SUPPLEMENTATION WITH SUCROSOMIAL® IRON AND FOLIC ACID REDUCING IL-6 LEVELS IN HEALTHY TRAINED ATHLETES

Elisa Brilli [1], Tindaro Bongiovanni [2], Giulio Pasta [2] and Germano Tarantino [1]

[1] Pharmanutra S.p.A., Pisa Italy, [2] Parma calcio 1913, Parma, Italy

Introduction:

Interleukin-6 (IL-6) is the major cytokine produced under conditions of intense physical stress. Recent data have suggested that IL-6 is the main promoter of hepcidin, a liver produced hormone that plays a key role in iron metabolism. The inflammatory mediated increase of hepcidin ultimately result in rapid decreases in plasma iron concentrations. Thus, in such conditions commonly used oral iron supplements have lower absorption rate with unabsorbed iron leading to frequent gastrointestinal side effects. Sucrosomial® Iron represents an innovative formulation of oral ferric pyrophosphate carried by a phospholipid bilayer membrane plus a sucrose esters of fatty acid matrix, that provides gastro-resistance and allows the iron to be highly absorbed at the intestinal mucosae. Some data showed that Sucrosomial® Iron absorption does not seem to be affected by hepcidin levels. Recently has been demonstrated that Sucrosomial® Iron absorption doesnít induce any pro-oxidative effects and doesnít increase inflammatory markers (IL-6, Socs-3) after administration. Therefore, Sucrosomial® Iron could be taken in consideration in cases of inflammatory conditions and in professional athletes undergoing intense training and physical stress. Interestingly, it has previously been shown that short-term supplementation could have unfavorable effects on iron metabolism.

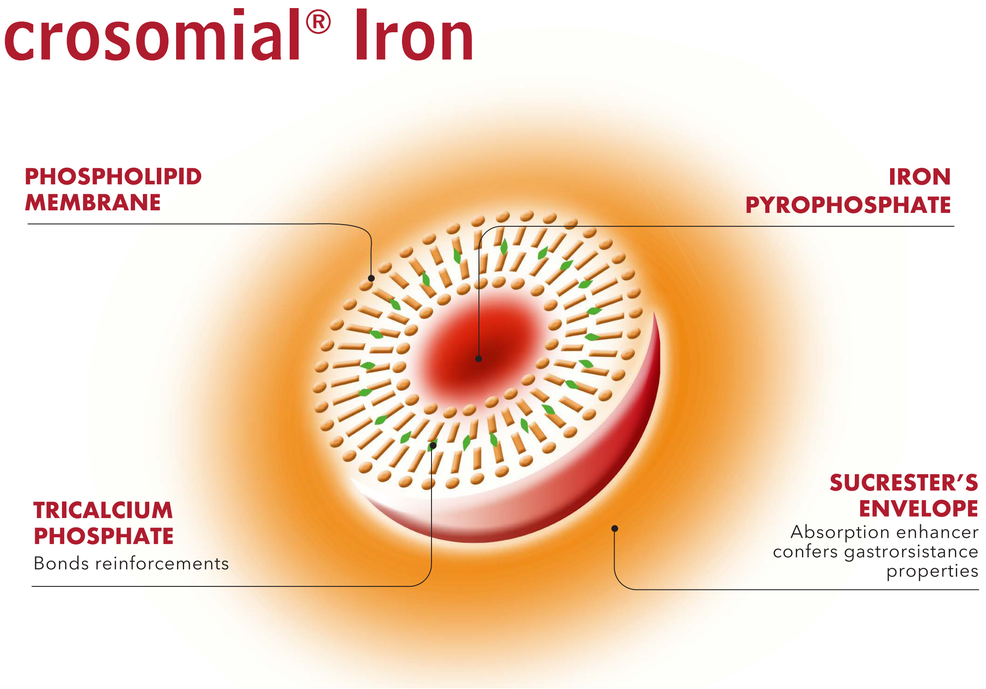
Materials and Methods:

Fifteen professional male athletes from an Italian national soccer team (meanstandard deviation age 28.81.3 years; height, 180.24.5 cm; fat mass, 7.170.9 kg; VO2max, 52.22.9 mL/kg1/min-1) were included in the study. Eleven accepted to assume SI supplement (21mg iron/day plus folate 400 mcg/day, Sideral® Folico, Pharmanutra S.p.A.), for 5 days a week, for a period of 18 weeks. Visit and blood sampling were repeated at 3 time points: T0 (pre-season sample) 14 weeks before iron and folate supplementation; T1 (in-season sample) 18 weeks after iron and folate supplementation. T2 (after-season sample) 10 weeks after the last dose of product supplementation. Iron and hematological parameters have been analyzed. Furthermore, C-reactive protein and IL-6 were determined.

Results:

Iron and biochemical parameters did not significantly change in both groups.Vitamin B12 and folate concentration increased significantly after Sideral® Folico supplementation while they did not change in untreated group (Table 1). IL-6 increased in untreated group (Figure 1), although such increase was not statistically significant. In the treated group a different trend was observed: in T1 IL-6 level was lower than at the baseline and turned again up to baseline value after season ended. Therefore, while IL-6 values were similar between groups at baseline, they became significantly higher in untreated compared to treated group immediately after the end treatment (T1). Interestingly, IL-6 levels were still greater in untreated than treated group longer after supplement interruption and at the end of playing season.

Sucrosomial® Iron



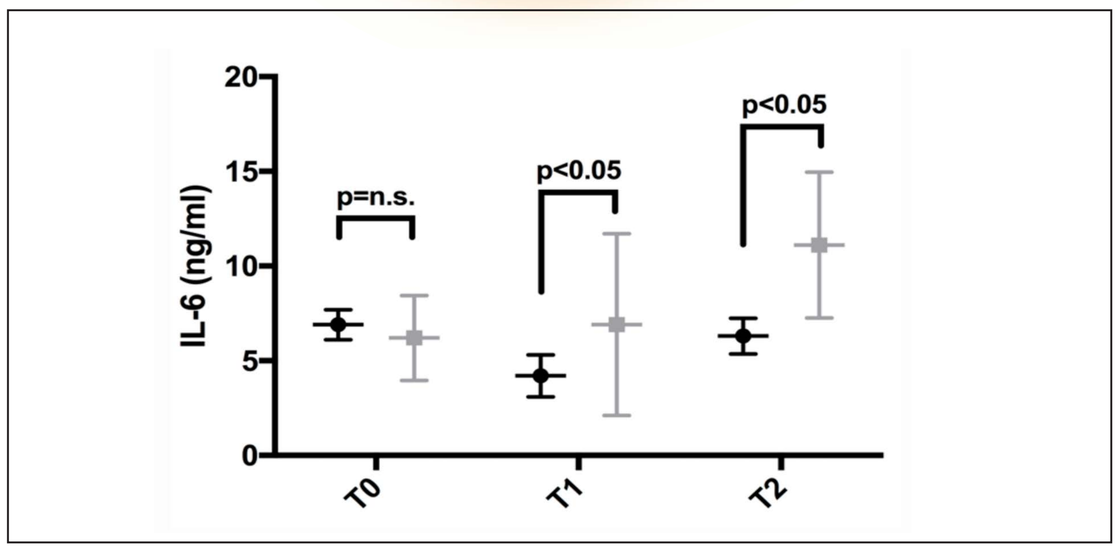


Figure 1
IL-6 Expression Results are expressed in ng/ml and values are presented as meanSD. Statistical significance difference ($p<0.05$) between the group unexposed compared to exposed to iron supplement.

Parameters	Sucrosomial® Iron supplement	T0	P between groups	T1	P between groups	T2	P between groups	P for trend
Iron indices								
Serum ferritin (ng/mL)	Y	117.9±60.4	NS	131.5±67.2	NS	135.7±68.7	NS	NS
	N	119.2±43.7		150.8±44.4		182.5±30.5		NS
Transferrin saturation (%)	Y	33.0±11.7	NS	33.4±9.1	NS	32.5±7.4	NS	NS
	N	42.7±12.4		42.1±13.7		42.8±9.3		NS
Transferrin (mg/100 mL)	Y	244.6±34.9	NS	230.0±28.0	NS	216.1±31.5	NS	**0.004**
	N	222.8±25.2		210.3±21.0		208.5±6.4		NS
Biochemical parameters								
Hb (g/dL)	Y	14.9±0.5	NS	14.9±0.6	NS	15.0±0.8	NS	NS
	N	14.8±1.2		14.6±1.0		15.7±0.4		NS
RBC (x10^6/µL)	Y	5.1±0.2	NS	5.2±0.3	NS	5.1±0.3	NS	NS
	N	4.9±0.3		5.0±0.2		5.2±0.1		NS
WBC (x10^3/µL)	Y	6.0±1.2	NS	5.9±1.0	NS	5.8±1.0	NS	NS
	N	5.9±0.3		5.8±1.0		5.9±1.2		NS
HCT (%)	Y	45.6±2.2	NS	45.7±2.0	NS	43.6±2.2	NS	**0.002**
	N	46.0±3.2		45.3±2.1		44.8±1.7		NS
MCV (fL)	Y	85.5±1.4	NS	87.2±1.7	**0.01**	85.8±1.8	NS	**0.005**
	N	87.2±2.5		91.0±3.5		86.4±2.1		NS
MCH (pg)	Y	28.9±0.6	NS	28.4±0.7	NS	29.5±0.5	NS	**0.001**
	N	29.6±1.6		29.2±1.4		30.2±0.3		NS
MCHC (g/dL)	Y	33.4±0.6	NS	32.6±0.5	NS	34.4±0.5	NS	**<0.001**
	N	32.7±1.0		32.1±0.9		35.1±0.5		**0.01**
RDW (%)	Y	11.9±0.6	NS	11.7±0.4	NS	11.6±0.5	NS	NS
	N	12.1±0.7		11.6±0.3		11.0±0.0		NS
PLT (x10^3/µL)	Y	233.8±59.9	NS	237.4±73.6	NS	205.2±37.5	NS	NS
	N	218.3±11.4		219.3±22.0		192.5±2.1		NS
Folate (ng/mL)	Y	3.3±1.2	NS	5.7±3.1	NS	4.4±1.4	NS	**0.03**
	N	4.1±0.9		3.8±2.1		3.2±0.1		NS
Vitamin B12 (pg/mL)	Y	551.9±211.1	NS	969.0±510.3	NS	579.9±165.7	NS	**0.01**
	N	476.0±238.1		626.8±508.5		452±38.2		NS
AST (U/L)	Y	24.7±3.3	NS	27.2±4.7	**0.04**	25.7±7.3	NS	NS
	N	25.3±9.4		34.3±7.8		21.0±4.2		NS
ALT (U/L)	Y	26.2±10.2	NS	24.4±6.1	NS	22.1±8.3	NS	NS
	N	19.0±2.9		32.5±11.7		19.0±4.2		NS
BUN (mg/dL)	Y	24.1±9.7	NS	22.9±4.5	NS	20.7±4.7	NS	NS
	N	21.0±7.1		20.8±1.7		20.0±1.4		NS
Creatinin (mg/dL)	Y	1.0±0.1	NS	1.0±0.1	NS	1.0±0.1	NS	NS
	N	1.0±0.1		1.1±0.1		1.0±0.1		NS
CPK (U/L)	Y	243.8±145.2	NS	287.4±103.7	**0.03**	244.7±144.1	NS	NS
	N	315.0±51.0		518.5±282.8		189.0±73.5		NS
Inflammatory markers								
hsCRP (mg/dl)	Y	0.3±0.3	NS	2.9±3.6	NS	0.3±0.5	NS	**0.04**
	N	0.2±0.1		1.2±1.2		0.1±0.1		NS
IL-6 (pg/ml)	Y	6.9±2.6	NS	4.22±3.7	**0.04**	6.3±3.1	**0.04**	NS
	N	6.2±4.5		6.9±9.6		11.1±7.7		NS

Table 1
The IL-6 levels increase over the season in athletes that did not receive Sideral® Folico. Results are expressed in ng/ml and values are presented as meanSD. Statistical significance difference ($p<0.05$) between the group unexposed compared to exposed to iron supplement.

Conclusions:

This study showed for the first time that the supplementation with Sideral® Folico is able to reduce IL-6 levels during the sport season. Since intense stress may increase IL-6 levels, we can suppose that the increase in IL-6 observed in the controls is due to normal exercise during the season. This increase in cytokine levels was not observed in athletes who received Sideral® Folico. Furthermore, we did not observe change in iron parameters. These results showed that the positive effect of this supplement is independent of the iron status, it could be suggested even in the absence of an established deficit