Experience with a High-Dose Oral Iron Sulfate and Gluconate in Peritoneal Dialysis Patients

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Introduction

Iron deficiency is an important problem for patients on peritoneal dialysis. In PD patients iron absorption is diminished due to interreaction with other drugs such as phosphate binders or H2 blockers and edema of the gut .

Blood loss for laboratory investigations is about 30-60 ml blood/per month, or 900 mg of elemental iron on average[14,15]. Occult gastrointestinal losses occurred in about 7% PD patients. Reason for iron deficiency is improved erythropoesis following initiation of peritoneal dialysis treatment. Increased iron utilization is due to removal of toxins, especially middle molecules that are bone-marrow inhibitors resulting in absolute or relative iron deficiency. Oral iron alone is insufficient for HD patients[1,3,4], but for PD patients that is more practicable. This form of iron therapy may be adequate in patients not receiving erythropoietin, but some authors preferred oral iron in erythropoietin – treated peritoneal dialysis patient[10,11]. Iron overload may occure with recurrent intravenous iron dosing and may be associated with increased risk of bacterial infection and tissue iron deposition[5,9]. Noncompliance to oral iron supplementation is described in up to 32 % of cases, mainly because of gastrointestinal side effects[2]. Patients who are prescribed oral iron tablets, two or three times per day usually are noncompliant.

Patients and Methods

Twenty nine patients on CAPD were included in the study. The causes of chronic renal failure were the fololowing: noninsulin – dependant diabetes mellitus in 8 (27,58%) patients, insulin dependant diabetes mellitus in 3 (10,34%) patients , hypertensive glomerulosclerosis in 10 (34,48%), autosomal dominant polycystic kidney disease in 2 (6,89%), vasculitis in 1 (3,44%) chronic glomerulonephritis in 2 (6,89%), chronic pyelonephritis in 3 (10,34%) cases.

None of patients had received transfusion within 1 month prior the study and intramuscular or intravenous iron two weeks before test. Six patients were receiving erythropoietin. Patients who had receiving H2 blockers and phosphate binders were asked to stop it 24 hours before the test. Patient who had receiving oral iron were asked to stop it 7 days before the test and don't to eat meat one day before the test. On the day of the test 4 tablets of iron sulfate (Ferrogradumet) corresponding to 105 mg elemental iron were given orally at 7.oo h. Patients were asked to have an empty stomach and don't to eat during the test Blood samples for measurement of serum iron and TIBC levels were taken at baseline as well as 2, 4 and 8 hours after that. Blood samples for serum feritin were colected at baseline.

Test was repeted using VIII drinkable ampoules of iron gluconate (Tot hema- containing 50 mg elemental iron per ampoule) 7 days after.

Patients with serum feritin level less than 100 ug/l or with TSAT less than 20 % considered iron depleted. Patients with serum feritin level of more than 100 ug/l and TSAT 20% considered iron repleted.

Results are presented as mean values ± standard deviation (SD). For comparison between iron values after 2,4 and 8 hours during the test following intake of ferous sulfate and ferous gluconate a two tailled t-test was performed. Correlation coefficient was used to invastigate the association between iron absorption and serum iron level, serum feritin and TIBC. All tests are two-sided. A p value less than 0,05 considered significant.

Results

Comparing serum iron 2 hours after intake of 4 tablets of ferous sulfate and 2 hours after intake of ferous gluconate we found significant difference between the two groups. After 4 hours following oral intake of ferous sulfate and ferous gluconate difference was significant, but we found no significant difference after 8 hours.

Maximal level of serum iron after intake of 4 tablets of ferous sulfate one patient /3,44%/ reached after 2 hours, 17 patients /58,62%/ after 4 hours and 11 patients (37,935%) after 8 hours. After intake of VIII ampoules of ferous gluconate maximal level of serum iron 15 (51,72%) patients reached after 2 hours, 13 (44,82%) reached after 4 hours and 1 (3,44%) after 8 hours. Maximal increase in serum iron after intake of 400 mg ferous sulfate was113,51 % ± 103,37% versus 183,87 ± 137,38% after intake of 400 mg ferous gluconate.

Maximal increase in serum iron was significantly different between the two groups.

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Table 1.

	Fe F	Fe T
0	13,64±6,33	13,10±6,56
2	20,13±7,42	28,36±7,12
4	24,47±9,57	29,20±9,62
8	22,01±10,70	22,98±8,90
p2/0	<0,05	<0,01
p4/0	<0,01	<0,01
p8/0	<0,05	<0,05
p2/2	<0,01	
p4/4	<0,05	
P8/8	>0,05	

Only baseline serum iron level correlated significantly to the maximal increase in serum iron during the test. Between baseline serum feritin, TSAT and maximal increase in serum iron we found negative corralation, but it was not significant. Side effects after intake of ferous sulfate occured in 7 (24,13%) - nausea and vomiting in 4 (13,79%). During the test with ferous gliconate side effects registered only in 4 (13,79%) patients - nausea. There were 6 patients with baseline serum ferutin less than 100 ug/ml or TSAT less than 20%. Maximal increase in serum iron after intake of iron sulfate was 257,33% ± 223,68% in this group versus 94,75% ± 66,37% in other 23 patients. After intake og ferous gluconate maximal increase in serum iron was 364,10% ± 250,55% in iron depleted patients versus 156,04% ± 86,44% in iron repleted.

Discussion

PD patients have higher hemoglobin levels, a lower transfusion rate and lower erythropoietin

doses than hemodialysis patients. Reason for a lower incidence of iron deficiency may be the lower extent of iron loss. In our group of patients absolute iron deficiency was present only in 3/10,34%/ cases, and functional iron deficiency in other 2 /6,89%/ cases. In PD patients serum feritin levels are higher than in patients with renal insufficiency not receiving dialysis, esspecialy in cases of inflammation. Reason for iron deficiency in PD patients not receiving erythropoietin may be the improved erythropoesis after starting of peritoneal dialysis treatment. Erythropoietin treatment causes an increase in iron demand for erythropoesis wich can exceed the ability of of realising iron for erythropoesis[6,16,17]. Studies on hemodialysis patients showed both adequate or reduced iron resorption. Milman et al.[18] found that compared with healthy controls, the resorption rate was equal in peritoneal dialysis patients with reduced iron stores and significantly lower in those patients with normal iron content. Domoto and Martin[12] applied low dose of ferrous sulfate and ferrous fumarate to CAPD patients and control subjects. After two hours, there was only a significant increase of serum iron levels in the control subjects. Dittrich at al.[19] invastigeted absorption of high dose and low dose of ferrous sulfate in PD patient and helthy control subjects and found that there was no significant difference in iron absorbtion between the two groups. As known for healthy subjects, iron absorption was significantly better in PD patients with absolute iron deficiency compared to those with functional iron deficiency and iron repleted. They showes the lowest iron absorption, indicating that a high dose of oral iron did not overwhelm the abillity of the bowel to reject unneeded iron. Increasing oral iron dose from 100 to 400 mg was followed by a better response in a group of PD patients. A number of studies [7,8,13,] following hemoglobin levels, erythropoietin dose and iron stores during oral iron supplementation concluded that this form of therapy may be adequate in PD patients receiving and not receiving erythropoietin.The iron of food occures in a number of forms, of wich iron present in heme compounds and inorganic iron are the most important. Our study showed a significant increase in serum iron levels after intake 400 mg of ferous sulfate and ferous gliconate, but apsorption of ferous gluconate is signifficantly higher after 2 and 4 hours. Patients with baseline serum feritin level of less than 100 ug/ml and TSAT 20% showed an increase in serum iron after oral intake of ferous sulfate 257,33% ± 223,68% versus 364,10% ± 250,55% after intake of ferous gluconate. It is in agreement with the results of Dittrich et all[19]. Patients with baseline serum feritin of more than 100 ug/ml and TSAT 20% showed maximal increase in serum iron of more than 100% /that is usually detectable in healthy subjects/ only after intake of ferous gluconate (156,04% ± 86,44%%). Iron absorbtion is enhanced by including meat into diet, an affect atributed to the formation of soluble complexes of iron with amino acids. Six (20,68%) patients showed an increase in serum iron of more than 300% and in 15 (51,72%) patients serum iron increased between 100% and 300% .In 8 (27,58%) patients was an increase of less than 100% noted if iron gluconate is used. If iron sulfate is used only 2 (6,89%) patients showed an increase of more than 300%, 14 /48,27%/ patients between 100% and 300% and 13 (44,82%) patients of less than 100%. We found a negative statistically significant correlation between iron absorption and serum iron and negative not significant correlation between iron absorption and serum feritin and TSAT. This is not in contrast with other studies[19], but correlation between iron absorption and feritin/TSAT have not been significant. This may have been due to other factors influencing feritin and TSAT values. Feritin is relatively stable, but it is an acute phase reactant and can increase with infection.The percentage transferin saturation with iron varies with nutritioinal status and serum albumin level, factors we have not evaluated this time.

We can conclude that high dose of oral iron is well absorbed and tolerated in CAPD patients. Iron gluconate is better absorbed and tolerated than iron sulfate and we recommend it for oral supplementation in PD patients.

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