Clinical Efficacy Of Intravenous Ferric Carboxymaltose (FCM) In Restless Leg Syndrome Patients: An Observational Study

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Background: Restless leg syndrome(RLS) is a sensory-motor disorder. The time course of the effect of IV iron with its exact dosing to be used for its response in RLS is not yet proven.

Objective: Present study was done to determine impact of single dose of 500mg IV ferric carboxymaltose(FCM) on RLS severity, sleep and quality of life.

Methods: Individuals were assessed for RLS on International RLS Study Group(IRLSSG) diagnostic criteria and those having low ferritin(<100 nanogm/l) were invited to participate. Single dose of IV FCM was administered to 50 RLS individuals and change in RLS severity was evaluated using International RLS severity scale, improvement in sleep(nocturnal and daytime) by Pittsburgh Sleep Quality Index(PSQI) and Epworth sleepiness Scale(ESS), while quality of life was assessed using RLSQoL(Quality Of Life Scale) questionnaire at baseline, 1month and 3month.

Socio-demographic characteristics	
Age (years)	Percentage(N)
18-30	20%(10)
31-40	20%(10)
41-50	24%(12)
51-60	16%(8)
61-70	12%(6)
71-80	8%(4)
Mean Age (Mean ± SD)	45±15.6 years
Height(cm)	158(156-165.75)
Weight(kg)	68(63-74.75)
BMI (Kg/m^2)	26.58(24.03-28.64)
Family History	
Positive	36%(18)
Negative	64%(32)
Co-morbidities	
No comorbidity	38%(19)
Migraine	22%(11)
Fibromyalgia	8%(4)
Diabetes mellitus	12%(6)
Hypertension	20%(10)
PD	4%(2)
CVA	2%(1)
Radiculopathy	2%(1)
Hypothyroidism	6%(3)

Table- Status of Haematological parameters at baseline among individuals with restless leg syndrome.

Parameters	Mean ± SD (N=50)	Parameters	Mean ± SD (N=50)
Hemoglobin(gm/dL)	12.29 ± 1.45	Total protein(g/dL)	7.22 ± 0.48
TLC (per micL)	7595.2 ± 2244.49	Albumin(g/dL)	4.06 ± 0.34
HCT (%)	37.03 ± 4.01	A/G ratio	1.32 ± 0.26
MCV (fL)	83.4 ± 8.67	Serum calcium(mg/dL)	12.23 ± 16.48
MCH	27.75 ± 3.66	CRP (mg/L)	3.19 ± 1.52
MCHC	31.18 ± 2.11	ESR	9.38 ± 3.51
RDW (%)	16.87 ± 18.99	FBS (mg/dL)	93.73 ± 19.04
Urea(mg/dL)	21.69 ± 9.28	PPBS	118.28 ± 14.31
Creatinine(mg/dL)	0.79 ± 0.3	Serum Iron(µg/dL)	55.75 ± 22.44
SGPT(U/L)	28.1 ± 13.52	TIBC (micg/dL)	417.79 ± 87.29
SGOT(U/L)	26.59 ± 13.45	Transferrin saturation	14.29 ± 7.19
Total bilirubin(mg/dL)	0.72 ± 0.31	Serum Ferritin(ng/mL)	24.31 ± 20.93

Table- Transformation in Severity of RLS , Daytime Sleepiness, sleep Quality and Quality of life of individuals with RLS at baseline and in subsequent visits after administration of IV FCM.

Variables	Scores at baseline (N=50)	Scores at 2nd Visit (N=49)	Scores at 3rd Visit (N=47)	P- Value
RLS severity	29.9 ± 8.19[bc]	10.31 ± 11.54[a]	9.11 ± 11.28[a]	<0.0001
Daytime Sleepiness	11.68 ± 4.97[bc]	6.63 ± 3.87[ac]	5.96 ± 3.91[ab]	<0.0001
Sleep Quality	10.42 ± 4.93[bc]	5.51 ± 4.68[ac]	5.17 ± 4.65[ab]	<0.01
Quality of Life	59.05±23.88 [bc]	84.39±22.02[a]	86.28±21.58[a]	<0.001

Data is presented as mean± SD; P value <0.05 is significant; Friedman test with post hoc comparison by Wilcoxon Signed Ranks test was used for group comparison;
a- significant difference with baseline score; b- significant difference at 1month(2nd visit); c- significant difference at 3 months(3rd visit).

Table-Correlation of Haematological parameters with RLS severity, Sleep Quality, Sleepiness and QOL.

Variables		Correlation (r)	Significance (P Value)
Haemoglobin	Serum Iron	0.396	0.004**
	Serum Ferritin	0.377	0.007**
	Transferrin	0.499	0.0001**
	IRLSSG	-0.129	0.374
	ESS	-0.018	0.901
	PSQI	0.026	0.860
	RLSQOL	-0.180	0.211
IRLSSG	Haemoglobin	-0.129	0.374
	Serum Iron	-0.146	0.311
	Serum Ferritin	-0.098	0.498
	Transferrin	-0.186	0.195
	ESS	0.661	0.0001**
	PSQI	0.653	0.001**
	RLSQOL	-0.709	0.001**

Spearman correlation (r); P value <0.05 is significant.

CONCLUSION:

While the causal relationship between iron and RLS remains unproven, the present study has observed that a single 500 mg dose of IV FCM can significantly improve not only RLS symptoms but also sleep quality and sleepiness in individuals who have ferritin deficiency. This improvement can lead to an overall better QOL for RLS patients. Subsequent large-scale studies may be conducted in future to identify the subgroup of population that will respond the most to intravenous iron treatment.