Iron-deficiency anemia is undervalued and undertreated in many different clinical conditions. In oncology, for example, 60% of European cancer patients have iron deficiency. Although iron deficiency is so frequent and it is a well-known condition, its treatment, the use of iron and its delivery are not yet well known and not according to the international guidelines. The international debate on how to manage chemotherapy-induced anemia and anemia of chronic diseases is still open. The presentation of the phase III EPO-ANE-3010 Study at San Antonio Breast Cancer Symposium (December 9–13, 2014) on anemia treatment in anemic patients with metastatic breast cancer, demonstrates how actual is the problem. Anemia in oncologic patient is mostly multifactorial but the iron deficiency seems to be the principal cause and frequently a consequence of chemotherapy and biological drug treatments. The problems are similar also in chronic inflammatory diseases, such as inflammatory bowel diseases (IBD), cancer, and heart failure.

A recently published European Consensus on the Diagnosis and Management of Iron Deficiency and Anemia in Inflammatory Bowel Diseases (Journal of Crohn’s and Colitis, 2015) established that anemia is the most common systemic complication and extraintestinal manifestation of inflammatory bowel disease (ulcerative colitis, Crohn’s disease), mainly due to combination of chronic iron deficiency and anemia of chronic disease. A significant impact of iron deficiency on the quality of life is often seen in chronic kidney disease (CKD) patients and in heart failure syndrome.

Iron-deficiency anemia in CKD patients can be due to an inadequate endogenous erythropoietin production and an absolute or relative iron deficiency as a consequence of a reduced intestinal iron absorption or its mobilization from the stores. Specifically, iron deficiency has a prevalence from 25 to 70% in patients with CKD.

An estimated 37–50% of patients with chronic heart failure are iron deficient. Iron deficiency is a common comorbidity of heart disease, which has a significant and detrimental effect on clinical outcome.

Patients with iron deficiency have an associated risk of heart transplantation, increased morbidity, and reduced exercise capacity. Furthermore, iron deficiency has been independently associated with a marked increase in mortality in patients with heart disease. As such, the successful treatment of iron deficiency in patients with chronic heart failure has the potential to significantly improve overall clinical outcome, reducing morbidity and mortality rates, as well as restore quality of life.

Recently, researchers have focused on preoperative anemia that is emerging as a common and important public health issue.

In a study of 227,425 patients undergoing major noncardiac surgery, 30% were anemic preoperatively and the presence of even mild preoperative anemia was associated with a threefold increase in risk of mortality (Musallam KM et al. Lancet 2011) with a negative impact on patient morbidity and length of hospitalization (Myers E et al. Arch Orthop Trauma Surg 2004).

Besides over 80% of preoperatively non-anemic patients became anemic after elective orthopedic surgery (Lasocki S et al. Euroanaesthesia 2012), increasing the need of iron supplementation or increasing the risk for perioperative blood transfusion.

Hence comes the need to organize this fifth Course, addressed to oncologists, hematologists, cardiologists, nephrologists, anesthesiologists, and orthopedics (50% European/50% Italian), to focus on anemia’s problems and increase the knowledge of its clinical importance.

New therapeutic perspectives are given by a new type of oral iron supplementation, such as oral sucrosomial iron, which is more comfortable, has a better tolerability and effectiveness, with lower risks compared to intravenous iron therapy. Furthermore, on the risk of intravenous iron treatment the European Medicines Agency issued in June 2013 ‘New recommendations to manage risk of allergic reactions with intravenous iron-containing medicines.’

Therefore, the expected result is a better knowledge of the physiopathology, the clinical experience and up to date on iron deficiency therapy in patients with kidney disease, chronic inflammation, cancer, heart failure, and all the patients undergoing main surgery interventions.

The final and evident aim is to improve patients’ treatment, care, and quality of life. All this is possible thanks to an international faculty with a specific experience and knowledge of the problem.

ABSTRACTS

Cost analysis of patient blood management & MCQs
Andrea Kleineruschkamp, Kai Zacharowski, Claudia Ettwein, Markus M Müller, Christof Geisen, Christian Friedrich Weber and Patrick Meybohm
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**Background**

Patient blood management (PBM) is a multidisciplinary approach focusing on the diagnosis and treatment of preoperative anemia, the minimization of blood loss, and the optimization of the patient-specific anemia reserve to improve clinical outcomes. Economic aspects of PBM have not yet been sufficiently analyzed.

**Objectives**

The aim of this study is to analyze the costs associated with the clinical principles of PBM and the project costs associated with the implementation of a PBM program from an institutional perspective.

**Methods**

Patient-related costs of materials and services were analyzed at the University Hospital Frankfurt for 2013. Personnel costs of all major processes were quantified based on the time required to perform each step. Furthermore, general project costs of the implementation phase were determined.

**Results**

Direct costs of transusing a single unit of red blood cells (RBCs) can be calculated to a minimum of €147.43. The process flowchart of transfusion of RBCs is depicted in graph 1. PBM-associated costs varied depending on individual patient requirements. The following costs per patient were calculated: diagnosis of preoperative anemia €48.69–123.88; treatment of preoperative anemia (including iron-deficiency anemia and megaloblastic anemia) €12.61–127.99; minimizing perioperative blood loss (including point-of-care diagnostics, coagulation management, and cell salvage) €3.39–1901.81; and costs associated with the optimization of the tolerance to anemia (including patient monitoring and volume therapy) €28.62. General project costs associated with the implementation of PBM were €24,998.24.

**Conclusions**

PBM combines various alternatives to the transfusion of red blood cells and improves clinical outcome. Costs of PBM vary from institution to institution and depend on the extent to which different aspects of PBM have been implemented. The quantification of costs associated with PBM is essential in order to assess the economic impact of PBM, and thereby, to efficiently reallocate healthcare resources. Costs were determined at a single university hospital. Thus, further analyses of both the costs of transfusion and the costs of PBM principles will be necessary to evaluate the cost-effectiveness of PBM.

**Patient blood management: from theory to practice**

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**Introduction**

Patient Blood Management (PBM) has recently become of primary medical interest, due to the need of optimizing patients’ prognosis and minimizing costs and risks of allo- genetic blood transfusions.

The 3 recognized ‘pillars’ of PBM are:

1. Implementing red blood cell (RBC) mass, i.e. reducing anemia (if present) and ensure adequate iron and vitamin reserves
2. Minimizing hemorrhage during and after surgery
3. Optimizing tolerance to mild/moderate grades of anemia

PBM guidelines have been recently proposed by several national and international blood authorities and scientific societies such as the European Society of Anesthesia (ESA) and, in Italy, the Blood National Bank (Centro Nazionale Sangue – CNS). However, a strict application of the guideline is not easy. Indeed, each hospital must verify its feasibility considering aspects such as its logistic (e.g. the location of the operative theaters, emergency and obstetrics, presence/absence of 24h open blood bank, etc.), the experience of each surgical team and the characteristics of the patients. General and local guidelines, moreover, should not be imposed, but shared by competent multidisciplinary teams of anesthesiologists, surgeons, and transfusionists, and an adequate training of the involved personnel should be ensured before applications.

**Objective**

We report here our experience in San Raffaele hospital, with particular regard to the vascular surgery, which is a national reference center.
Results

The first step in PBM is the preoperative phase (Figure 1).

Depending on patient’s comorbidities and/or hematologic diseases, gender, and underlying pathology, preoperative anemia may be present in up to 20–50% of cases, and represents an independent risk for morbidity and mortality (Munoz et al. Blood Transfus. 2012; Spahn et al. Anesthesiology 2010), due to higher infection rate, longer recovery time, prolonged hospitalization, and decreased quality of life. Implementing the RBC mass is the most important target of this phase. Patients at risk of massive bleeding are the ones undergoing major cardiac and vascular surgery; for those patients, the aim is to minimize the need of blood support. Our data suggest that patients with Hb 12 g/dL or above before surgery have 20% probability of not being transfused for a TAAA (thoraco-abdominal aorta aneurysm) with a median perioperative support of 3 RBC units, whereas this percentage decreases to only 2% in patients with less than 12 g/dL with a median support of 5 RBC units. Other patients undergoing liver, oncologic, or orthopedic surgery, instead, may completely avoid transfusion, if they are correctly supported before surgery. Special care must be taken to optimize anticoagulant and antiplatelet therapy. As ESA guidelines suggest, patients undergoing surgery with potential transfusion need to be evaluated 6–8 weeks before surgery, in order to have time to correct anemia and restore iron storage resources. However, in the majority of Italian hospitals, the preoperative routine tests are usually done about 3–4 weeks before surgery, while patients coming from other regions referred to larger university hospitals for second-level surgery, in spite of their complications and comorbidities, may be evaluated shortly before surgery.

We are currently applying the approved CNS-suggested algorithm for patients undergoing elective major vascular, cardiac, liver, and orthopedic surgery. The hematologist works together with the anesthesiologists in the presurgery ambulatory check for all patients undergoing elective surgery, providing iron and/or vitamin support as need.

We normally suggest oral supplementation with Sucrosomial® Iron, due to its efficacy and tolerability profile, as well as its broad spectrum of efficacy in different underlying conditions such as chronic diseases and cancer (D’Amico e al. EHA 2015; Pisani et al, Barni et al, Gascon et al 3rd Mediterranean Multidisciplinary Course on Iron Anemia); our data are at the moment under evaluation.

In particular situations when there is no enough time to ensure an adequate restore of hemoglobin levels or in case of documented iron malabsorption, we prefer the use of intravenous iron administration (Pisani et al al 3rd Mediterranean Multidisciplinary Course on Iron Anemia). Even if the use of EPO is suggested in order to implement RBC mass, possible side effects and lack of patients’ confidence toward this drug lead us to reserve this treatment to very selected cases.

The second step of PBM is in the perioperative phase.

According to the suggestion of our regional sanitary system, the above cited multidisciplinary teams have revised the data and identified for each operation the Maximum Surgical Blood Order Schedule (MSBOS). This allowed to reduce the amount of blood units preemptively brought to the operating theater.

In the TAAA subset, for example, the MSBOS have been reduced from 10 to 5 or 7 according to patients’ characteristics. In the case of cardiac surgery, 3 patient groups have been identified: only patients undergoing high-risk surgery preemptively have their RBC units brought into the theater, whereas all the others do immunohematology standard tests and receive RBC only on demand.

Figure 1. Flowchart of preoperative process for implementing PBM.
The results of this approach are still under evaluation. However, one may speculate that a better education of surgeons and anesthesiologists, as well the direct presence of a smaller amount of blood in the operating theater, may reduce the number of effectively transfused RBC units.

The main target of PBM during this phase is to minimize hemorrhage and at San Raffaele Hospital a strong collaboration has been built up among the emergency room, the cardiac/vascular surgery and obstetrics on shared thromboelastometry-based management protocols. The aim of those protocols is to optimize the use of plasma and platelets units and prevent/treat massive hemorrhage with fibrinogen concentrates.

Considering only the vascular surgery subset, this led to a reduction in the use of intraoperative plasma from 2000 to 1500 mL and blood from 3 to 2 units, with a significant expense decrease and no negative impact on patients’ prognosis.

The final, but not less important step in PBM, is the postoperative phase.

Even if the intraoperative use of RBC units has been reduced, many patients are transfused during the intensive care unit stay or readmission, especially after major surgery. In some cases, this procedure is mainly preemptive, since referring patients to transfusional or to hematology unit after discharge is logistically complicated.

For the TAAA subset, in our hands, 70% of patients were transfused after surgery, with median Hb level at transfusion of 8.9 g/dL, but in 7% of cases it was 10 g/dL or more. Therefore, we are currently planning a workflow in which blood test of selected patients associate to the standard postoperative surgical ambulatory controls. In the unlikely probability of transfusion need, those patients would be managed in the hospital Transfusion Center; much more frequently they would be given an appropriate oral iron and/or vitamin support plus follow-up indications for their general practitioner.

A cost-effective implementation of preoperative protocol with Sucrosomial® iron supplementation

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Introduction

Low perioperative Hb values in orthopedic surgery patients are associated to a longer hospital stay, higher transfusion rates, and mortality. Timely prevention of perioperative anemia and iron deficiency can improve patient outcome. We evaluated the efficacy of Sucrosomial® iron supplementation in prosthetic hip surgery patients on recovery hemoglobin levels, length of hospital stay, and blood transfusion.

Materials and methods

Retrospective study on prosthetic hip surgery 648 patients (non-anemic and with no major comorbidities) between 2011 and 2016. Preoperative protocol of Sucrosomial® iron was gradually implemented from 2011 to 2016. At preoperative visit 21–28 days prior to surgery, full blood exams were performed (CRP and ferritin included). If ferritin levels were <100 mcg/L and Hb levels <14 g/dL for male and 13 g/dL for female, patients were prescribed with Sucrosomial® Iron (Sideral® Forte, 1 cps/day) for 21\28 days before and 7\10 after surgery.

Results

Sucrosomial® iron supplementation was associated with a reduction in the length of hospital stay from an average of 15 days in 2011 to 10 days in 2016, was associated with a faster recovery in the hemoglobin levels during the postoperative period. The amount of blood transfusions significantly decreased from 10% in 2011 to 0% units in 2016 in this type of population. Estimated saving for the shorter length of hospitalization could be calculated in 2000 euro/patient (plus additional saving gained from more efficient use of hospital beds).

Discussion

Preoperative Sucrosomial® iron supplementation 4 weeks prior to elective surgery in non-anemic patients was associated with a fall in postoperative Hb levels and a faster recovery of hemoglobin levels and functional recovery after surgery, corresponding to a shorter length of hospital stay and decreased surgery-related costs.

Figure 1. Representation of LOS (blue) and free beds (orange) between 2015 and 2017. Full color available online.
Response to Sucrosomial® oral iron supplementation in patients underwent bariatric surgery

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Introduction

In the postoperative period, all the techniques of bariatric surgery induce a significant reduction in the intake or absorption of most of the nutrients. Therefore, bariatric surgery can be associated with a risk of nutritional deficiency, which increases over the years. One of the nutrients whose absorption is affected in a significant way is iron, and the women of childbearing age are the most vulnerable. The daily recommendation of iron intake in adults is 8 mg a day for men and women of more than 50 years, and 18 mg per day for women of age less than 50 years. The incidence of iron deficiency and anemia after bariatric surgery is variable according to the type of surgery and the time after the surgery. For instance, after a Y-de-Roux gastric by-pass, iron-deficiency anemia is diagnosed between 10 and 40% of all the cases [1–6]. Bariatric surgery techniques produce changes of the digestive tract and dietary habits that favor iron deficiency [7,8]. These changes are: (a) intolerance to red meat, leading to intake decrease, (b) decreased gastric acid secretion by resection of the proximal stomach, with the consequent relative deficit of parietal cells and iron absorption deficiency, (c) exclusion of the duodenum, which is the main place of molecular iron and heme iron absorption. Most of the patients, especially women of childbearing age, require oral iron supplementation after bariatric surgery. Additionally, a non-negligible percentage of women, who previously underwent bariatric surgery, require parenteral iron therapy supplementation until the establishment of the menopause. This fact is due in part to lower presurgery iron deposits in obese patients, which also translates into a great variability in the time of occurrence of the deficit (from months to years) [7]. Also, most of the obese women, who undergo bariatric surgery, restore the menstrual period in almost 40% of the cases after a 4.6% weight loss [9]. In many cases, despite taking high oral doses of conventional iron supplementation, often causing gastrointestinal intolerance, they fail to achieve optimal levels, requiring therefore chronic parenteral therapy [10]. In our series of patients (1100 patients, who underwent bariatric surgery from 2000 up to today), about 120 women of childbearing age require chronic parenteral treatment with intravenous iron every 3 months until the menopause is installed. The administration of intravenous iron, in a day-hospital setting, takes between 2 and 3 h for 2 consecutive days, every 3 months, which represents an important distortion of work and daily life for the patients. Sucrosomial® oral iron may represent a treatment alternative in these cases. Due to its innovative technology, based on an alternative way of absorption, the ‘usual mechanisms’ of intestinal iron absorption, such as gastric acid secretion and duodenum section are not fundamental. Therefore, the bioavailability of Sucrosomial® iron rises to 3.5 times compared to conventional iron. Sucrosomial® iron has also been proven to be effective and well tolerated, compared to oral supplements of conventional iron in pregnancy, newborn, infant, chronic kidney disease, and inflammatory bowel disease. This form of oral iron demonstrated its effectiveness even against conventional intravenous iron therapy [11].

Objective

To our knowledge, to date there is no study using Sucrosomial® oral iron in patients undergoing bariatric surgery. Thus, Sucrosomial® iron supplementation was evaluated in this population.

Materials and Methods

In order to shed light on this issue, we have designed a single-center, open, prospective, interventional trial, including 40 women of childbearing age, who previously underwent Y-de-Roux gastric by-pass and currently require chronic intravenous iron therapy. The subjects were divided into 2 parallel groups: 20 cases and 20 controls matched by age, previous level of hemoglobin (Hb), years after surgery and percentage of weight lost. The 20 cases were discontinued from the parenteral iron treatment and were treated with Sucrosomial® oral iron 28 mg/day for 3 months. The 20 controls continued with 300 mg iron sucrose intravenously every 3 months. Total hemoglobin (Hb), ferritin, and transferrin saturation index (TSI) were determined before and after 3 months of treatment in both groups, as well as tolerability. We have performed an additional pilot study in pregnant women, who previously underwent bariatric surgery and who required previous chronic parenteral iron therapy. We have included 3 patients of 29.66 ± 3.3 years of age, with a presurgery BMI of 39.22 ± 4.1 kg/m2 and % EWL of 61.22 ± 2.4% after 5 years, who discontinued the parenteral iron therapy between week 6 and 8 of pregnancy and were switched to Sucrosomial® iron, 60 mg/day.

Results

No significant differences were seen between the levels of Hb (12.67 g/dL ± 1.06 g/dL vs. 12.267 g/dL ± 1.35 g/dL, p = 0.081), ferritin (101.67 ng/dL vs. 88.89 ng/dL, p = 0.069) and TSI (24.11% vs. 26.28%, p = 0.55) before and after the 3 months of treatment with Sucrosomial® iron. We did not find any adverse effect during this period in the case group.

In the additional pilot study, the tolerability was excellent in all patients. The initial (T0) level of total Hb was 13.3 g/dL versus 12.7 g/dL after 3 months of treatment (T3), ferritin was 64.66 ng/dL at T0 and 37.33 ng/dL at T3 and TSI was 50.33% at T0 while 37% at T3. The results after 3 months of treatment with Sucrosomial® iron are reported in Table 1.

Table 1. Preliminary results on pregnant women.

| Age (years) | 29.66 ± 3.3 |
| Previous BMI (kg/m2) | 39.22 ± 4.1 |
| %EWL (1 year) | 61.22 ± 2.4 |
| Hb (g/dL) | 13.3 |
| Ferritin | 64.66 |
| SaT index | 50.33 |
Conclusion
Our study suggests that Sucrosomial® oral iron might represent an alternative therapy in patients who require parenteral iron treatment after bariatric surgery, including during pregnancy. Moreover, it might help to reduce healthcare costs and improve the quality of life of these patients; however, further studies are needed to confirm it.

References

Implementation of a PBM program in oncology patients
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Transfusion of blood and blood products are one of the most frequently performed procedures during hospitalizations. Clinical research has demonstrated that a restrictive transfusion strategy results in patient outcomes similar to those associated with more liberal strategies, which may even improve outcomes. At the same time, retrospective studies have suggested an association between transfusions and patient morbidity – increased hospital-acquired infections and length of stay. In economic terms, unnecessary transfusions have been shown to translate to poor use of resources and increased costs.

Patient Blood Management (PBM) can be described as the application of evidence-based medical and surgical concepts to achieve measurable improvements in patient safety and clinical outcomes, using an interdisciplinary care team to manage anemia, optimize hemodynamic stability, tissue oxygenation, and hemostasis in a patient-specific manner (Figure 1).

PBM should consider the patient’s entire course to determine whether the reason for transfusion could be avoided in the first place and/or possibly treated in another manner. The patient’s involvement in the decision-making process is also important.

Anemia in cancer patients may be multifactorial and treatments should be directed based on etiology. The approach to anemia should focus on simultaneous interventions – stimulate erythropoiesis, enhance hemostasis, and control or prevent ongoing blood losses. The application of PBM principles in patients with malignant disease might achieve similar results. However, this population presents unique challenges, thus the impact of a PBM program on blood usage and patient outcomes in cancer patients, particularly in the setting of restricted use of erythropoiesis-stimulating agents (ESAs), should be considered.

We will address the main issues related with the implementation of a PBM program in the oncologic setting.

Iron deficiency and anemia: definitions and diagnosis
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Introduction
Anemia is defined by the World Health Organization as a hemoglobin (Hb) concentration <130 g/L for men and <120 g/L for nonpregnant women [1]. These definitions are used in most epidemiological studies. However, this may not be reliable for females undergoing cancer surgery with moderate-to-high blood losses. Consequently, a preoperative Hb level ≥130 g/L should be desirable, in both genders, to minimize the risk of transfusion and unfavorable outcomes [2].

In cancer patients, anemia is highly prevalent (40–60%) and can be attributed to chronic hemorrhage, chemotherapy, or radiotherapy, and nutritional deficiencies, usually iron deficiency...
These may be exacerbated by activation of the immune system with the release of inflammatory cytokines [4, 5].

**Definitions**

Iron deficiency (ID) without anemia refers to a reduction in total body iron with normal Hb, as levels of erythroid iron are still sufficient to sustain erythropoiesis [4, 5]. There is emerging evidence that ID without anemia is a disease in its own right, and should not be overlooked [6]. Functional iron deficiency (FID) refers to insufficient mobilization of iron from stores in the presence of increased demands [4, 5]. Iron sequestration refers to decreased iron mobilization from stores due to inflammation-induced hepcidin synthesis [5].

In contrast, true iron-deficiency anemia (IDA) is a more severe condition in which decreased iron stores result in decreased Hb and microcytic hypochromic red cells, though these RBC indexes are not reliable for diagnosing or treating IDA [4, 5, 7]. However, a reticulocyte production index greater than 2 is not compatible with IDA [7].

**Diagnosis**

A serum ferritin level <30 μg/L is the most sensitive and specific test used for the identification of ID (with or without anemia), independently of any other parameter (Figure 1) [3, 4]. A transferrin saturation (TSAT) <20% further indicates insufficient iron supply to support normal erythropoiesis [4, 5]. In contrast, ferritin 100–500 μg/L and TSAT <20% usually indicate iron sequestration or decreased iron availability, as seen in anemia of chronic inflammation (ACI) (Figure 1) [5]. However, though ferritin values >100–200 μg/L argue against concurrent absolute ID in the setting of inflammation (e.g. C-reactive protein (CRP) >5 mg/L), its diagnostics value is imperfect. Thus, ferritin levels between 30 and 100 μg/L (200) and TSAT <20% and any elevated inflammatory marker (CRP) may reflect ID associated with inflammation. Other tests, such as low reticulocyte Hb content (CHR <28 pg), high proportion of hypochromic red cells (HYPO >5%), low red cell Hb density (LHD >4%), or the ratio of serum transferrin receptor (sTfr) to the log of ferritin (sTfr/log Ferritin >2) must be utilized to evaluate for a component of true ID, which if present suggests a benefit of iron supplementation [5, 8]. Some guidelines recommend administration of iron even at ferritin concentration as high as 500 or 800 ng/mL if the response to ESAs is not adequate [9–11]. Intermediate ferritin levels (30–100 μg/L), in the presence of inflammation and/or TSAT <20%, strongly suggest anemia of inflammation with absolute iron deficiency (ACI+ID) (Figure 1) [5]. When anemia cannot be explained by IDA, ACI, or ACI+ID, it is paramount to consider other causes that would demand specific treatment. In these cases, further testing should include vitamin B$_12$, lactate dehydrogenase, and serum creatinine (estimated glomerular filtration rate) to exclude other nutritional deficiencies, hemolysis or renal disease. If malabsorption or severe malnutrition, a red cell folate may also be useful [12]. Bone marrow aspiration may be useful if hypoplasia/aplasia or invasion is suspected.

**References**


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**Figure 1. Anemia classification.**

**Effect of Oral Sucrosomial® Iron Versus Intravenous Iron for Treatment of Iron-Deficiency Anemia in CKD Patients: A Randomized Trial**

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**Introduction**

Iron deficiency is a common cause of anemia in nondialysis chronic kidney disease (ND-CKD) patients. Controversies exist about the optimal route of administration for iron therapy. Sucrosomial® iron, a new generation of oral iron with high gastrointestinal absorption and bioavailability and a low incidence of side effects, seems to be a promising new strategy of iron replacement.

**Objective**

Therefore, we conducted a study to determine whether Sucrosomial® iron, compared to intravenous (IV) iron, improves anemia in ND-CKD patients.

**Methods**

In this randomized, open-label trial, 99 patients with CKD (stage 3–5, not on dialysis) and iron-deficiency anemia (hemoglobin (Hb) ≤12 g/dL, ferritin ≤100 ng/mL, transferrin saturation ≤25%) were assigned (2:1) to receive oral Sucrosomial® iron (30 mg/day, OS group) or a total dose of 1000 mg of IV iron gluconate (125 mg infused weekly) (IV group) for 3 months. The patients were followed up for the entire treatment period and 1 month after drug withdrawal. The primary end point was to evaluate the effects of the two treatments on Hb levels; the iron status, compliance and adverse effects were also evaluated.

**Results**

The short-term therapy with IV iron produced a more rapid Hb increase compared with Sucrosomial® iron, although the final increase in Hb was similar with either treatment; the difference between the groups was statistically significant at the first month and such difference disappeared by the end of treatment. After iron withdrawal, Hb concentrations remained stable in the IV group, while recovered to baseline in the OS group. The replenishment of iron stores was greater in the IV group. The incidence of adverse event was significantly lower in the oral group (p < 0.001) and the adherence was similar in the two groups.

**Conclusions**

Our study shows that oral Sucrosomial® iron is a safe and efficacious alternative to IV iron gluconate to correct anemia in ND-CKD patients, although its effects on repletion of iron stores and on stability of Hb after drug discontinuation are lower.

**Efficacy and tolerability of oral Sucrosomial® iron in CKD patients with anemia**

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**Introduction**

Iron deficiency is one of the main causes of anemia in patients with chronic kidney disease (CKD), and iron supplements along with the erythropoietin constitute the basis of its therapy [1]. The clinical consequences of untreated severe anemia in nondialysis CKD patients can be significant, but disparities exist in the anemia treatment guidelines and position papers issued from working groups and associations across the world [1]. These differ in hemoglobin target and iron levels and they focus on various iron markers and other clinical outcomes. Moreover, there is an ongoing debate regarding oral versus intravenous administration of iron [1]. The above facts led new oral compounds to arise, which show different rates of absorption with possibly different efficacy and improved tolerability. The main representative is oral Sucrosomial® iron, a preparation of ferric pyrophosphate carried inside a phospholipid and sucrosester membrane, which is characterized by higher gastrointestinal absorption and bioavailability than other oral formulations, as well as lower incidence of side effects.

**Objective**

The study purpose was to assess the efficacy and tolerability of the treatment with Sucrosomial® iron in iron-deficiency anemic nondialysis CKD patients.

**Methods**

30 patients (mean age 74.21 years, range: 39–86 years) with CKD stage 3–5 (not in dialysis, eGFR <60 ml/s/min, range: 12–48) and anemia along with ferritin level <200 ng/mL not attributable to other causes (neoplasms, infections, bleeding, hemopathies, hepatopathies), were enrolled in our prospective study. Hematological profile, renal function, and bone-
mineral data were recorded at the beginning of the study and every 2 months until the end of the study protocol. The primary efficacy end points of the study included the change in Hct values from baseline to the end of the treatment. Secondary end points were an estimation of iron repletion and bone–mineral parameters. Adverse effects and compliance data were reported from the beginning to the end of treatment. Data were analyzed using t-test (SPSS). We separated our population in 2 groups: one with eGFR over 30 mils/min and another with eGFR below 30 mils/min and we compared their clinical-laboratory behavior regarding all the parameters of the protocol.

Results

During a study period of 18 months, all patients had stable renal function, did not need transfusion or admission to hospital for any reason and received oral Sucrosomial® iron (Sideral®) once daily, according to the therapeutic protocols of the clinic. During our study period of 18 months, Hct levels increased from 33.3 ± 1.87% at the beginning of the protocol to 36.61 ± 2.72% (p < 0.05). Hemoglobin levels were 10.98 ± 0.73 g/dL at the beginning of the study and ended to be 11.86 ± 0.71 g/dL (p = NS) (Figure 1). Ferritin levels, which are one index of iron stores, also increased from 42.73 ± 24.47 mcg/dL to 98.89 ± 126.99 mcg/dL (p = NS) (Figure 2). Renal function (eGFR) of our patients remained stable, without significant changes during the 18 months period of the study. PTH levels declined over the study period from 359.05 ± 447.24 pg/mL to 163.72 ± 89.12 pg/mL (p = NS) (Figure 3). Ca, K, and Na levels remained stable without significant changes. We did not notice any significant changes concerning Hct, Hb, and ferritin fluctuations during protocol period. Oral iron was well tolerated and no significant adverse effects were recorded. None of our patients dropped out from the study for any reason.

Conclusions

It is noticeable that its behavior related to GI effects seems to differ favorably compared to other iron compounds. Oral Sucrosomial® iron seems to be a safe and efficacious alternative in managing CKD patients with anemia. Despite the small amount of patients in our study protocol, the low rate of adverse events with Sucrosomial® iron and its practicality suggest that this formulation has all the potential to be the first step to correct anemia in stable CKD patients. Along with the other follow-up parameters in CKD patients, it might be somehow of help for the stabilization of renal function. Further larger studies are needed to investigate Sucrosomial® iron effects in complicated CKD patients and help scientific community to reach solid conclusions.
Iron deficiency has been recognized in the last years as one of the most prevalent comorbid conditions in chronic heart failure [1]. When anemia is considered, the prevalence of iron deficiency ranges from 43 to 61% depending on populations under study and the definition used for iron deficiency [1,2]. These estimates include both absolute iron deficiency (in which iron stores are low) and functional iron deficiency (in which iron supply is inadequate to meet the demand for erythropoiesis and other cellular functions despite normal iron stores). A decreased iron status is also associated with heart failure severity assessed by NYHA functional class and NT-pBNP level [1–3].

Although, attention is focus on the effect of inadequate iron supply on erythropoiesis and the resulting risk of anemia, it is necessary to remember that iron is an essential cofactor for heme and nonheme proteins involved in cellular activities such as oxygen storage (as component of myoglobin), or generation of cellular energy (as part of mitochondrial respiratory chain proteins) in skeletal muscle and myocardiocytes [3].

Recent research has shown deterioration in heart function when myocardial iron content is reduced. Moreover, iron deficiency is also associated with lower peak oxygen consumption and worse exercise tolerance in patients with heart failure, even in absence of anemia. This negative influence of iron deficiency on heart failure could be linked to non-hematopoietic effects of iron, such as mitochondrial dysfunction in cardiomiocytes and skeletal myocytes.

The major concern about anemia and iron deficiency in heart failure is their relationship with mortality. All-cause mortality and hospitalization are higher in anemic compared with non-anemic patients with chronic heart failure. However, not only anemia, but also iron deficiency without anemia has been shown to worsen prognosis, symptoms, exercise capacity, and quality of life in patients with heart failure. For these reasons, iron deficiency was considered a potential therapeutic target in patients with heart failure.

In recent years, several studies have investigated the effects of intravenous iron therapy in iron-deficient patients with heart failure. Nowadays, four randomized, controlled, and double-blinded trials demonstrated improvement of clinical status on patients with heart failure and iron deficiency treated with intravenous iron compared to placebo. Parenteral iron therapy resulted in an alleviation of heart failure symptoms and an improvement in quality of life (assessed by specific questionnaires for heart failure and for general medical condition evaluation), and an improvement in exercise capacity (as reflected by longer 6 min walking test distance). Despite a reduction on heart failure hospitalization was observed, analysis revealed no effect on either all-cause or cardiovascular mortality [3–5].

After review of all these data, European Society of Cardiology has included in current guidelines the recommendation to treat with parenteral iron patients with symptomatic heart failure, reduced ejection fraction and iron deficiency (defined by ferritin <100 μg/L or ferritin <300 μg/L and TSAT <20%) [6].

It is important to point out that no study has been conducted to evaluate the possible beneficial effect of iron therapy (oral or parenteral) in heart failure patients with preserved ejection fraction, thus further investigation is required.

Despite the fact that oral iron is still often the first-line therapy for many clinicians, the evidence related to this therapy is limited. The reasons for oral therapy preference are that routine administration of parenteral iron is expensive and poses logistical challenges. Until now, only two studies evaluated the use of oral iron to treat iron deficiency in heart failure patients. The first one, the IRON-HF, compared the efficacy and safety of oral ferrous sulfate (at a dose of 200 mg of iron three times a day for 8 weeks) versus intravenous iron sucrose (200 mg iron/week for 5 weeks) [7]. Oral iron failed to achieve an increase in peak oxygen consumption after a 3-month follow-up period, while a significant increase was observed in parenteral iron arm. An increase in hemoglobin and ferritin was observed in both groups; however, the increase in iron availability (measured by TSAT) was less pronounced in the oral iron group [7]. Recently, IRONOUT trial tested an oral iron polysaccharide (150 mg twice daily) against placebo in patients with symptomatic heart failure and depressed ejection fraction [8]. Despite low drug-discontinuation rate, the degree to which iron stores and TSAT changed in response to oral iron was minimal and it also fails to achieve an improvement in peak oxygen consumption at week 16 (primary end point) and did not show any clinical benefit on quality of life or hospitalizations. The investigators observed that in the two highest hepcidin quartiles response to oral iron was null [8].

The reasons, why oral iron therapy could fail, are linked to the pathophysiology of iron deficiency in heart failure, a topic that is still not well understood. Several factors seem to be related to iron deficiency in heart failure, such as higher hepcidin levels in the early stages of disease, high prevalence of malnutrition, and reduced iron absorption due to interactions with several drugs or intestinal edema. As discussed above, hepcidin may play a major role in iron deficiency since heart failure is recognized as an inflammatory state. However, recent research observed an increased bowel wall thickening in heart failure patients compared with controls. These morphological changes are associated to altered intestinal function represented by increased permeability, decreased absorption, and augmented bacterial colonization [9].

New oral formulations such as Sucrosomial® iron could offer a new opportunity to oral iron therapy for patients with heart failure and iron deficiency. With a different mechanism of absorption and delivery, Sucrosomial® iron could overcome
the mentioned factors related with iron absorption impairment. Despite Sucrosomial® iron has proven its efficacy in chronic renal failure (with similar pathophysiological mechanisms), specifically designed studies to confirm this hypothesis are required.

Bibliography


Oral Sucrosomial® Iron in Post Cardiac Surgery Patients. Efficacy and Tolerability in a Follow up of 3 Months

Roberto Testa a, Elio Venturini a, Cecilia Sansoni a, Elena Pera b and Germano Tarantino b

aCardiology and Rehabilitation O.U. Cecina Hospital, Leghorn, Italy; bPharmanutra SpA, Pisa, Italy

Introduction

Anemia is a common condition after cardiac surgery with consequences on the rehabilitation program. The management of iron supplementation can be difficult if intravenous (IV) or it can give side effects if oral. Sucrosomial® Iron (Cardiosideral® – Pharmanutra S.p.A) was not inferior to intravenous iron in different patient sets.

Objective

The aim of the study was to evaluate the efficacy and duration of Sucrosomial® Iron supplementation in the correction of post cardiac surgery anemia.

Methods

We studied 28 patients (17M) aged 73 ± 9 years (9 diabetic, 8 hypertensive, 21 coronary artery disease, 2 left ventricular dysfunction, 2 chronic kidney disease, 2 with preexisting anemia, 2 with previous stroke), who underwent cardiac surgery (14 coronary artery bypass graft, 12 valves and 2 valve and coronary artery bypass graft) and were admitted after surgery in our inpatient and then outpatient rehabilitation. Seven patients had postoperative bleeding and 11 had received blood transfusions. The protocol consisted in 1-month therapy followed by 1 month of placebo and further 1 month of therapy. The parameters evaluated were: complete blood count, serum iron, serum creatinine, CRP, BNP, transferrin, 6 min walk test (6MWT), arterial pressure, heart rate, ECG at baseline (B), 1 month (1), 2 months (2), and 3 months (3), and a questionnaire on quality of life (QoL) at (B) and (3).

Results

Results showed an increase of hemoglobin level from 10 ± 1.2 g/dL to 12.4 ± 1.5 g/dL after 3 months of treatment. Similarly, serum iron increased from 35 ± 14 mcg/dL to 56 ± 16 mcg/dL and 6MWT from 262 ± 96 to 392 ± 83 m. Ferritin decrease back to a normal range (from 334 ± 235 mcg/dL to 63 ± 55 mcg/dL) together with a decrease in CRP levels from 4.4 ± 3.7 mg/L to 0.7 ± 1.4 mg/L and in BNP levels (from 436 ± 372 pg/mL to 153 ± 103 pg/mL). QoL was not significantly different.

Conclusions

Cardiosideral® was effective and well tolerated in the post cardiac surgery anemia (no side effects) and is a valid option in these patients. The duration of therapy should be at least 3 months as

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline (B)</th>
<th>1 month (1)</th>
<th>2 months (2)</th>
<th>3 months (3)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC (×1000)</td>
<td>3449 ± 406</td>
<td>3896 ± 468</td>
<td>4210 ± 88</td>
<td>4404 ± 53</td>
<td>p &lt; .001: B vs.1–2–3</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>10 ± 1.2</td>
<td>11 ± 1.2</td>
<td>11.9 ± 1.2</td>
<td>12.4 ± 1.5</td>
<td>p &lt; .001: B vs.1–2–3</td>
</tr>
<tr>
<td>Sideremia (mcg/dL)</td>
<td>35 ± 14</td>
<td>46 ± 18</td>
<td>47 ± 15</td>
<td>56 ± 16</td>
<td>p &lt; .01; B vs. 1–2–3</td>
</tr>
<tr>
<td>Ferritin (mcg/dL)</td>
<td>334 ± 235</td>
<td>164 ± 152</td>
<td>91 ± 68</td>
<td>63 ± 55</td>
<td>p &lt; .001; B vs. 1–2–3</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>4.4 ± 3.7</td>
<td>1.5 ± 2.1</td>
<td>0.5 ± 0.5</td>
<td>0.7 ± 1.4</td>
<td>p &lt; .001; B vs. 1–2–3</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.07 ± 0.4</td>
<td>1.06 ± 0.35</td>
<td>1.0 ± 0.24</td>
<td>0.96 ± 0.2</td>
<td>p ns: B vs. 1–2–3</td>
</tr>
<tr>
<td>BNP (pg/mL)</td>
<td>436 ± 372</td>
<td>242 ± 198</td>
<td>170 ± 106</td>
<td>153 ± 103</td>
<td>p &lt; .002: B vs. 1–2–3; ns 1vs. 2, 2 vs. 3</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>262 ± 96</td>
<td>352 ± 84</td>
<td>378 ± 64</td>
<td>392 ± 83</td>
<td>p &lt; .001; B vs. 1–2–3; ns 1vs. 2, 2 vs. 3</td>
</tr>
<tr>
<td>QoL</td>
<td>144.4 ± 30.3</td>
<td>149.6 ± 26</td>
<td></td>
<td></td>
<td>p ns</td>
</tr>
</tbody>
</table>
evidenced by the decrease in the recovery of Hb between 1 and 2 months (placebo) and the gradual improvement of the BNP and the 6MWT. It confirms the futility of ferritin in these patients as marker for martial heritage due to the inflammatory state as demonstrated by CRP level. Serum iron, however, could be a useful tool to guide therapy. The improvement of QoL does not reach the significance; this, in part, could be due to the already high levels for QoL at baseline.

Oral Sucrosomial® iron in heart failure patients with iron deficiency
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\textsuperscript{a}Department of Cardiology, General Hospital 'G. Gennimatas', Greece; \textsuperscript{b}Department of Cardiology, Attikon University Hospital, Greece

Introduction
Iron deficiency is a frequent comorbidity in heart failure (HF) patients and has been associated with impaired functional capacity, poor quality of life, and increased mortality. Iron is poorly absorbed from oral preparations in HF patients and can be complicated by gastrointestinal side effects. Sucrosomial\textsuperscript{®} Iron is a new-generation oral iron based on a sophisticated technology that uses sucrose as a carrier. The result is that iron never comes into contact with gastrointestinal mucosa and the sucrose is directly absorbed by M cells of the small intestine. Sucrosomial\textsuperscript{®} technology offers two important advantages, which are high gastrointestinal absorption and low incidence of side effects.

Objective
We sought to evaluate the efficacy and safety of oral Sucrosomial\textsuperscript{®} iron, a formulation that seems to overcome intestinal iron malabsorption, in HF patients with iron deficiency.

Materials and methods
We studied 10 patients with chronic HF with reduced left ventricular ejection fraction (40\% or less; mean, 22 ± 3\%), New York Heart Association (NYHA) class II or III, iron deficiency (ferritin level <100 ng/mL or serum ferritin between 100 and 299 ng/mL with transferrin saturation <20\%), and hemoglobin level between 10 and 13.5 g/dL in females and 10 and
15 g/d in males. All patients were on stable, evidence-based medical therapy for HF for at least 1 month. All patients received oral Sucrosomial® iron, containing 28 mg of iron, once daily for 3 months. Clinical and laboratory parameters were evaluated at baseline and at 3 months.

**Results**

At baseline, 50% of patients were in NYHA class II and 50% in class III, while the corresponding distribution at 3 months was 78% and 22%, respectively (Figure 1). In addition, 6-minute walking distance (6MWD) test, serum ferritin, serum iron, and hemoglobin increased significantly at 3 months, while B-type natriuretic peptide (BNP) decreased significantly and serum creatinine remained stable (Table 1). No adverse events were reported throughout the study period.

**Conclusion**

Oral Sucrosomial® iron for 3 months was effective in improving iron status, along with NYHA class, exercise capacity, and neurohormonal activation in HF patients with reduced ejection fraction and iron deficiency, without causing any adverse events.

**Materials and Methods**

Permeation study was done using ex vivo isolate rat intestine model mounted in a Ussing chamber (Figure 3(a)). This model gives a good representation of the complex in vivo morphology and of the different kind of processes involved in the in vivo intestinal tissue. To show the efficacy and compliance of Sucrosomial® Iron in IDA HL patients, 25 subjects were retrospectively analyzed (all were staged 2B or higher, according to Ann Arbor classification, none of them showed bone marrow infiltration). A continued treatment with oral Sucrosomial® Iron (Sideral Forte 30mg/day) was performed for the whole period of chemotherapy. Statistical analysis was performed with two-way ANOVA followed by Dunnett’s multiple comparison test.

**Results**

Sucrosomial® Iron (Sideral®) is an innovative preparation of ferric pyrophosphate covered by phospholipids plus sucrose esters of fatty acids matrix (Figure 1(a)). Field-emission gun scanning electron microscope (FEG-SEM) morphological analysis shows that Sideral® is a powder with slight different nanostructures. In water, it forms spherical nanostructures (Figure 1(b)). We have performed gastroresistance experiments in simulated

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**Table 1. Results.**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After 3 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-MWD (m)</td>
<td>282 ± 63</td>
<td>294 ± 66</td>
<td>0.009</td>
</tr>
<tr>
<td>Serum ferritin (ng/mL)</td>
<td>48.1 ± 22.4</td>
<td>101.9 ± 57.5</td>
<td>0.005</td>
</tr>
<tr>
<td>Serum iron (mg/mL)</td>
<td>49.7 ± 17.8</td>
<td>68.0 ± 16.4</td>
<td>0.028</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>12.8 ± 1.1</td>
<td>13.4 ± 1.1</td>
<td>0.009</td>
</tr>
<tr>
<td>BNP (pg/mL)</td>
<td>9598 ± 8498</td>
<td>3214 ± 2601</td>
<td>0.008</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.4 ± 0.7</td>
<td>1.3 ± 0.6</td>
<td>0.281</td>
</tr>
</tbody>
</table>

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**Posters – Preclinical research**

**Sucrosomial® iron is able to promote Fe³⁺ absorption: preclinical and clinical studies**

Elisa Brilli¹, Angela Fabiano², Giovanni Tosi², Alessandra Romano², Barbara Ruozzi², Ylenia Zambito², Francesco Di Raimondo² and Germano Tarantino¹

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<sup>¹</sup>Pharmanutra S.p.A. Pisa, Italy; <sup>²</sup>Department of Pharmacological Sciences, University of Pisa, Italy; <sup>³</sup>Department of Life Sciences, University of Modena and Reggio Emilia, Modena, Italy; <sup>⁴</sup>Hematological Division, University di Catania, Italy.
Figure 1. Structure and gastroresistance of Sucrosomial® Iron. Bioavailability experiments on CACO-2 cells (Figure 2(a)) showed that cells treated with Sucrosomial® Iron significantly increase ferritin expression compared to cells treated with other iron salt formulations (data are shown as mean, ****p < 0.0001) (Figure 2(b)).

Figure 2. Bioavailability experimental plan and results. Sucrosomial® technology is able to transport Fe3+ from the apical to basolateral side of the isolate rat intestine and the transport is effective thanks to carrier composition (*p < 0.05 ***p < 0.001) (Figure 3(b)).

Figure 3. Permeation study and results. Data from clinical study showed that Sucrosomial® Iron is well tolerated and effective in patients with advanced-stage HL (data not shown). All the iron parameters tested at the end of the planned treatment showed a significant increase compared to baseline (*p < 0.05) (Table 1).
Iron to a phospholipid-
iron (Sideral® 20% of the administered dose), iron appears to show gastroresistance proper-
iron,® Forte) is preferable, Capua (Ce) Forte) administered during prehospi-
iron (Sideral® – iron,® – Clinica Forte a day or more for one month before surgery in
iron (Sideral® 8.5 ± 0.5 g/
iron (Sideral® iron at 1
iron (Sideral® iron (Sideral® iron, there was not only the
iron
iron
Results of Sucrosomial
preparation, such as Sucrosomial
intestinal level. However, with the introduction of a new oral martial therapy, administered orally (with
is a key element for the correction of anemia in these subjects. Until few years ago, the martial therapy, administered orally (with an intestinal absorption equal 15–20% of the administered dose), had, in many patients, important side effects especially at gastro-intestinal level. However, with the introduction of a new oral preparation, such as Sucrosomial® iron, there was not only the decline of gastrointestinal side effects, but also a high absorption of the administered dose, thereby reducing the risk of post-operative blood transfusion.

Conclusions
Sucrosomial® Iron is a new, patented ingredient that shows an alternative mechanism of absorption, thanks to its unique formulation. We have showed that Sucrosomial® Iron is able to promote Ferric pyrophosphate absorption in conditions where ferric iron is usually not absorbed, overcoming the limits of conventional iron supplements. Furthermore, Sucrosomial® Iron appears to show gastroresistance properties and bioavailability. On the basis of our data, we can suggest Sucrosomial® Iron as an alternative of oral iron sup-

Posters – Transfusional Medicine
Effectiveness of oral Sucrosomial® Iron (Sideral® Forte) administration in patients undergoing hip replacement
Mauro Di Costanzo
U.O responsible for Orthopedics and Traumatology – Clinica Villa Fiorita – Capua (Ce)

Introduction
Many orthopedic interventions, including hip replacement, are procedures that result in a certain amount of blood loss leading to postoperative anemia, which can delay rehabilitation and postoperative recovery. Anemia is a much more frequent and premature complication in older patients with lower hemoglobin levels before the operation. Having said that, pre- and post-operative iron supplementation, either orally or intravenously, is a key element for the correction of anemia in these subjects. The effectiveness was evaluated using the lowest dose (1 capsule daily) for one month prior to surgery. The study was carried out on 20 patients divided in two groups. Group A: 10 patients, scheduled for hip replacement surgery, visited one month before the operation with Hb values between 11 and 12 g/dL, aged between 65 and 70 years (5 males and 5 females), were treated before surgery with 1 capsules of Sucrosomial® iron (Sideral® Forte) a day for a month. Group B: 10 patients, undergoing hip replacement surgery, were not treated with iron therapy. Their Hb values were between 11.5 and 12.5 g/dL, aged between 65 and 70 years (5 males and 5 females). The baseline characteristics of the patients studied were hemoglobin, hematocrit, and red blood cells. Side effects or contraindications were also assessed.

Results
No side effects were reported during treatment with Sucrosomial® iron (Sideral® Forte) and none discontinued therapy. After surgery, the mean value of hemoglobin in group A (treated with Sideral® Forte) was about 8.5 ± 0.5 g/dL with no transfusion request, while the average value of Hb in group B was about 7.5 ± 0.5 g/dL and 4 required transfusion (Table 1). The supplemented group with Sucrosomial® iron, despite a lower hemoglobin level (10.5 ± 0.5 g/dL) at baseline compared to the control group (12 ± 0.5 g/dL), had a lower decline of Hb during the postoperative phase compared to the control group. The treatment with Sucrosomial® iron at 1 capsules showed a higher Hb level compared to the control group during the postoperative period. This therapeutic effect could have been even more evident using at 2 capsules of Sideral® Forte a day or more for one month before surgery in order to correct eventual iron deficiency in time.

Conclusions
In patients undergoing hip prosthesis, a preventive treatment with oral Sucrosomial® iron (Sideral® Forte) is preferable, since other studies have showed that Sucrosomial® iron appear to be better compared to other oral martial therapy showing few side effects (abdominal pain, gastralgia, nausea,}

| Table 1. Results of Sucrosomial® Iron supplementation on HL patients. |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
|                             | T0      | T1      | Blood transfusions n (%) |
| Hb (g/dL)                   | 10.2    | 12.8*   |                           |
| TIBC (μg/dL)                | 244     | 264*    |                           |
| Iron (μg/dL)                | 35      | 95*     |                           |
| Ferritin (ng/mL)            | 90      | 277*    |                           |

| Table 1. Results. |
|-------------------|------------------|------------------|------------------|
| Group of patients | Hb baseline | Hb preop | postop | Blood |
| (n)               | (g/dL)       | (g/dL)   | (g/dL) | transfusions n (%) |
| Control (10)      | 12 ± 0.5     | 12 ± 0.5 | 7.5 ± 0.5 | 4 (40%) |
| Oral Iron         | 10.5 ± 0.5   | 11.5 ± 0.5 | 8.5 ± 0.5 | 0 (0%)  |

Objectives
The aim of the study is to evaluate the effectiveness of Sucrosomial® iron (Sideral® Forte) administered during prehospitalization in a group of patients undergoing hip replacement surgery.

Materials and methods
The effectiveness was evaluated using the lowest dose (1 capsule daily) for one month prior to surgery. The study was carried out on 20 patients divided in two groups. Group A: 10 patients, scheduled for hip replacement surgery, visited one month before the operation with Hb values between 11 and 12 g/dL, aged between 65 and 70 years (5 males and 5 females), were treated before surgery with 1 capsules of Sucrosomial® iron (Sideral® Forte) a day for a month. Group B: 10 patients, undergoing hip replacement surgery, were not treated with iron therapy. Their Hb values were between 11.5 and 12.5 g/dL, aged between 65 and 70 years (5 males and 5 females). The baseline characteristics of the patients studied were hemoglobin, hematocrit, and red blood cells. Side effects or contraindications were also assessed.
vomiting, and diarrhea) and to be able to reduce blood transfusion. The study, even if performed on a small number of patients, showed superior efficacy with a significant increase in hemoglobin compared to untreated patients with Sideral® Forte and a reduction in postsurgical blood transfusions. The Hb values of patients treated with Sucrosomial® iron during the post-intervention was 1–1.5 g/dL higher than the hemoglobin values found in untreated patients, a demonstration of the bioavailability of Sucrosomial® iron. In conclusion, the work done suggests a benefit from treating patients undergoing hip replacement, with oral Sucrosomial® iron, which is well tolerated and has proven effective and safe for patients with less clinical risk compared to those untreated.

Improving the patient blood management (PBM) program in our center: a seven months experience

Fabio Marletto, Rita La Grotta, Alessandra Russo and Ilvana Scuvera

Immunohematology and Transfusion Medicine, Cardinal Massaia Hospital – ASL AT, Asti

Introduction

In patients undergoing major orthopedic surgery (knee and hip replacement), preoperative anemia, perioperative bleeding, and a liberal transfusion policy are the main risk factors for requiring red blood cell transfusion (RBCT). The clinical and economic disadvantages of RBCT have led to the development and implementation of multidisciplinary, multimodal, individualized strategies, collectively termed patient blood management, which aim to reduce RBCT and improve patients’ clinical outcome and safety. Within a patient blood management program, low preoperative hemoglobin is one of the few modifiable risk factors for RBCT.

Objective

Based on available clinical evidence and our experience, we tried to optimize preoperative hemoglobin levels, in order to minimize the risk of patients requiring RBCT. To this purpose, after reviewing the diagnostic value and limitations of available laboratory parameters, we developed an algorithm for the detection, classification, and treatment of preoperative anemia, with a patient-tailored approach that facilitates decision-making in the preoperative assessment.

**Figure 1. Flow Chart.**

| Lowering Hb (man<13 g% woman<12 g%) |
| History of liver/kidney disease, internal bleeding |
| Treat disease |
| Blood test |
| Peripheral blood smear |
| MCV=80 fl (alcoholism, thyroid, liver, …) |
| VitB12, Folic acid suppi |
| Homocysteine, iron, FTN suppi |
| BMB, EPO, transfusion |
| Chronic disease anemia (EPO, sucrosomial iron) |
| Suspect Iron deficiency anemia (dose VitB12, folic acid) |
| Supplementation therapy; BMB if not responding |

BMB: bone marrow biopsy, FTN: ferritin, Sat: transferrin saturation,
Methods
The algorithm, designed by our center and subjected to pre-admission to the orthopedics department, provides that patients undergoing elective orthopedic surgery (hip and knee prosthesis) perform blood chemistry routine with complete control blood count and reticulocyte count, clotting time, protein electrophoresis, creatinine, iron, transferrin, ferritin, vitamin B12, and folic acid. Patients are subjected to our evaluation about a month before the surgery. Based on the detected values, patient can start a supplementation therapy with oral Sucrosomial® iron (30 mg daily), folic acid (5 mg daily), IM cyanocobalamin 5000 UI weekly or IV ferric carboxymaltose (dosage depending on total iron deficit evaluated by Ganzoni equation) until the intervention. Values are then rechecked at admission for surgery. In the period July 2016–January 2017, 46 patients were evaluated (Figure 1).

Results
46 patients were evaluated (M 20–43%, F 26–57%, mean age 71 years, mean Hb 13.5 g/dL data before treatment): 28 patients (60%) did not receive transfusion, 9 (20%) received one RBC unit and 9 (20%) received 2 or more RBC units, with significant improvement of our data prior to the introduction of the PBM protocol (47% the average transfusion rate and 0.88 unit the average of RBC units transfused in anemic patients before the introduction of the PBM program). 6 patients (13%) had abnormalities in protein electrophoresis. 43 patients (93%) started supplementation with Sucrosomial® iron until surgery (only 3 patients had Hb >14.5 g/dL and were not supplemented), 7 patients (15%) received IV iron in addition to oral iron, while 6 patients (13%) received folic acid and/or vitamin B12 supplementation in addition to oral/IV iron.

Conclusions
To reduce transfusion rates, patient blood management needs a comprehensive preoperative, intraoperative, and postoperative approach, considering the state of each patient. Because blood management is closely connected with prognosis, it has become a new challenge in the management of orthopedic patients.

Iron supplementation in the perioperative period: preliminary results for general surgery
Christian Franzini, Lorenzo Casali, Alessio Rollo and Caterina Santi
U.O.C. Chirurgia Generale, Ospedale di Vaio, Fidenza (PR)

Table 1
<table>
<thead>
<tr>
<th>Group of patients</th>
<th>Mean Hb preop (g/dL)</th>
<th>Mean Hb post (g/dL)</th>
<th>Blood transfusions (units/patients)</th>
<th>Mean hospital stay (days)</th>
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<tbody>
<tr>
<td>2015</td>
<td>13.1 ± 1.82</td>
<td>11.2 ± 1.55</td>
<td>0.41 ± 0.07</td>
<td>12.4 ± 1.88</td>
</tr>
<tr>
<td>Oral Iron supplementation</td>
<td>11.5 ± 1.72</td>
<td>11.3 ± 1.45</td>
<td>0.20 ± 0.03</td>
<td>17.3 ± 2.96</td>
</tr>
</tbody>
</table>

Introduction
Anemia frequently occurs in patients undergoing general surgery, in particular for gastrointestinal surgery [1]. The impact of anemia and iron-deficiency abdominal surgery outcomes is well documented in literature [2,3]. Perioperative iron supplementation is usually administered intravenously [4].

Objectives
Aim of this study is to determine if oral Sucrosomial® iron supplementation in the perioperative period enables better results in terms of recovery, length of hospital stay, and need of blood transfusions compared to an historical population with the same characteristics.

Methods
We prospectively collected data of patients needing major gastrointestinal surgery in the four-month period from October 2016 to January 2017. Patients scheduled for colorectal surgery (right hemicolectomy, left hemicolectomy, segmental colonic resection, anterior rectal resection) or gastric surgery (total or subtotal gastrectomy) with anemia at preoperative blood exams (hemoglobin <13 g/dL for women and <14 g/dL for men) were recommended the supplementation of Sucrosomial® iron (1 capsules a day, for one to three weeks prior to surgery) [5]. 22 patients were initially enrolled for the study. Four patients were ruled out because of intraoperative findings of advanced neoplastic disease. Three patients were ruled out because of postoperative anastomotic bleeding (two patients required transfusions as a consequence of bleeding). Five patients were excluded because of poor adherence to the supplementation prescribed. Thus, the postoperative results of ten patients were analyzed in terms of hemoglobin values, blood transfusions, and hospital stay against comparable data from the previous year (major digestive surgery in 2015). Patients who underwent major elective gastrointestinal surgery were selected. Patients who received palliative intervention and those with hemorrhagic postoperative complications were excluded. For 2015, 82 patients matched the selection criteria. They were not pair matched.

Results
Table 1 shows mean preoperative hemoglobin values (data collected 1 week before surgery and corresponding to at least 1 week after beginning of iron supplementation; Hb value at diagnosis was not available), mean postoperative hemoglobin values, blood transfusions, and mean hospital stay in the two groups of patients. Comparative data analysis highlights a smaller decrease in hemoglobin values after surgery in patients taking oral Sucrosomial® iron...
implementation (0.2 g/dL vs. 1.9 g/dL) and lower need of blood transfusions (0.20 units/patient vs. 0.41 units/patient). Mean hospital stay was longer in the group on iron supplementation, but this result is biased by two patients whose longer hospitalization was not due to anemia: in one case the reason was lack of place in the intensive care unit, while the other case was a 94-year-old patient lacking home caregivers.

Conclusions
Preliminary results do not allow us to establish actual efficacy of oral iron intake in improving surgical outcomes. However, early data suggest the efficacy of oral therapy with Sucrosomial® iron in terms of lower need for blood transfusions in digestive surgery. Extension of the study in order to collect more data regarding patients treated in perioperative period with oral iron supplementation and increasing the dose (2 capsules a day) will clarify if this approach can be effective in reducing the need for blood transfusions and enhancing recovery after major digestive surgery.

Bibliography

Sucrosomial® iron vs. different iron oral formulation in iron-deficiency anemia due to gastrointestinal bleeding: multicentric randomized study
Giulio Giordano, Donata Berardi, Giuseppe Berardi, Giuseppe Di Gregorio, Bruno Carabellese, Antonietta Licianti, Marilù Magri, Rosanna Gigli, Giovanna Niro and Luigi Di Marzio

Background
There are several different oral iron formulations with different mechanisms of uptake known or supposed (DMT1 for iron sulfate, microencapsulated iron and sunactive iron, transcellular and lymphatic way for Sucrosomial® iron, heme and peptones carrier for heminic chelated bisglycinate iron, peptones carrier for chelated bisglycinate iron).

Objective
Data regarding absorption and effectiveness for each kind of iron are lacking. Aim of this study is to see if there is some difference regarding effectiveness and tolerability among different oral iron formulation.

Methods
This study is a multicenter randomized study. 300 patients with iron-deficiency anemia and gastrointestinal bleeding were randomized 1:1:1:1:1:1 to receive iron sulfate (65 mg of elemental iron oíd), microencapsulated iron, sunactive iron, Sucrosomial® iron, heminic chelated bisglycinate iron (30 mg of elemental iron tid), chelated bisglycinate iron (15 mg of elemental iron tid). Patients’ characteristics were similar in all six groups. Hemoglobin trend and side effects were recorded in general patients population and in C-reactive protein (CRP) high-level patients.

Figure 1. Overall Hb levels.
Results

Median Hb value at start of treatment was 8.2 g/dL. In a group of patients with high CRP, median Hb value was 7.8 g/dL. Median follow up was 4.5 months (R 3–6). The Hb increase rate in the first two weeks of treatment was the same in the group of Sucrosomial® iron, bisglycinate chelated iron and heminic bisglycinate iron (Figure 1). However, from the third to the sixth week, Hb increase rate was higher in the Sucrosomial® iron group (Figure 1). In this group, from the sixth to the twelfth week the Hb increase rate was still higher, but with a slight decrease (Figure 1). In all group Hb level achieved a plateau phase after three months (Figure 1) and ferritin level starts to increase. At three months, higher levels of hemoglobin were shown by Sucrosomial® iron (13.2 g/dL), heminic chelated bisglycinate iron (11.7 g/dL) and chelated bisglycinate iron (11.3 g/dL) (Figure 1). In a group of patients with high CRP level (>30 ng/mL), the Hb increase is higher in Sucrosomial® iron group from the tenth week, it is continuous until the sixth month (Hb 12.5 g/dL) (Figure 2) and is linked to a marked CRP-level decrease after three months of treatment. Further investigation is needed to confirm the results.

Conclusion

Among different oral iron formulation in iron-deficiency anemia, Sucrosomial® iron appears to have a faster activity, a higher efficacy, more evident in patients with high CRP value linked to a marked CRP-level decrease after three months of treatment. Further investigation is needed to confirm the results.

Posters – Gastroenterology

Sideral® Forte – the first experience of 3 month therapy of anemia in inflammatory bowel diseases

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aRUDN-university, Moscow, Russia; bMoscow Clinical Scientific Practical Center, Moscow, Russia

Introduction

The article describes the modern view on the etiology and treatment approaches of anemia in inflammatory bowel...
diseases (IBD). Standard iron drugs' low efficacy and poor tolerability due to malabsorption and chronic inflammation of the intestinal wall are discussed.

**Objective**
The aim of this work is to determine the pathogenetic validity, efficacy, and tolerability of the novel oral Sucrosomial® iron (Sideral® Forte) in IBD patients with anemia.

**Methods**
We have currently analyzed the results of 6 anemic patients treated with oral Sucrosomial® iron, Sideral® Forte. The therapy was prescribed after hospital discharge under the supervision of a hematologist. The drug was given as one capsule (30 mg of elemental iron) two times a day when the serum ferritin level was less than 100 µg/L. The result was evaluated before and after 1 and 3 months of treatment. We used erythrocyte indices and routine parameters for iron metabolism as laboratory markers of the treatment effectiveness. Clinical efficacy and tolerability of
Sideral® Forte was determined according to the severity of anemia, sideropenic symptoms, complaints associated with the manifestation of IBD before and after 3 months of treatment. With this purpose, a special questionnaire was developed and filled out by patients. It included three main groups of anemia and IBD symptoms with point ranging from 1 to 5 depending on the severity of the symptoms. The questionnaire was assessed by calculating mean value for each item, then the average value for three groups of complaints.

**Results**

Laboratory efficacy of Sideral® Forte was suggested by an increase in hemoglobin (Hb, from 11.1 ± 1.4 g/dL to 12.4 ± 1.6 g/dL) (Figure 1), mean corpuscular hemoglobin (MCH, from 26.3 ± 2.6 to 29.4 ± 3.0 pg) (Figure 1), serum iron (SI, from 4.6 ± 1.6 mkmol/L to 8.1 ± 4.1 mkmol/L) (Figure 2) and serum ferritin (SF, from 12.4 ± 13.3 mkg/L to 20.2 ± 33.9 mkg/L) (Figure 2) levels and by a decrease in erythrocyte sedimentation rate (ESR, from 30.8 ± 1.2 to 20.8 ± 7.4 mm/h) (Figure 1) and total iron-binding capacity of serum iron (TIBC, from 56.4 ± 10.9 to 51.7 ± 4.9 mkmol/L) (Figure 2), thus, showing normalization of Hb, MCH, and SF levels after 3 months of treatment.

Questionnaire results for the five patients receiving Sideral® Forte showed, after 3 months of treatment, a decrease in the average scores (average manifestations) for anemic symptoms (from 3.0 ± 1.2 to 1.7 ± 0.6), sideropenic symptoms (from 2.4 ± 1.6 to 1.6 ± 0.3) and IBD gastrointestinal manifestations (from 2.5 ± 0.8 to 1.8 ± 0.3). The most significant changes were seen in the reduction of anemic (to 2.1 ± 0.5) and sideropenic (to 1.6 ± 0.4) manifestations already after 1 month of treatment.

**Conclusions**

Clinical symptoms of IBD also had positive dynamics and none of the patients abandoned the treatment. Mean Hb increase leads us to conclude that Sucrosomial® iron might be an effective drug for anemia in IBD patients. MCH increase was significant, which may be explained by the quick increase of iron availability, needed for erythropoiesis, and normalization in hemoglobin formation with Sideral® Forte treatment. Despite the sharp increase of exogenous iron utilization, SF increase, during therapy, is an efficacy criterion for the treatment of iron-deficiency anemia (IDA). Thus, these findings suggest that Sideral® Forte is an effective (by laboratory and clinical data) and safe treatment for anemia in patients with IBD. This preparation may be adequate for the treatment of anemia and may help changing the paradigm of relatively poor tolerable iron supplements. Further research is necessary to allow recommending Sideral® Forte as the main drug for the treatment of anemia associated with IBD.

**Introduction**

Morbid obesity has a dramatic increase worldwide over the last 20 years, becoming eventually epidemic (globesity). Bariatric surgery is the only effective way to treat these patients in the long term, with sustained and prolonged BMI decrease. Several bariatric procedures are commonly performed with this aim, with some drawbacks regarding mainly a reduced absorption of nutrients. Most common occurrences are iron, vitamin D, and vitamin B12 deficiencies, therefore, requiring supplementation of these nutrients. More specifically, one of the most common bariatric operations, Roux-en-Y gastric bypass (RYGBP), prevents the alimentary transit in the duodenum and proximal jejunal loop, that are the main sites of iron absorption and in some cases iron anemia may occur. Moreover, many patients are young fertile women in whom anemia is worsened by menstruations, and oral or intravenous iron supplementations are, therefore, often needed.

In our Obesity Surgery Center, about 2000 patients were operated in the last 20 years, the vast majority being RYGBP and gastric banding. The observation of iron-deficiency anemia (IDA) after gastric banding is uncommon and related to poor iron intake. Vice versa, up to 15% of patients of our cohort operated on with RYGBP showed iron-deficiency anemia and needed iron supplementations. Common oral iron (iron sulfate) is frequently low tolerated and poorly effective and requires long-time treatment due to low absorption in distal jejunum and ileum, since duodenum is excluded from the alimentary transit and in few cases with reduced oral tolerance the patients had to be treated with parenteral iron. Sucrosomial® iron seems to represent a better therapeutic option because its absorption, due to its particular structure, is not limited to the excluded loop but is maintained over the entire small bowel.

**Objective**

We decided to initiate a program of treatment on our patients with IDA during the follow up from RYGBP, with the aim of confirming the efficacy of oral Sucrosomial® iron treatment in operations that determine a partial malabsorption in the proximal intestinal loop.

**Methods**

20 patients operated on with RYGBP and showing postoperative IDA (Hb<12 g/L, ferritin <15 ng/mL), will be enrolled in this study. All patients will attend visits with the hematologist and the endocrinologist according to our perioperative protocol. During the follow up, hematological parameters (hemoglobin, serum iron, and ferritin) will be collected at 3, 6, 12, and 18 months postsurgery, as well as malabsorption parameters (Vitamin B12, Vitamin D, albumin, and cholinesterase) and weight loss. Multivitamin tablets containing 5 mg of fumarate iron will be routinely given to all patients up to 6 months postoperatively. In case of IDA, based on the evidence of efficacy available for Sucrosomial® iron, this supplement will be administered orally with the following protocol: hemoglobin range 11–12 g/dL: 30 mg daily (1 capsule) for

A protocol for the treatment of iron anemia after bariatric surgery with Sucrosomial® iron

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3 months; hemoglobin range 8–11 g/dL: 60 mg daily (2 capsules) for 1 month, then 30 mg for 2 months; hemoglobin >12 g/dL and Ferritin <15 ng/mL: 30 mg daily (1 capsule) for 3 months; hematological parameters will be controlled after 1 and 3 months from the beginning of treatment.

Results

9 patients out of 20 patients showing IDA occurring between 3 and 12 months postoperative were enrolled so far. Only 3 patients have already concluded the 3-month treatment and preliminary data in these cases showed a mean hemoglobin increase from 11.4 g/dL to 12.6 g/dL, a mean ferritin increase from 6.7 ng/mL to 19 ng/mL, a mean serum iron increase from 46.5 mcg/dL to 61.3 mcg/dL (Table 1). The other malabsorptive parameters remained unchanged and all patients were doing well. The oral iron administration was well tolerated and completed without side effects in all patients.

Conclusions

The study is still in progress and these preliminary data are insufficient to draw any conclusion, but they show that Sucrosomial® iron administered orally seems to allow an improvement on IDA in a short time span, showing that in operations in whom the main sites of iron absorption are excluded we might more successfully use a specific iron that is absorbed all over the jejunum and ileum. Further data are needed to confirm these preliminary observations.

Iron replacement in bariatric surgery: a long-term perspective

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Objectives

We aimed at evaluating iron supplementation efficacy in bariatric surgery patients and to underline the differences between ferrous sulfate (FS) and Sucrosomial® iron (SI) regarding effectiveness.

Table 1. Preliminary results.

<table>
<thead>
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<th>Serum iron pre-therapy</th>
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</table>

Methods

34 subjects, who underwent bariatric surgery (94.1% gastric bypass surgery, 6% sleeve-gastrectomy; 91% female, and mean age at surgery 41 ± 8 years), were divided in two subgroups according to the nature of supplements: FS, prescribed right after surgery (105 mg/day for the first month, then 105 mg/day for 10 days a month) and SI (14 mg/day for the first month, then 14 mg/day for 10 days a month), prescribed 3–76 months postsurgery (median time of 9.5 months due to FS inefficacy or intolerance). SI is prescribed several months after surgery because of FS intolerance and side effects or inefficacy. Hemoglobin (g/dL) and serum ferritin (ng/mL) at t0 (time of the prescription) and peak values reached within 2 years of iron replacement (t1) were evaluated. For the statistics, they used mean, SD, and statistical significance (p-value <0.05) obtained through two-tailed Student’s t-test.

Results

After 2 years of iron replacement, the whole sample showed a significant improvement in Hb (p-value <0.0001) but not in serum ferritin (p-value = 0.1). Considering the two subgroups, there is no significant difference in Hb and serum ferritin peak values. Both groups had an 88% of subjects reaching or preserving good Hb values within 2 years of treatment, and FS led to a higher increase in Hb (p-value = 0.03). In contrast, only 29.4% of the SI group and 24% of the FS group could reach or kept normal ferritin levels. Moreover, among those subjects it was shown a later decrease of ferritin below 50 ng/mL in 20% (SI group) and 25% (FS group) of cases. SI-treatment led to a noticeable improvement in serum ferritin (p-value = 0.016) in patients refractory to previous FS treatment, as denoted by low serum ferritin values at t0 (p-value = 0.007) (Figure 1).

Discussion

Managing iron deficiency in bariatric patients is complicated because of its malabsorptive nature, but also because of the
need of long-term follow up and therapy, resulting in poor compliance to treatment. A large part of our sample was represented by women of fertile age, which could result in a further obstacle to an effective iron replacement. Our analysis highlights a prevailing difficulty in reaching and keeping stable iron storage. Patients who were refractory to FS, as denoted by markedly low ferritin levels at 10 (despite previous iron treatments), benefited from SI, as denoted by a significant increase in this marker, even if peak values are still below the lower tolerance limit. These data suggest that long-term SI supplements could allow a more stable maintenance of serum ferritin levels >50 ng/mL, compared to FS (which more frequently leads to temporary results).

Conclusions

In conclusion, we underline the importance of long-term follow up (monitoring Hb and ferritin levels) and continuous supplementation, while promoting and motivating patients’ adherence to treatment. A main limitation of the present study is represented by the time gap between surgery and SI prescription, while FS supplementation was started right after surgery. Further studies are needed to find additional evidence to our preliminary conclusions.

POSTERS – ONCOLOGY

Sucrosomial® iron for transfusion prevention in cancer patients on chemotherapy

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Introduction

Anemia is a cancer-related condition and associated with antineoplastic treatments. Its management is based on iron prescription plus or minus erythropoiesis stimulating agents (ESAs) according to Hb value, with red blood cell transfusions (RBCT) reserved only for severe anemia due to potential detrimental effect in cancer patients. Sucrester and phospholipids-based iron capsules (Sucrosomial® Iron – Sideral® forte) appears to be significantly more bioavailable than other oral formulations with better tolerability.

Objectives

We started a prospective study to evaluate if administration of Sucrosomial® iron 30 mg/day could prevent Hb fall to <10 g/dL and the use of ESAs or transfusions in cancer patients starting chemotherapy with Hb values 10–12 g/dL.

Methods

Patients with solid tumors starting chemotherapy with Hb level 10–12 g/dL and transferrin saturation (TSAT) 15–50% were included. Treatment continued for 3 months. Iron parameters were checked at 6 and 12 weeks.

Results

Up to February 2017, 16 patients were enrolled. In n = 3 cases, treatment lasted <12 weeks. At baseline, medium Hb level was 11.18 g/dL. After 6 and 12 weeks (in n = 12 pts with both data evaluable), medium Hb levels were 10.9 g/dL. TSAT increased from 13.45 to 20.1% and 20.6% at 6 and 12 weeks, respectively. No patient was transfused or received ESAs.

Conclusion

In this prospective series of patients with baseline mild anemia, the intake of Sucrosomial® iron for 3 months maintained Hb level above 10 g/dL and avoided any ESAs or RBCTs. Use of Sucrosomial® iron could be considered in cancer patients on chemotherapy.

Administration of Sucrosomial® iron in patients with localized prostate cancer treated with whole pelvis radiotherapy: improvement of fatigue and quality of life

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Introduction

Radical radiotherapy is commonly used in the treatment of localized prostate cancer. The treatment is painless but it can cause side bowel and bladder dysfunction, fatigue, skin reactions, bruising, urethral stricture, bone marrow suppression, and bleeding. Modern radiation oncologists can direct higher radiation doses at prostate cancer cells, while reducing exposure to normal, healthy tissue. The fatigue is one of the most common side effects of radiation therapy and it is typically more severe 2–4 h after treatment. However, the etiology of cancer-related fatigue is poorly understood. Studies linking inflammatory processes to fatigue in cancer survivors led us to test the hypothesis that activation of the proinflammatory cytokine network is associated with fatigue symptoms during radiation therapy for prostate cancer. The fatigue may be caused by anemia, poor appetite, depression, or it may be related to toxic substances that are produced when cancer cells break down and die. Low blood cell counts occur because of radiation’s damaging effect on the bone marrow, where blood cells are made. Blood counts are more likely to be affected when the pelvic bones lie in the treatment area. Fatigue in disease-free patients was significantly associated with gender, physical distress, pain rating, sleep quality, functional disability, psychological distress, and depression. Several studies show that cancer patients with higher hemoglobin levels experience less fatigue and have more favorable perceptions of their quality of life. Although many factors can induce or exacerbate cancer-related fatigue, anemia is one of the most common etiologies. Sucrosomial® iron is a preparation of ferric pyrophosphate carried within a phospholipid and sucroester membrane. Compared to other oral formulations, it is well absorbed from the gut and demonstrates high bioavailability together with a lower incidence of side effects.
Objectives

The aim of our study is maintaining or improving patient quality of life during and after therapy, thanks to the administration of Sucrosomial® iron during radiotherapy.

Methods

In this preliminary study, we enrolled 20 consecutive patients affected by clinically localized prostate cancer, naive for chemotherapy, treated with whole pelvis hypo-fractionated intensity-modulated radiotherapy. Although the use of hypo-fractionation in the treatment of localized prostate cancer has attracted significant attention in recent years, its use, with high equivalent doses, is a relatively recent approach. Sucrosomial® iron (Sideral® Forte, 1 capsules/day) has been administered for 8 weeks during radiotherapy and the hemoglobin value has been monitored weekly. Furthermore, fatigue level has been reported.

Results

Preliminary results on 5 patients revealed that the patients (mean age 70 years) have completed radiation therapy without interruption (Total 62 Gy/3.1 Gy per fraction). The weekly control of blood count showed a constant value of hemoglobin (the value was always higher than 12 g/dL), reducing the percentage of patients experiencing anemia (Figure 1). Only one patient had gastrointestinal pain thus supplementation was suspended. Considering the fatigue level, none of them needed to stop daily activates or substantially change lifestyle.

Conclusions

Among patients with prostate cancers, the percentage of patients experiencing anemia increased during the course of radiotherapy. Nevertheless, correcting mild-to-moderate anemia may have positive effects on quality of life. The fatigue may be caused by anemia. The addition of Sucrosomial® iron might be useful to not worsen fatigue symptoms and quality of life in patients with prostate cancers planned to receive whole pelvis radiotherapy.

Effectiveness of two different dosage regimes of Sideral® forte in anemic patients with solid tumor

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Introduction

Anemia is a frequent condition in patients with solid tumor and treatment with chemotherapy. The martial intravenous supplement can be difficult to manage.

Objective

In this study, Sucrosomial® iron (Sideral® Forte – Pharmanutra S.p.A.) had a therapeutic efficacy in both single and double administration. With the latter, it can be seen a considerable increase in iron concentration. The aim of the study was to evaluate its effectiveness with various dosages.

Methods

We studied thirty patients (16 M, 14 F) aged between 30 and 70 years old with solid tumors (8 suffering from colon cancer, 7 breast cancer, 2 pancreas cancer, 1 oral cancer, 3 rectum cancer, 1 stomach cancer, 3 lung cancer, 1 kidney cancer, 1 larynx cancer, 1 prostate cancer, 1 esophagus cancer, 1 bladder cancer) and chemo-related anemia, divided into two groups (1:1). The protocol consisted in three months of

<table>
<thead>
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<th>Table 1. Results.</th>
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<tr>
<td>Hb (g/dL)</td>
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<tr>
<td>Serum iron (mcg/dL)</td>
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</tbody>
</table>

Figure 1. Weekly control of hemoglobin for each patient.
treatment with Sideral® Forte: group A received one capsule a day and group B received two capsules a day.

Results
Group A showed a hemoglobin (Hb) of about 10.5 g/dL and serum iron of about 50 mcg/dL, while group B showed an Hb of about 9.8 g/dL and serum iron of approximately 40 mcg/dL. The results are reported in Table 1. No major adverse events were observed, except for some patients with modest dyspepsia and some diarrheal episodes.

Conclusion
Sideral® Forte proved to be effective and well tolerated in postsurgical anemia in patients with solid tumor treated either with 1 or 2 capsules. As showed by the results, the use of two capsules increases the effectiveness of treatment.

Preventive Sucrosomial® iron supplementation in an elder patient undergoing exclusive radiation therapy treatment for nasopharyngeal cancer with laterocervical lymph node metastasis: clinical case

Nicola Ricottone
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Introduction
A 78-year-old man, with a medical history of chronic obstructive pulmonary disease (COPD), hypertension, coronary angioplasty, malaria, dyslipidemia, diabetes mellitus treated with oral hypoglycemic agents and a low-grade pT2a bladder cancer, affected by nasopharyngeal carcinoma with laterocervical lymph node metastasis underwent head-and-neck exclusive radiation therapy treatment. The diagnosis was obtained thanks to an otorhinolaryngology examination with a biopsy followed by a total body CT scan, a head-and-neck MRI and FDG-PET scans. These exams confirmed the nasopharyngeal cancer and the presence of bilateral neck metastatic lymph nodes, cT3, cN3a. The patient underwent two induction chemotherapy cycles with Carboplatin and Gemcitabine in another hospital. A month after chemotherapy a CT scan showed a partial response for both the primary tumor and the metastatic lymph nodes. A week before the start of radiation therapy, the patient was in sufficient clinical conditions (ECOG 2), showing hemoglobin (Hb) value of 8.9 g/dL, mean corpuscular volume (MCV) of 79.7 fl and mean corpuscular hemoglobin concentration (MCHC) of 26.5 pg, thus, indicating a sideropenic anemia. Patients undergoing radiation therapy treatment for head-and-neck cancer are subject to several side effects such as mucositis, pharyngodynia, and dysphagia, which lead to malnutrition and, as a consequence, the onset of a state of sideropenic anemia.

Objectives
To counterbalance this initial condition of sideropenic anemia, we administered to the patient a daily dose of 30 mg of Sucrosomial® Iron as concomitant supportive therapy during radiation therapy cycle.

Methods
About two months after chemotherapy, the patient underwent PET simulation before starting radiation therapy treatment. Radiation therapy was delivered with a Volumetric Arc Therapy (VMAT) technique and a Simultaneous Integrated Boost (SIB) in 33 fractions for a total dose of 54.45 Gy + 15.51 Gy on nasopharyngeal cancer and PET positive nodes (total dose 69.96 Gy). A week before the beginning of radiation treatment and for the entire course, the patient was supplemented with 30 mg of oral Sucrosomial® Iron.

Results
Fifteen days after the beginning of radiation therapy, a blood sample was taken to check the Hb value, which was Hb 10.3 g/dL with an MCV of 83.5 f and MCHC of 27.2 pg. Another blood test was done on the 25th day of radiation therapy showing the following results: Hb = 13.2 g/dL (Figure 1), MCV = 85.5 fl and MCH = 28.6 pg. During the radiation therapy course, the patient suffered moderate mucositis and had no weight loss.

Conclusions
This clinical case shows an improvement of patient anemia condition with the administration of oral Sucrosomial® Iron. Hemoglobin value determines blood oxygenation, which is fundamental in limiting the degree of mucositis, dysphagia, and fatigue. This resulted in a better compliance and avoided radiation therapy interruptions, which have a detrimental impact on the prognosis. Another point in favor of administering oral Sucrosomial® Iron was due to the negative effect of anemia on the efficacy of radiation therapy. Preserving the hemoglobin level allows for better local control and survival.
Effect of oral Sucrosomial® iron supplementation in an elderly anemic patient treated with platinum-based chemotherapy for metastatic lung cancer: a case report

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Thoracic Department of Istituto Nazionale Tumori di Napoli

Introduction
Platinum-based chemotherapy is the cornerstone of treatment of advanced non-small-cell lung cancer (NSCLC) patients [1,2]. In people over the age of 70 with advanced NSCLC who do not have significant comorbidities, increased survival with platinum combination therapy needs to be balanced against higher risk of major adverse events when compared with non-platinum therapy [1,2]. In this report, we describe the effect of addition of oral sucrosomial® iron supplementation to epoietin therapy in improving Hb levels in an elderly patient treated with platinum schedule chemotherapy.

Case report
A 74-year-old man with a long history of cigarette smoking and ischemic heart disease treated with aspirin has referred from his general practitioner for cough and asthenia. After a preliminary clinical evaluation, he underwent a thorax X-Ray followed by total body CT scan, which showed a lung mass in the right lower lobe of lung, mediastinal node bulky disease and bone metastasis (clinical stage cT4N2M1). The histological exam confirmed a poor differentiated adenocarcinoma, EGFR wild type. In view of good PS and normal heart function, the patient underwent first-line chemotherapy, with age-modified schedule of a low-dose platinum-based therapy. A baseline evaluation demonstrated an Hb level of 10.6 g/dL. After first cycle of the chemotherapy, the Hb levels dropped to 8.7 g/dL, resulting in increased asthenia. To prevent worsening of his condition, we started therapy with alfa biosimilar epoietin (40,000 IU) and oral supplementation of oral Sucrosomial® iron, 30 mg per day. After six weeks, the Hb levels increased to 9.4 and after 9 weeks to 10.2 g/dL, resulting in improved fatigue and appetite. The patient was able to complete six cycles of therapy, achieving a partial remission of disease.

Conclusions
Recent studies have demonstrated that, among patients with metastatic non-small-cell lung cancer, early palliative care led to significant improvements in both quality of life and mood [3]. Moreover, as compared with patients receiving standard care, patients receiving early palliative care had longer survival. Correct and prompt management of anemic status related to chemotherapy is of paramount importance to improve quality of life and ensure the treatment outcomes [4]. This clinical case showed an increase in Hb levels with an epoietin plus Sucrosomial iron treatment, which allowed the patient to complete the radiotherapy cycles.

Bibliography

Safety and efficacy of Sucrosomial® iron in cancer patients with anemia

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Hospital Universitario Parc Taulí de Sabadell

Introduction
Anemia is the main hematologic complication of patients with cancer and it shows a great prevalence [1–5]. Oral Sucrosomial® iron is a dietary supplement that is considered to be an alternative to the ferrous and ferric salts present on the market, whose principal problem is their poor digestive tolerance responsible for low adherence to treatment. It appears to have a higher percentage of absorption and better tolerability, which could be reflected in better compliance and effectiveness.

Objective
The primary end point is to describe the tolerability of oral Sucrosomial® iron in patients with anemia and cancer. Secondary end points are to:

- Describe changes in the analytical levels in relation to pretreatment
- Describe if there is reduction of treatment with IV iron and transfusions
- Describe compliance to the treatment

Method
This is a single-center, prospective, observational study with no medication carried out at outpatient palliative care consultations at Universitario Parc Taulí Hospital in Sabadell. The studied population is represented by patients with solid neoplasia undergoing treatment with chemotherapy who presented total or functional iron deficiency confirmed by recent analyses and who have started treatment with Sucrosomial® iron in the last two weeks.

A descriptive data analysis was carried out for all the variables collected, both quantitative and qualitative, using SAS®9.3 statistical package.
Results

20 patients were recruited. Of these 8 were excluded, 1 abandoned the study, and in 2 data were not completed. The average age was 63 years and 55.6% of patients presented a Palliative Performance Scale (PPS) of 90–100%. Two-thirds of the population presented a gastrointestinal neoplasia, none with bone metastasis involvement. The Hb values show a mean of 98.1 g/L before the treatment outset and an average increase of 107 g/L after 8 weeks of treatment. No patient presented nausea or vomiting either before or after the treatment; only 1 presented constipation. Statistically significant differences were found in the iron saturation transferrin, serum iron, erythrocyte sedimentation rate and CRP levels. 77.8% presented good therapeutic compliance, rising to up to 88.9%. No patient required IV iron. One patient required transfusion.

Conclusions

Good tolerance and adherence to the treatment were observed. Improvement in the anemia parameters was observed without transfusion or parenteral iron therapy being required. Improvement in inflammatory parameters was reported.

Bibliography


POSTERS – NEPHROLOGY

Comparison of Oral Sucrosomial® Iron vs. Iron Sulphate effect in Chronic Kidney Disease Stage 5 Patients: A Retrospective Cohort Study

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Introduction

Sucrosomial® iron (SI) is a preparation of ferric pyrophosphate conveyed through a matrix of phospholipid and sucrose esters of fatty acids that shows a favorable absorption profile and is well tolerated. Clinical experiences have been performed both in the onco-hematologic and nephrological settings. A randomized clinical trial comparing SI vs. intravenous (IV) iron showed a more rapid and sustained effect with the IV formulation, but the hemoglobin target was also reached with SI [1]. Many lesser studies with few patients have compared the effect of SI vs. other oral formulations [2]. In our facility, iron sulfate is the first-line oral iron therapy, but many patients are intolerant to this compound, thus, since 2015 we have administered Sucrosomial® iron to these patients.

Objectives

In this study, we reviewed the effectiveness and the tolerance of SI in patients with chronic kidney disease stage 5 both in conservative treatment and renal replacement therapy (RRT) as compared to oral ferrous sulfate (FS). The aim of the study was to compare the increase of hemoglobin and ferritin levels in the patients treated with SI, one 30 mg tablet per day and FS, one 80 mg tablet per day, at three and six months with or without ESA.

Methods

We reviewed the clinical files of all patients with chronic kidney disease stage 5 treated with oral iron compounds in 2015 and 2016 in our Unit. A cohort of 45 patients was extracted. Oral iron treatment and its changes (hemoglobin, ferritin, transferrin saturation, PTH, urea, creatinine and eventual modality of RRT) were recorded for each patient at the start of iron therapy and at three and six months. Moreover, age and sex were considered. Adverse effects, in particular, gastrointestinal and the causes of interruption of the therapy were recorded. Descriptive statistics were performed for all the study variables a time 0 (start of therapy), at three months and at six months. The comparison between the two treatments was performed with analysis of variances for repeated measures. Since the retrospective study design, a repeated measure mixed model has been performed to adjust for possible confounders. Tests for simple effects and pairwise comparison were also performed. All statistical analyses were conducted with STATA 13.

Results

45 patients underwent oral iron treatment during 2015 and 2016 for at least six months: 18 with SI and 27 with FS. Patients treated with SI were older (median age 68 vs. 62), more anemic and with lower iron deposits (Table 1). The analysis of variance for repeated measures on the primary outcome (hemoglobin) showed a significant effect for both treatment and time: patients treated with SI started from lower levels of hemoglobin, but reached the same level as FS patients at three months and maintained it at six months; hemoglobin increased significantly along the time only in SI group. No interaction was detected between treatment and time, showing a similar increase trend in both treatments (Table 2, Figure 1). Simple effects test confirmed
that SI effect on hemoglobin was significant at three and six months, while the FS effect was not. We did not observe any significant effect on ferritin (Figure 2) or transferrin saturation.

The same results were also obtained after adjustment for age, RRT modality and ESA dose. Three patients on FS treatment dropped out, showing intolerance, while there were no dropouts in SI group. No adverse effect was observed in the SI group.

Discussion
Many experts claim that Sucrosomial® iron is probably the most effective oral formulation and, thus a randomized control trial (RCT) comparing SI vs. IV iron was performed [1]. Probably the oral bioavailability of SI is high, but not as high as IV administration; as a matter of fact, the RCT showed the equivalence between the two treatments at three months, but the effect of IV iron was more rapid and more sustained.

Many observations suggest that SI is more tolerated than other formulations [1–3], consequently in our facility, we reserved this therapeutic option to patients unable to take oral iron without interruption and for whom IV administration was not comfortable. This selection is apparent, since the SI group starts from lower levels of hemoglobin. Nonetheless, at three months, the response in terms of hemoglobin is similar in the two groups and it is maintained at six months. Ferritin is not affected by iron administration, indicating that the dosage delivered is sufficient to guarantee erythropoiesis, but not to increase iron deposits, since almost all patients were on ESA.

This real-world study shows that the dynamics of hemoglobin increase in SI patients is similar to the one observed in the RCT, reaching a peak at three months. Although Parisi et al. 2016 [3] carried out an observational study on SI versus other iron formulation, there have been no randomized clinical trials as yet.

Conclusions
Our study gives some interesting information: in CKD patients a good response to oral SI is observed, the response reaches a peak at three months, adverse effects are negligible. These observations suggest that performing an RCT comparing SI versus other oral iron compounds in CKD patients would be useful.

References

Effects of substitution intravenous iron therapy with oral Sucrosomial® pyrophosphate iron in HD-CKD patients with hyperferritinemia – results at 15 months
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S.C. di Nefrologia Dialisi P.O. di Alghero, ASL 1 Sassari – CD San Camillo
Introduction

Patients with chronic kidney disease (CKD) in hemodialysis (HD) have a relative deficiency of erythropoietin production in response to anemia. Therapy with erythropoiesis stimulating agents (ESAs) is generally effective, but attenuated by inflammation and comorbidity, and leads to a constant increased demand for iron supplementation. In the HD population, intravenous iron (IV), as iron gluconate, is usually used, both for practical reasons, and because many studies showed the advantage of the IV iron treatment compared to conventional oral iron therapy. However, prolonged administration of iron and inappropriate IV doses generates increased the sequestration of iron into tissue deposits and hyperferritinemia may occur. Moreover, the Italian Medicine Agency (AIFA) released in 2013 new on the use of IV iron formulations highlighting their risks, which may be even serious. Oral therapy, mainly iron sulfate, is often less effective, due to its reduced absorption and frequent gastrointestinal disorders that reduce patient’s compliance. The oral Sucrosomial® pyrophosphate iron, conveyed within a phospholipid membrane and sucres- ters, is able to increase iron bioavailability and tolerability.

Methods

12 CKD patients, having HD three times a week, were enrolled; two deceased due to cancer and cardiovascular event. All patients were treated with ESA and IV iron supplementation (sodium ferric gluconate, FERLIXIT®, 31.25–125 mg/week) and showed hyperferritinemia (1705 ± 1114 ng/mL; range = 543–3822 ng/mL) and Hb within target values (12.1 ± 0.85 g/dL). They had serum iron in a high-normal range (107.5 ± 37.6 mcg/dL) and elevated TSAT (49 ± 16.5%). PCR was normal. At time 0 (T0), the IV iron therapy was suspended and oral iron supplementation with Sucrosomial® pyrophosphate iron (SIDERAL® FORTE) was introduced at the dose of 30 mg/day. Values of Hb/Ht, ferritin, serum iron, TSAT%, PCR and erythropoietin dose were monitored monthly. All data are expressed as mean ± SD. The statistically significance was calculated using paired t-test.

Results

In the ten patients who completed the follow up after 15 months (T15), the decrease in ferritin levels was quick and progressive from the third month onwards (587 ± 254 ng/mL (T15) vs. 1705 ± 1114 ng/mL (T0), p < 0.001). Hb/Ht levels remained steadily within target range, but a slight reduction was seen after 6 months (11.2 ± 0.4 g/dL), which increased after optimization of ESA dose (11.7 ± 0.3 g/dL after 12 months). A slight significant decrease, within normal values, in serum iron (66.1 ± 15.8 mcg/dL vs. 107.5 ± 37.6 mcg/dL, p < 0.03) and TSAT% (32.7 ± 13.9% vs. 49.5 ± 15.6%, p < 0.03) were observed. After 15 months, ESA dose was reduced significantly (from 5400 ± 5232 IU to 1333 ± 1366 IU/week, p < 0.01). There were no changes in PCR values, always within normal range.

Conclusions

The substitution of IV iron supplementation with Sucrosomial® pyrophosphate iron (SIDERAL® FORTE) in HD-CKD patients with hyperferritinemia was effective in lowering ferritin levels, while maintaining Hb, serum iron and TSAT% levels within target range. The results were obtained despite an evident ESA dose reduction.

Advantages of therapy with oral Sucrosomial® pyrophosphate iron in the management of chronic kidney disease in ‘conservative’ therapy: our experience

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Introduction

Patients with chronic kidney disease (CKD) in advanced stages generally develop an erythropoietin production deficit, resulting primarily in hyporegenerative anemia. The administration of erythropoiesis stimulating agents (ESA) for therapeutic purposes is indicated in this case. Such therapy is variously effective depending on the subject matter and is affected by the presence of comorbidity, a possible systemic inflammatory state, and the bioavailability of other elements and/or factors involved in erythropoiesis chain. One of these factors is represented by iron. This leads to carry on a therapeutic supplementation with this element in order to avoid its deficiency in the course of stimulation with ESA. In the population of CKD subjects in the hemodialysis, iron therapy is administered intravenously mainly for practical reasons. In the pre-dialysis chronic renal failure stages, instead, it is necessary or appropriate to administer oral iron. In such circumstances it becomes essential the actual extent of iron absorption from the gastrointestinal tract, that is often affected by a poor adherence to therapy, due to gastrointestinal disorders arising from the ingestion of the iron-containing drugs. The administration of Sucrosomial®

<table>
<thead>
<tr>
<th>Table 1. Results.</th>
<th>Initial Values (T0)</th>
<th>Final Values (T 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferritinemia</td>
<td>1705 ± 1114 ng/mL</td>
<td>587 ± 254 ng/mL</td>
</tr>
<tr>
<td>Hb</td>
<td>12.2 ± 0.4 g/dL</td>
<td>11.78 ± 0.3 g/dL</td>
</tr>
<tr>
<td>Serum iron</td>
<td>107.5 ± 37.6 mcg/dL</td>
<td>66.1 ± 15.8 mcg/dL</td>
</tr>
<tr>
<td>TSAT %</td>
<td>49.5 ± 15.6%</td>
<td>32.7 ± 13.9%</td>
</tr>
<tr>
<td>PCR</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>ESA</td>
<td>5400 ± 5232 IU/week</td>
<td>1333 ± 1366 IU/week</td>
</tr>
</tbody>
</table>
pyrophosphate iron, which is conveyed within a phospholipid and sucrosester membrane and appears to have characteristics of greater absorption and bioavailability and reduced incidence of side effects, could be beneficial in the treatment of anemia as important supportive therapy with the administration of ESA in patients in the pre-dialysis.

**Objectives**

We aim to evaluate the effects of oral therapy with Sucromomial® Iron (SIDERAL® FORTE) in anemic subjects with CKD in pre-dialysis ‘conservative therapy’ treated with ESA, in comparison with other oral iron preparations.

**Methods**

48 patients with CKD in conservative therapy in pre-dialysis 3b-5 K/DOQI stage, anemic with ESA treatment, were enrolled and divided into two homogeneous groups according to age and the presence of comorbidities. Those subjects with evidence of bleeding events and or inflammatory status during follow up were excluded. The observation period was 18 months. Both groups were treated with the long-acting ESA. Patients in the first group were supplemented with different oral iron preparations, with the possibility of switching one another, and at adequate dosage to meet the therapeutic needs, while the other group of patients was treated only with Sucromomial® pyrophosphate iron (SIDERAL® FORTE) at a dose of 30–60 mg/day in single or twice-daily administration. The study was conducted by detecting every two months the values of Hb/Ht and by varying, if necessary, the dose of ESA in relation to the predetermined therapeutic target. Simultaneously with the assessment of the degree of anemia, we proceeded to evaluate serum iron, ferritin, transferrin, folic acid, and vitamin B12, with subsequent prescription of therapeutic ‘adjustments,’ mainly regarding martial supplementation to maintain normal degree of transferrin saturation (TSAT), calculated by applying the following formula: serum iron/(transferrin × 1.42) × 100, to prevent vitamin deficiencies accidents on the red cell maturation.

**Results**

All patients completed follow up and none of them had bleeding events and/or significant changes in serum creatinine levels during the observation period. In the group treated with SIDERAL® compared to the group receiving other oral iron preparations; the martial status was more stable and Hb/Ht values showed a more favorable trend for the attainment and subsequent maintenance of the therapeutic target (Figure 1); ESA quantities necessary to optimize treatment were on average lower in the group treated with SIDERAL® compared to the other group (Figure 2). Adherence to oral iron therapy was significantly greater with the use of SIDERAL®, with a lower occurrence of adverse and/or side effects reactions (Figure 3).

**Conclusions**

In our experience, the administration of oral Sucromomial® pyrophosphate iron (SIDERAL® FORTE), in comparison with other iron preparations administered orally, in patients with CKD in pre-dialysis conservative treatment, in the absence of inflammatory state, was more effective in maintaining iron bioavailability for the synthesis of hemoglobin along during
erythropoiesis. We believe that this can be correlated with various factors, among which an important role is played by a better absorption and higher gastrointestinal tolerability compared to traditionally used iron salts and with a greater ‘adherence to therapy’ by the patient. In clinical practice, this can be translated into greater effectiveness on the ‘totality of care’ for the patient with CKD, with positive effects on cost savings due to a lower ESA consumption.

POSTERS – CARDIOLOGY

Sucrosomial® iron: short-term efficacy compared to administration of 4 capsules/day for 7 days vs. 2 capsules/day for 14 days in post cardiac surgery patients for myocardial revascularization

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Introduction
In patients undergoing myocardial revascularization by coronary artery bypass grafting (CABG), postoperative anemia is a condition that occurs in almost all patients. This condition limits the functional recovery and needs special attention, as often they must be resolved through transfusions of red blood cells or periods of martial intravenous or enteral supplementation. The recovery of acceptable values of serum hemoglobin occurs some weeks after surgery and, often, therapy with iron preparations is poorly tolerated by patients due to side effects such as abdominal pain, dyspepsia, diarrhea, and phlebitis at the site of infusions.

Objectives
We wanted to test, in our experience, the efficacy and tolerability of Sucrosomial® iron (Cardiosideral® Pharmanutra) in patients undergoing myocardial revascularization with CABG. Aim of the study was the assessment of acute postoperative correction of anemia by taking Sucrosomial® iron.

Methods
We studied 16 patients (12 M and 4 W) undergoing CABG, 67 ± 8 years of age, 6 had diabetes, 13 hypertension, 15 dyslipidemia, 8 had ejection fraction (EF) <50% and 5 were transfused with red blood cells after surgery. We considered hemoglobin (Hb g/dL) values from baseline to the 7th postoperative day (POD) and we treated 8 patients with 4 capsules/day for 7 days and 8 patients with 2 capsules/day for 14 days. The following parameters were taken into account: 6-minute walking test (6MWT, meters) and Hb at the 7th and 14th POD in the group of patients who received 4 capsules/day (G1) and at the 7th and 21st POD in the group of patients who received 2 capsules/day (G2).

Results
The results are reported in Table 1 and graphed in Figure 1.

Conclusions
Sucrosomial® iron was effective in the short-term treatment of anemia after heart surgery with no side effects. For the postoperative state was considered only the hemoglobin as a marker of therapy effectiveness. The improvement in performance of the 6MWT seems still very influenced by the POD and reconditioning exercise.

Management of iron deficiency and anemia in patients undergoing transcatheter aortic valve replacement (TAVR): a case report

Felice Gragnano, Andreina Carbone, Mario Crisci, Maurizio Cappelli Bigazzi, Renatamaria Bianchi, Donato Tartaglione, Simona Sperlongano, Francesco Natale, Fabio Fimiani, Claudia Concilio, Arturo Cesarro, Ivana Pariggiano, Vincenzo Diana, Giuseppe Limongelli, Mariagiovanna Russo, Enrica Golia and Paolo Calabrò
Division of Cardiology, Department of Cardio-thoracic and Respiratory Sciences, University of Campania ‘Luigi Vanvitelli’, A.O. dei Colli Monaldi Hospital, Naples, Italy.

Table 1. Results.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>G1 (S M and 3 W) 4 capsules/day for 7 days</th>
<th>G2 (6 M and 2 W) 2 capsules/day for 14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>113.13 ± 23.29</td>
<td>106.25 ± 12.46</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>14th POD</td>
<td>21th POD</td>
</tr>
<tr>
<td>11.00 ± 0.48</td>
<td>393.13 ± 39.09</td>
<td></td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>p value</td>
<td>p value</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0000001</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline</td>
<td>9.66 ± 0.45</td>
<td>10.00 ± 0.48</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>2 capsules/day</td>
<td>21 capsules/day</td>
</tr>
<tr>
<td>2 capsules/day for 14 days</td>
<td>10.35 ± 0.50</td>
<td>11.00 ± 0.31</td>
</tr>
</tbody>
</table>

Figure 1. Transcatheter aortic valve replacement (TAVR).
Introduction
Symptomatic aortic stenosis (AS) is an emerging problem of contemporary populations. Patients with AS assigned for transcatheter aortic valve replacement (TAVR) commonly demonstrated both non-cardiovascular and cardiovascular comorbidities, all significant modifiers of clinical outcomes. In this context, the most important ones are comorbidities that can be effectively treated. Iron deficiency and anemia have received particular attention in patients with AS, appearing to be highly prevalent (20–30% of patients) and bearing unfavorable prognostic consequences. Most importantly, some attempts to correct anemia seemed to be effective in improvement of clinical status. The recent evidence may position iron deficiency and anemia as therapeutic targets and a potentially correctable comorbidity in AS.

Clinical case presentation
An 84-year-old female with aortic stenosis and history of iron deficiency and microcytic anemia presented at our observation. She was a previous smoker, with a history of diabetes, hypertension, and peripheral artery disease. She had chronic kidney disease (3° stage) and paroxysmal atrial fibrillation on NOAC. She presented severe aortic stenosis (transvalvular mean gradient 65 mmHg, AVA 0.8 cm$^2$), symptomatic for dyspnea and chest pain, with a recent episode of pulmonary edema. Angiography excluded coronary artery disease. During our evaluation, we confirmed the diagnosis of iron deficiency and anemia. Considering the high surgical risk (EUROSCORE2: 18.5%; STS: 11%), TAVR was performed, with an excellent result (Figure 1).

Management of iron deficiency in TAVR
Considering the history of iron deficiency and anemia, the patient started therapy with oral Sucrosomial® iron (CardioSideral®) 2 months before TAVR. On admission (Figures 2 and 3), we found a net increase in hemoglobin (Hb), iron, and ferritin values. During hospitalization, the patient continued CardioSideral® supplementation. After TAVR, we observed a slight decline in Hb, ferritin, and iron values (Figures 2 and 3). On discharge, we recommended to the patient to continue therapy with oral Sucrosomial® iron. At 3-months follow up, Hb, iron, and ferritin results increased, with a resolution of iron-deficiency status.

Conclusions
This case report showed that the use of iron supplementation with oral Sucrosomial® iron (CardioSideral®) in a patient undergoing complex percutaneous procedures, as TAVR, appeared to be fundamental. In patients with AS, iron deficiency and anemia have high prevalence and can severely impact the outcome. Preventive, periprocedural, and long-term therapy with iron supplementation may be useful to improve anemia, clinical status and outcome. Non-anemic but iron-deficient patients with AS would probably also benefit from iron supplementation. Future studies are needed to further explore the potential benefit of Sucrosomial® iron in patients with AS undergoing TAVR.
Sucrosomial® iron supplementation can be a useful support treatment in patients with heart failure and anemia

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Introduction

Many studies have shown that anemia is an independent risk factor for death and rehospitalization in patients with heart failure (HF) [1] with an increased risk of undergoing cardiac transplantation [2]. Several factors can lead to anemia and it has been shown that iron deficiency is the most common cause of anemia in advanced HF patients. The prevalence of iron deficiency in patients with HF ranges from 30 to 50% independently of anemia [3,4]. The European Society of Cardiology (ESC) guidelines recommend systematic monitoring of iron parameters for all patients with HF [5]. Conventional iron supplements represent an important health problem. The effect of intravenous (IV) or conventional oral (PO) iron supplementation can be difficult to manage or may give side effects. Sucrosomial® iron (CardioSideral®, PharmaNutra S.p.A.) was found to be not inferior to intravenous iron supplementation in some set of patients.

Objectives

The aim of the present observational and single-center study was to evaluate the effects of Sucrosomial® iron supplementation in patients admitted to the hospital for heart failure.

Methods

Nine patients with anemia, aged from 64 to 92 years, with left ventricular dysfunction (EF 39%), were enrolled in the study. NYHA class was I–II in 6 and III–IV in 3 cases. The patients were adjusted for NYHA classes (I, II, III, IV), presenting iron-deficiency anemia (Hb < 13 g/dL for men and 12 g/dL for women with serum iron < 59 µg/dL) (World Health Organization (WHO) 2001).

According to our protocol, the patients received iron supplementation: Sucrosomial® iron (30 mg twice a day via oral administration – PharmaNutra, Pisa). Evaluated parameters were: hemoglobin, serum iron, ferritin, BNP (Brain natriuretic peptide), and CRP (C-reactive protein). Baseline values were compared to 1-month control. Pairwise comparison was performed with Wilcoxon test (p < 0.005 was considered as statistical significance). Data are reported as median value and quartiles.

Results

One-month results were associated with a significant improvement of hemoglobin, serum iron, and ferritin along with significant reduction of BNP and CRP (Table 1).

Conclusions

This preliminary study seems to support the hypothesis that treating anemia in patients with heart failure could be another tool to take into account. The small sample size is the main limitation of this study and surely further investigations in this sense are warranted.

References


Oral Sucrosomial® iron supplementation in patients underwent percutaneous coronary intervention: safety, efficacy and tolerability

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Introduction

Anemia is present in 15–30% of patients hospitalized because of acute coronary syndrome (ACS), with a further increase during hospitalization after myocardial revascularization with percutaneous coronary intervention (PCI) and on dual antiplatelet therapy (DAPT). At the best of our knowledge, the correlation between anemia and poor outcome is clarified and it is due to higher incidence of major adverse cardiovascular events at follow up. It is still unclear whether anemia is just another marker of severity of cardiovascular disease or a condition responsible for the increase in mortality and myocardial infarction.

Table 1. Results.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>1-month</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP (mg/L)</td>
<td>26 (11–68)</td>
<td>8.4 (2.5–15)</td>
<td>0.043</td>
</tr>
<tr>
<td>BNP</td>
<td>3245 (1675–7892)</td>
<td>345 (127–624)</td>
<td>0.010</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.3 (9.6–10.6)</td>
<td>11 (11–11.6)</td>
<td>0.008</td>
</tr>
<tr>
<td>Serum iron (mg/mL)</td>
<td>24 (17–37)</td>
<td>38 (29–100)</td>
<td>0.033</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
<td>32 (26–51)</td>
<td>67 (35–153)</td>
<td>0.012</td>
</tr>
</tbody>
</table>
Objectives
Objective of this study is to compare efficacy and tolerability of iron supplementation with Sucrosomial® iron (Cardiosideral®-Pharmanutra S.p.A) and ferrous sulfate in hospitalized patients with ACS underwent PCI on DAPT, since, it is well known that blood transfusion does not contribute to improve prognosis, but, instead, it is associated with a greater number of major adverse cardiovascular events.

Methods
We included in our analysis 50 patients admitted to Cardiology Department of Augusta between January and December 2016 and affected by ACS and iron-deficiency anemia, treated with PCI. Patients had 81 ± 6-year old, 4 had stage-3 chronic renal disease, 30 were diabetic. All patients had anemia at admission (Hb = 9 ± 1.5 g/dL), worsen during hospitalization, even if without evident bleeding (Table 1). All patients were treated with oral iron supplements and 3 patients underwent blood transfusion, because they were hemodynamically unstable. The patients were divided into two homogeneous groups: group A was supplemented with Sucrosomial® iron 30 mg/day (Cardiosideral® – Pharmanutra S.p.A), while group B with ferrous sulfate 105 mg/day. In all patients, iron supplementation was prescribed at discharge for 3 months and all patients underwent cardiology evaluation: EKG, blood tests, such as blood count, serum creatinine, serum iron, ferritin, and transferrin performed, after 1 and 3 months.

Results
In both groups, an increase of hemoglobin level of 1 g/dL was obtained in about 4 weeks, with a further increase of 1 g/dL after 3 months. In group A, iron therapy was well tolerated in all patients (Table 2); in group B, 8 patients reported side effects (3 gastralgia, 5 diarrhea).

Conclusions
Iron supplementation with Sucrosomial® iron is safe, well tolerated and achieves a similar effect with 1/3 of the dose, representing an effective and reliable therapeutic option in patients with ACS and iron deficiency. The levels of serum iron and hemoglobin appear to be reliable parameters in the follow up to guide the duration of therapy.

Role of anemia and iron supplementation on in-hospital and long-term prognosis and on management of elderly STEMI patients. a single-center experience
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Introduction
Elderly patients admitted with diagnosis of S-T elevation myocardial infarction (STEMI) presented a very high risk for both in-hospital and long-term morbidity and mortality. Comorbidities play a key role in influencing prognosis and in particular anemia (preexistent or acquired) is a more and more emerging clinical element able to influence morbidity, mortality and clinical management. Nevertheless, the role of anemia in elderly STEMI patients is not completely clarified.

Objectives
Aim of the present study is to observe the role of anemia and its therapy by iron supplementation in a very-old population of acute STEMI patients followed for 1 year after hospital admission for the above event.

Methods
We considered all STEMI patients admitted in the Coronary Care Unit of the Policlinico of Milan in 2015–2016 and we selected only people aged >80-years old (n = 150). Hemoglobin (Hb, g/dL) values were considered at admission (T0), at hospital discharge (T1) and after (approximately) 6 month (T2). In-hospital and 1-year mortality, treatment by primary coronary angioplasty (PCI), major bleedings (Thrombolysis in Myocardial Infarction -TIMI criteria), need of transfusion, double antiplatelet therapy (DAPT) discontinuation were considered and compared between groups of patients with anemia (group A, Hb <13.5 for men and <12 for women at T1) and without (group NA). Type of iron supplementation (Sucrosomial® or not) and its tolerability (expressed as % of discontinuation) were considered only for group A. Data were expressed as mean ±SD or % values.

Results
26 patients (group A – 17%) presented anemia at T0 (66% were women), TIMI major in-hospital bleeding were observed in 7 of
Introduction

In the Cardiac Rehabilitation Unit, the percentage of hospitalized patients having anemia is equal to 20–30% of the observed population if a red cells number <3,500,000/mm$^3$ is considered as a criterion for diagnosis, while it is equal to about 50% if considering an hemoglobin level <11 g/100 mL.

Objectives

Evaluate effectiveness and time of action using Sucrosomial® iron compared to other iron-based constituents taken orally and entered into the hospital formulary availability in a cohort of patients referred to rehabilitation and preventive cardiological population.

Methods

The study design provides randomization of a total of 100 patients divided into two consecutive arms by random selection. Each patient pertaining to cardiac rehabilitation or preventive cardiology with hemoglobin of between 8.5 g/dL (9.0 g/dL in ischemic patients) and 11.9 g/dL (excluding patients with active peptic ulcer, erosive gastritis, ulcerative colitis and other inflammatory bowel disease or malabsorption diagnoses) was supplemented either with ferrous sulfate (Ferrograd) 1 table/day corresponding to 105 mg of elemental iron or Sucrosomial® iron (Cardiosideral®) 1 capsule twice a day, corresponding to 60 mg of elemental iron or 2 capsules twice a day in case of Hb lower than 10.5 g/dL. The study was performed to evaluate the patient blood count, serum iron, ferritin, transferrin, and reticulocytes percentage at hospital admission time (basal), at 15 days corresponding to the end of the first rehabilitation cycle (mid-term) and at 30 days after beginning of oral therapy.

Preliminary Results

We have preliminary results on 16 patients with a comparable age (Figure 1(a)) and with a comparable baseline hemoglobin (9.5 vs. 9.2 g/dL (Figure 1(b))). These patients completed the first cycle of rehabilitation and the first 14 days of treatment. The mid-term results did not show a significant difference (10.1 vs. 9.9 g/dL) in hemoglobin recovery. Moreover, transferrin levels were significantly higher, despite the baseline, in the ferrous sulfate (174 vs. 194 mg/dL) (Figure 1(c)) even though they were not pathological. Ferritin values, instead, were high but with greater stability in the 14-day treatment of patients treated with Sucrosomial® iron (503–408 vs. 603–875 ng/mL) (Figure 1(d)). Two patients (33%) left the oral ferrous sulfate arm about one week after the beginning of treatment for gastrointestinal disorders.

Conclusions

In elderly STEMI patients: (1) anemia at hospital admission influences in-hospital major bleedings and need of blood transfusions, (2) anemia at hospital discharge seems to affect DAPT discontinuation and long-term mortality, (3) use of Sucrosomial® iron reduces probability of discontinuation of long-term iron supplementation therapy.

Hospital protocol for evaluating effectiveness and timing of use of Sucrosomial® iron in cardiac rehabilitation departments

Leopoldo Pagliani, Seena Padayattil, Lucia Marigo, Antonella Gesmundo, Gabriele Luzza, Laura Groppo, Roberta Pascon, Gabriela Ottiman, Silena Catto, Alban Liška, Ada Della Libera and Francesco Perissinotto

Cardiovascular Prevention Unit and Cardiology Department Motta di Livenza, High Specialization Rehabilitation Hospital

Table 1. In-hospital prevalence of gender, mortality, TIMI major bleedings, and blood transfusion in A and NA group.

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>26</td>
<td>124</td>
</tr>
<tr>
<td>Women (%)</td>
<td>17 (66%)</td>
<td>47 (38%)</td>
</tr>
<tr>
<td>Death</td>
<td>5 (18%)</td>
<td>21 (17%)</td>
</tr>
<tr>
<td>TIMI major bleedings</td>
<td>7 (27%)*</td>
<td>10 (8%)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>5 (19%)*</td>
<td>7 (5%)</td>
</tr>
</tbody>
</table>

*p < 0.05 vs. NA

Table 2. Post-discharge prevalence of gender, 1-year mortality, TIMI major bleedings, and DAPT discontinuation in A and NA group.

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
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<td>21 (17%)</td>
</tr>
<tr>
<td>TIMI major bleedings</td>
<td>7 (27%)*</td>
<td>10 (8%)</td>
</tr>
<tr>
<td>DAPT discontinuation</td>
<td>8 (30%)*</td>
<td>8 (10%)</td>
</tr>
</tbody>
</table>

*p < 0.05 vs. NA

them and 5 required blood transfusion (27 and 19%, respectively) whereas 10 patients (group NA) did not present anemia (8% with 5% required blood transfusion) (Table 1). In-hospital mortality was similar between anemic and non-anemic (18 vs. 17%) (Table 1). Twenty-five patients presented mild anemia at T1 (16% in group A) and mean age was similar to group NA (years, 86 ± 4 vs. 85 ± 5, ns). In group A, 7 patients (28%) died during follow up whereas 15 (14%) died in group NA. The number of patients treated with primary percutaneous transluminal coronary angioplasty (PTCA) (31% in group A vs. 39% in group NA, ns) was similar. Early DAPT discontinuation occurred in 8 patients of group A and in 10 of group NA (33 vs. 13%, respectively, p < 0.001) (Table 2). In group A, 19 patients were discharged with indication to long-term iron supplementation therapy, 8 of them with Sucrosomial® iron 30 mg/day (Cardiosideral®). Incidence of discontinuation of supplementation therapy was 12% (1 patients) for Sucrosomial® iron vs. 45% (5 patients, p < 0.001) for non-Sucrosomial® iron.

Conclusions

In elderly STEMI patients: (1) anemia at hospital admission influences in-hospital major bleedings and need of blood transfusions, (2) anemia at hospital discharge seems to affect DAPT discontinuation and long-term mortality, (3) use of Sucrosomial® iron reduces probability of discontinuation of long-term iron supplementation therapy.
preparations are better adapted to the clinical reality of cardiac patients. It remains solid the assumption of how the Sucrosomial® iron are better tolerated without loss of effectiveness. Long-term assessment also for serum iron values, transferrin, ferritin, and reticulocytes percentages will complete the analysis giving fundamental inspiration also to understand the real homeostatic mechanisms changed by different molecules.

**Effect of Sucrosomial® iron in early time after cardiac surgery**

Dario Buioni, Saveno Nardella and Daniele Maselli
Department of Cardiac Surgery. Casa di Cura Villa Sant’Anna Catanzaro

**Introduction**

Anemia is common in patients with cardiac disease and also in those undergoing cardiac surgery. Postoperative anemia frequently persists for months after Coronary Artery Bypass Graft (CABG) surgery and is associated with an impaired outcome also in the rehabilitation program. Iron therapy has been variably employed by medical centers over the years but can be difficult if intravenously (IV) administered or it can give side effects if orally supplemented. Sucrosomial® Iron (Cardiosideral® – Pharmanutra S.p.A) is known to be not inferior to intravenous iron in different patient sets.

**Objectives**

The aim of the study was to evaluate the efficacy of Sucrosomial® Iron supplementation up to 4 capsules (cps) in the correction of post cardiac surgery anemia in early postoperative period in order to avoid blood transfusions. Side effects were also monitored.

**Methods**

We analyzed 22 patients (median age 59 ± 3): 10 had diabetes, 18 hypertensive, 14 coronary artery disease (CAD), 4 left ventricular dysfunction, 4 CKD. 12 underwent CABG, 2 CABG + VALVES, 2 WHEAT, 6 VALVES. The study included the use of up to 4 cps of Cardiosideral® in the early postoperative period either during hospital stay after intensive care unit (ICU) or rehabilitation period. The values considered were: serum iron, complete blood count, blood transfusion, 6MWT and serum creatinine at admission, postoperative day (POD) 0, POD3, discharge and rehabilitation. The treatment last 20 days and considered the early postoperative and rehabilitation period.

**Results**

Results are reported in the table below. After an initial reduction in Hb level, it is evident at discharge an increased values for Hb, serum iron. No patient required blood transfusion.
Conclusions
The use of 4 cps of Cardiosideral® was well tolerated by patients, representing a potential alternative to the use of intravenous iron. The number of patients and the need for a greater follow up are the main limitations of this study.

Benefits of Sucrosomial® oral iron in patients with heart disease and concomitant iron-deficiency anemia
Giuseppe Putortì
cardiology specialist ASP 5 reggio Calabria

Introduction
Patients with hypertensive heart disease, treated with antihypertensive medications (ACE inhibitors or sartans), can sometimes have symptoms such as fatigue, shortness of breath and palpitations, often due to iron deficiency or iron-deficiency anemia. The treatment of this condition with the conventional oral iron formulations may be difficult, because accompanied by a poor compliance and side effects. Sucrosomial® pyrophosphate iron (CARDIOSIDERAL®) is a new oral iron technology, which does not present these side effects and showed increased duodenal iron absorption and thus, it may be useful in the correction of these forms of anemia in cardiac patient.

Objectives
Aim of this study is to assess the benefits of Sucrosomial® iron (CARDIOSIDERAL®) in patients with iron-deficiency anemia and concomitant heart disease, in terms of increase in hemoglobin (Hb) levels, serum iron and reduction of symptoms such as fatigue, shortness of breath and palpitations.

Methods
Eight patients aged 58 ± 10 years with iron-deficiency anemia and hypertensive heart disease were enrolled. They were already receiving antihypertensive medications (ACE inhibitors or sartans). Symptoms such as fatigue, shortness of breath and palpitations were taken into account. They were carried out blood tests (complete blood count (CBC), serum iron, transferrin and ferritin) and instrumental examinations (ECG and echocardiography), before and after treatment for 5 weeks with Sucrosomial® iron 60 mg/day (corresponding to 2 capsules/day). Patients with diabetes, dysthyroid, heart failure (NYHA class 2/3/4), and treated with beta-blockers or calcium channel blockers were excluded from the study.

The values at the first assessment are reported in Table 1.

Results
All patients completed the treatment, no side effects were registered and all values examined after treatment for 5 weeks improved (Table 2).

Conclusions
This small work showed that iron-deficiency anemia correction in patients with heart disease is important to improve the health of these individuals and to reduce symptoms such as fatigue, shortness of breath and palpitations. Sucrosomial® pyrophosphate iron (CARDIOSIDERAL®) could be useful for this purpose as it increased blood values.

Table 1. Patients’ characteristics.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Symptoms</th>
<th>ECG</th>
<th>Echo</th>
<th>CBC</th>
<th>Serum iron (µg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>58 ± 10</td>
<td>8 palpitations 8 fatigue 4 shortness of breath</td>
<td>6 sinus rhythm 90 ± 5 b/min</td>
<td>8 with diastolic dysfunction of the left ventricle; 2 with mild mitral regurgitation</td>
<td>Red blood Cells 4,000,000 ± 100,000/mL; Hb levels 10.5 ± 0.5 g/dL</td>
<td>35 ± 10</td>
</tr>
</tbody>
</table>

Table 2. Results.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Symptoms</th>
<th>ECG</th>
<th>Echo</th>
<th>CBC</th>
<th>Serum iron (µg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>58 ± 10</td>
<td>0 palpitations 2 fatigue 0 shortness of breath</td>
<td>8 sinus rhythm 75 ± 5 b/min</td>
<td>8 with diastolic dysfunction of the left ventricle; 2 with mild mitral regurgitation</td>
<td>Red blood Cells 4,100,000 ± 100,000/mL; Hb levels 11.5 ± 0.5 g/dL</td>
<td>50 ± 10</td>
</tr>
</tbody>
</table>
remarkable efficiency, in fact, it is for us the current reference point for the control of multifactorial anemia. Before the use of Sucrosomial® Iron (Sideral® Forte), the occurrence of side effects could limit the use of oral iron therapy, in particular due to toxicity, heartburn, and constipation/diarrhea, smell or metallic taste, which they occurred in 60% of patients.

Objectives
To evaluate the response, in terms of efficacy and tolerability, of Sucrosomial® Iron (Sideral® Forte) treatment in a population of patients with multifactorial anemia.

Methods
We performed an observational study on 4 patients (1 male and 3 females) referred to our Outpatient Hematology Clinic for anemia. The male was 89 years and the average age of females was 39.6 years. Patient 1 was seventh month pregnant and was suffering from dysphagia toward solid food due to Schizophrenia and she was followed by the Mental Health Service of her city. Her blood count at the first visit showed a white blood cells (WBC) count of 5600 cell/µl, red blood cells (RBC) count of 2,900,000 cell/µl, a hemoglobin (Hb) of 87 g/l, a mean corpuscular volume (MCV) of 70 fl, a platelet (PLT) count of 255,000 cell/µl, serum iron of 15 µg/dL and ferritin of 10 ng/mL. From her clinical history, she had poor nutrition (only chopped food and/or liquids) as she had dysphagia to solid food from young age, she had digestion and regular bowel function. Patient 2 was a female suffering from breast cancer (radio-treated) and menometrorrhagia and her clinical history reported heavy periods, varied diet, stable weight, treated with proton pump inhibitors for reflux esophagitis and constipation. Her blood count showed a WBC count of 6,500 cell/µl, an RBC count of 3,210,000 cell/µl, an Hb of 87 g/l, an MCV of 64 fl, a PLT count of 322,000 cells/µl, serum iron equal to 6 µg/dL and ferritin of 5 ng/mL. Patient 3 was eight-week pregnant and she had a short menstrual cycle (every 25 days) abundant in quantity. She was blood donor from 2008 to 2010 and she reported dyspepsia, regular bowel function, but no rectorrhagia or melena. Her WBC count was 7300 cell/µl, RBC was 3,300,000 cell/µl, Hb was 97 g/l, MCV was 76 fl, PLT count was 235,000 cell/µl, serum iron was equal to 35 µg/dL and ferritin was 1.7%. Patient 4 was a male suffering from B cell chronic lymphocytic leukemia, duodenal ulcer, hemorrhoids, a left hemi-lymphocytic leukemia, duodenal ulcer, hemorrhoids, a left hemi-

Results
Results are reported in Table 1. All patients followed Sucrosomial® Iron (Sideral® Forte) therapy. The observational period of 2 months was completed by all patients without interruption or modifications. After 15 days of therapy with Sucrosomial® Iron, all patients did not report any side effects, typical of conventional iron therapy (diarrhea, vomiting, nausea, constipation and abdominal pain). Patient 1 had the following blood count: WBC count = 7300 cell/µl, RBC count = 3,130,000 cell/µl, Hb = 98 g/l, MCV = 79 fl, PLT count = 257,000 cell/µl, serum iron was 30 µg/dL, ferritin was 45 ng/mL and reticulocytes was 1.2%. Patient 2 had the following blood count: WBC count = 7235 cell/µl, RBC count = 4,325,000 cell/µl, Hb = 99 g/l, MCV = 78 fl, PLT count = 315,000 cell/µl, serum iron was equal to 20 µg/dL, ferritin was 30 ng/mL, and reticulocytes was 1.8%. Patient 3 had WBC count = 8300 cell/µl, RBC count = 3,630,000 cell/µl, Hb = 108 g/l, MCV = 82 fl, PLT count = 247,000 cell/µl, serum iron was 60 µg/dL, ferritin was 55 ng/mL, and reticulocytes was 1.7%. Patient 4 had WBC count = 23,500 cell/µl (W72%, many Gumprecht shadows), RBC count = 3,500,000 cell/µl, Hb = 106 g/l, MCV = 98.6 fl, PLT count = 104,000 cell/µl, serum iron 40 µg/dL, ferritin of 35 ng/mL and reticulocytes 1.5%.

After 60 days of martial therapy with Sucrosomial® Iron, all 4 patients did not report any side effect. Patient 1 reported the following blood count: WBC count = 8350 cell/µl, RBC

<table>
<thead>
<tr>
<th>Table 1. Single results per patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters</td>
</tr>
<tr>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Patient 1 (F, 37 years)</td>
</tr>
<tr>
<td>WBC</td>
</tr>
<tr>
<td>RBC</td>
</tr>
<tr>
<td>Hb (g/l)</td>
</tr>
<tr>
<td>MCV (fl)</td>
</tr>
<tr>
<td>PLT</td>
</tr>
<tr>
<td>Serum Iron (µg/dL)</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
</tr>
<tr>
<td>Reticulocytes (%)</td>
</tr>
<tr>
<td>Patient 2 (F, 45 years)</td>
</tr>
<tr>
<td>WBC</td>
</tr>
<tr>
<td>RBC</td>
</tr>
<tr>
<td>Hb (g/l)</td>
</tr>
<tr>
<td>MCV (fl)</td>
</tr>
<tr>
<td>PLT</td>
</tr>
<tr>
<td>Serum Iron (µg/dL)</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
</tr>
<tr>
<td>Reticulocytes (%)</td>
</tr>
<tr>
<td>Patient 3 (F, 37 years)</td>
</tr>
<tr>
<td>WBC</td>
</tr>
<tr>
<td>RBC</td>
</tr>
<tr>
<td>Hb (g/l)</td>
</tr>
<tr>
<td>MCV (fl)</td>
</tr>
<tr>
<td>PLT</td>
</tr>
<tr>
<td>Serum Iron (µg/dL)</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
</tr>
<tr>
<td>Reticulocytes (%)</td>
</tr>
<tr>
<td>Patient 4 (M, 89 years)</td>
</tr>
<tr>
<td>WBC</td>
</tr>
<tr>
<td>RBC</td>
</tr>
<tr>
<td>Hb (g/l)</td>
</tr>
<tr>
<td>MCV (fl)</td>
</tr>
<tr>
<td>PLT</td>
</tr>
<tr>
<td>Serum Iron (µg/dL)</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
</tr>
<tr>
<td>Reticulocytes (%)</td>
</tr>
</tbody>
</table>

We began to administer to our patients the following regimen of Sucrosomial® Iron (Sideral® Forte) 30 mg) for 10 days: 2 capsules at 8:00, 2 at 12:00, 2 at 15:00, 2 at 19:00, and 2 capsules at 23:00. After this period, patients were instructed to take 2 capsules in the morning and 2 capsules in the evening for the remaining two months.
count = 4,885,000 cell/μl, Hb = 128 g/l, MCV = 84 fl, PLT count = 265,000 cell/μl, serum iron was 80 μg/dL, ferritin 90 ng/mL, and reticulocytes 2.4%. Patient 2 had the following blood counts: WBC count = 8845 cell/μl, RBC count = 265,000 cell/μl, serum iron was equal to 88 μg/dL, ferritin was 65 μg/dL, and reticulocytes was 2.6%. Patient 3 had: WBC count = 18,300 cell/μl (W 67%, many Gumprecht shadows), RBC count = 4,000,230 cell/μl, Hb = 119 g/l, MCV = 102 fl, PLT count = 99,000 cell/μl, serum iron of 65 μg/dL, ferritin of 105 ng/mL and reticulocytes of 2.5%.

Conclusions

In this study, the use of iron therapy with Sucrosomial® Iron (Sideral® Forte) appeared to be effective and well tolerated for the treatment of multifactorial anemia. The protocol studied readily resumed blood counts of our patients without causing any side effects.


The usefulness of Sucrosomial® iron supplementation in severe iron-deficiency anemia associated with multiple chronic comorbidities: a case report

Lucia Calcabrini, Alessandro Saturni and Elena Giannini
U.O. Internal Medicine, Macerata General Hospital – Italy

Introduction

In June 2014, a woman of 47 years old with a recent onset of wrist and ankle arthritis had a medical history characterized by iron-deficiency anemia, Hashimoto thyroiditis and uterine fibromatosis. The anemia was microcytic, TSH was normal, and rheumatoid factor was absent. She had elevated Ab-CCP, APCA and SSA, elevated VES, PCR and fecal calprotectin. Moreover, she had vitamin B12 deficiency. Hemoglobin was 8.9 g/dL, MCV 79 fl and ferritin 4.3 ng/mL. The patient had taken daily dose of iron sulfate and ascorbic acid (525/500 mg) for six months.

<table>
<thead>
<tr>
<th>Iron sulfate (525 mg/day)</th>
<th>Sucrosomial® Iron (60 mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb increase (after 6 months)</td>
<td>+0.3 g/dL</td>
</tr>
<tr>
<td>Ferritin level (after 6 months)</td>
<td>9.4 ng/mL</td>
</tr>
<tr>
<td>Target Hb (12 g/dL) Side effects</td>
<td>Not reached Dyspepsia, vague abdominal pain and diarrhea</td>
</tr>
</tbody>
</table>

Table 1. Results.

Objectives

Our goal was to manage the arthritis and to treat iron-deficiency anemia.

Methods

Wrist and ankle X-ray showed multiple articular erosions. Endoscopic examination of upper and lower gastrointestinal tract showed chronic inflammation of gastric mucosa, no bowel inflammatory disease, no cancer, and no other intestinal lesion. Gynecologic examination confirmed uterine fibromatosis. The diagnosis was rheumatoid arthritis associated with autoimmune gastritis, Hashimoto thyroiditis, and uterine fibromatosis. The therapy was Methotrexate 7.5 mg/week, prednisone 25 mg/day, 15 mg/day of calcium folinate, B12 vitamin 5000 UI/week, iron sulfate and ascorbic acid (525/500 mg/day). After 6 months hemoglobin was 9.2 g/dL and ferritin 9.4 ng/mL and the patient reported dyspepsia, vague abdominal pain and diarrhea. Thus, iron sulfate was suspended and ascorbic acid and Sucrosomial® iron (30 mg) twice daily with ascorbic acid was started.

Results

After 6 months, the hemoglobin was 9.2 g/dL and ferritin 9.4 ng/mL; the patient reported dyspepsia, vague abdominal pain and diarrhea. We stopped iron sulfate and ascorbic acid and we started Sucrosomial® Iron (Sideral® Forte) 2cps/day with ascorbic acid. After 6 months of therapy, the hemoglobin was 12.1 g/dL, MCV 89 fl and ferritin 65 ng/mL (Table 1).

Conclusions

Despite multiple comorbidities, Sucrosomial® iron supplementation had superior efficacy in restoring hemoglobin and ferritin levels in this patient. The patient did not report any side effects; the therapy was well tolerated and did not required interruption.

Three different conditions of iron-deficiency anemia treated with oral sucrosomial® iron therapy

Gino Svanera
Hematology Unit, PO San Giuliano, ASL NA 2 NORD, Naples Italy
Introduction

Reported here are three clinical cases of iron-deficiency anemia treated with oral Sucrosomial® iron therapy. Sucrosomial® iron is a new formulation with high bioavailability and a low incidence of side effects and it is highly tolerated.

Case studies

(1) a 31-year-old woman affected by celiac disease and thalassemia trait with hemoglobin value of 8.2 g/dL and ferritin serum level prior to therapy of 1.5 mcg/L was complaining asthenia, fatigue, drowsiness, hair loss, and diarrhea. After 4 months of therapy with oral iron, hemoglobin improved from Hb of 8.2 g/dL to 12.3 g/dL with resolution of all symptoms and ferritin serum level after therapy showed a significant increase (123 mcg/L).

(2) a 51-year-old obese woman, who underwent gastric bypass, after surgery had hemoglobin level of 7.9 g/dL due to severe bleeding, but the patient refused intravenous iron therapy. After 4 months of oral iron therapy, her hemoglobin increased from 7.9 g/dL to 11.3 g/dL and her ferritin serum level improved from 2 mcg/L to 89 mcg/L.

(3) a Jehovah’s Witness man with hemorrhoidal disease with hemoglobin levels equal to 5.9 g/dL and ferritin serum level 1.4 mcg/L refused blood transfusion with leukocyte-depleted red blood cells. He underwent iron infusion therapy, but he had a severe allergic reaction; therefore, he was started on oral iron therapy as Sucrosomial® iron (Sideral® Forte, 1 cps/day). After 4 months, his hemoglobin increased significantly (Hb 10.2 g/dL).

Conclusion

In conclusion, my experience with oral Sucrosomial® iron suggests it could be effective to correct anemia with a low rate of adverse events.