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A RANDOMIZED CONTROL TRIAL TO ASSESS THE EFFICACY AND SAFETY OF IRON DEXTRAN AND IRON SUCROSE AMONG IDA AFFECTED PREGNANT WOMEN

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Abstract:

Objective: *The aim of the research was to draw a comparison of safety and efficacy of the total dose infusion profile iron dextran (low molecular weight) against distributed intravenous iron sucrose doses to manage pregnant women diagnosed with iron deficiency anaemia.*

Patients and Methods: *This research was a randomized control trial which was carried out at Mayo Hospital, Lahore from October 2017 to November 2018. We distributed the sample that consisted of pregnant women with a gestational age of (> 12 weeks) and these women were confirmed for Iron Deficiency Anemia (IDA). We managed Group – A with intravenous iron sucrose and iron dextran (low molecular weight) to Group – B. was given. We confirmed Post-infusion Hemoglobin (Hb) at the fourth week and at delivery. Pre to post Hb rise comparison was made through paired T-Test which was not significant.*

Results: *Mean Hb pre-infusion level for Group – A, mean increase and after four weeks of infusion were respectively (9.09 ± 0.83) gm/dl, (10.75 ± 1.097) gm/dl and (11.06 ± 0.866) gm/dl at delivery with a significant P-Value under 0.001. Mean Hb pre-infusion in Group – B was (8.735 ± 0.956) gm/dl, mean Hb increase at fourth week was (10.613 ± 1.22) gm/dl; whereas, an increase at the time of delivery was (10.859 ± 1.11) gm/dl (P-Value < 0.001).*

Conclusion: *Both iron sucrose and iron dextran (LMW) were equally effective for the management of IDA among pregnant women; however, the later has an advantage that there is no need for the second visit for the treatment of IDA as it manages the onset of IDA at the first visit.*

Keywords: *Pregnancy, Anemia, Iron Deficiency Anemia (IDA), Iron, Parental, Dextran, LMW (Low Molecular Weight) and Sucrose.*

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INTRODUCTION:

The deficiency of iron is a nutritional disorder especially in the underdeveloped countries which ranges from 12% to 43% around the world attributing in death and disability [1 – 3]. Haemorrhage tolerance and severe anaemia attribute in maternal deaths primarily by postpartum haemorrhage, antepartum haemorrhage and heart failure [4, 5]. Pregnancy often causes loss of blood which needs blood transfusion among these cases [6, 7]. Local research highlights this alarming situation and presents IDA prevalence as 43.1% [8]. IDA has so many other effects which include intrauterine growth retardation, preterm delivery, low birth weight, increased perinatal mortality & morbidity irreversible central nervous system damage and psychomotor development impairment [4]. Most women start gestation with low iron storage due to multiple reasons such as compliance issues, diet deficiency, multiparity and poverty [9]. An author also reported no women with satisfactory diet pattern [10]. Ayyub reported the IDA prevalence among all socioeconomic classes [11]. Normally patients use oral intake of iron as it is less expensive and safe as well as effective. WHO recommends regular iron supplementation [12]. Non-compliant patients receive intravenous iron management and most of the patients included in this research were non-compliant [13]. Oral iron therapy is also difficult at early and later stage of pregnancy due to hyperemesis and nausea at the early stage and heartburn at the later stage of the pregnancy. Intravenous treatment suits such cases due to rapid Hb increase and rapid body iron replenishment. Intravenous iron therapy also reduces the requirement of blood transfusion among IDA patient. Good quality literature is scarcely available even in the higher disease burden [14]. Therefore, the aim of the research was to draw a comparison of safety and efficacy of the total dose infusion profile iron dextran (low molecular weight) against distributed intravenous iron sucrose doses to manage pregnant women diagnosed with iron deficiency anaemia.

METHODOLOGY:

This research was a randomized control trial which was carried out at Mayo Hospital, Lahore from October 2017 to November 2018. We distributed the sample population (180 females) that consisted of pregnant women with a gestational age of (> 12 weeks) and these women were confirmed for Iron Deficiency Anemia (IDA). We managed Group – A with intravenous iron sucrose and iron dextran (low molecular weight) to Group – B. was given. We confirmed Post-infusion Hemoglobin (Hb) at the fourth week and at delivery. We included pregnant women with a gestational age of twelve weeks, confirm IDA cases, oral iron intolerability, non-compliant and irritable bowels syndrome patients. We did not include any patients other than iron deficiency, symptomatic anaemia, hemoglobinopathies, parenteral iron preparations allergy history, rheumatoid arthritis and allergic bronchospasm. In addition to that, we also excluded those women facing obstetric complications such as antepartum haemorrhage, multi-fetal pregnancy and hypertensive disorders. IDA was diagnosed on the basis of clinical findings of Hb (< 10.5) gm/dl, serum ferritin (< 12) µg/l, Mean Corpuscular Volume (< 76 fl) and peripheral smears reflecting microcytic hypochromic picture. Iron deficiency was calculated with this formula:

[*Weight (kg) X (11 gm/dl - actual hemoglobin (gm/dl) X 0.24 + 500 mg*]

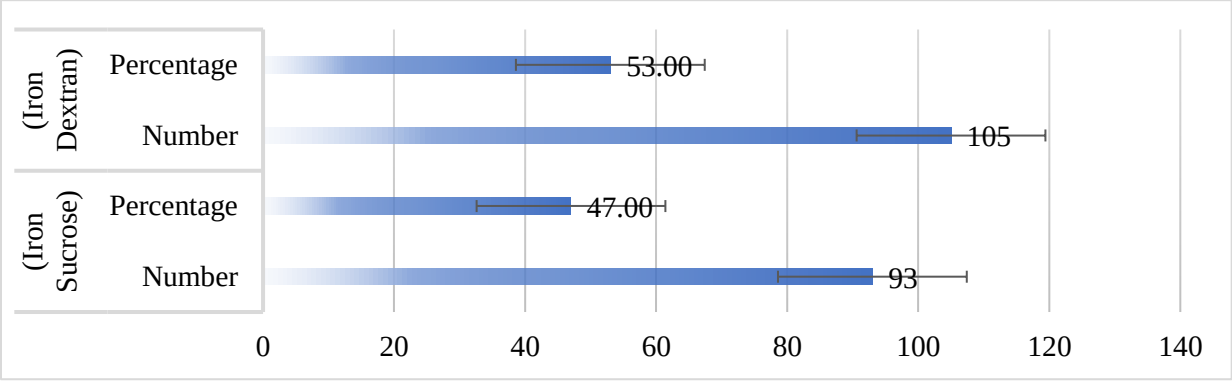
Addition of 500 mg for purely for the iron stores. Group – A was treated with 0.1 ml (normal saline "20 ml" diluted) iron dextran with the help of burette for more than twenty minutes and more than one hour. We also monitored possible side effects of the infusion procedure among patients. Among those who did not present any side effect, the treatment was continued till full dose; whereas, allergic cases were removed from the research. The dilution was made in normal saline (1000 ml) which was slowly administered from six to eight hours. Group – B received intravenous iron sucrose for starting twenty minutes and patients were monitored for allergic reaction with full dose insertion. Side effects were also monitored among patients for one hour after full dose insertion. Patients were also educated for possible reactions and also advised to report in case of any reaction. Post-infusion Hb was also monitored after four weeks and at delivery. Pre to post Hb rise comparison was made through paired T-Test which was not significant. SPSS software was also used for the outcome's analysis. The confidence interval was 95% and significant P-Value was < 0.05.

RESULTS:

Mean Hb pre-infusion level for Group – A, mean increase and after four weeks of infusion were respectively (9.09 ± 0.83) gm/dl, (10.75 ± 1.097) gm/dl and (11.06 ± 0.866) gm/dl at delivery with a significant P-Value under 0.001. Mean Hb pre-infusion in Group – B was (8.735 ± 0.956) gm/dl, mean Hb increase at fourth week was (10.613 ± 1.22) gm/dl; whereas, an increase at the time of delivery was (10.859 ± 1.11) gm/dl (P-Value < 0.001). Table – I, II & III present a detailed analysis of the research outcomes.

Table – I: Group-Wise Stratification of Parity, Serum Ferritin and Gestational Age

Details		(Iron Sucrose)		(Iron Dextran)	
		Number	**Percentage**	**Number**	**Percentage**
Group	Distribution	93	47.00	105	53.00
Gestational age weeks	≥ 33	65	69.89	59	56.19
	≤ 33	28	30.10	46	43.80
Parity	Primigravida	30	32.25	38	36.19
	2 to 3	38	40.86	31	29.52
	4 to 7	23	24.73	34	32.38
	≥ 8	2	2.15	2	1.90
Serum ferritin	≤ 6 µg/l	48	51.61	51	48.57
	≥ 6 µg/l	45	48.38	54	51.42



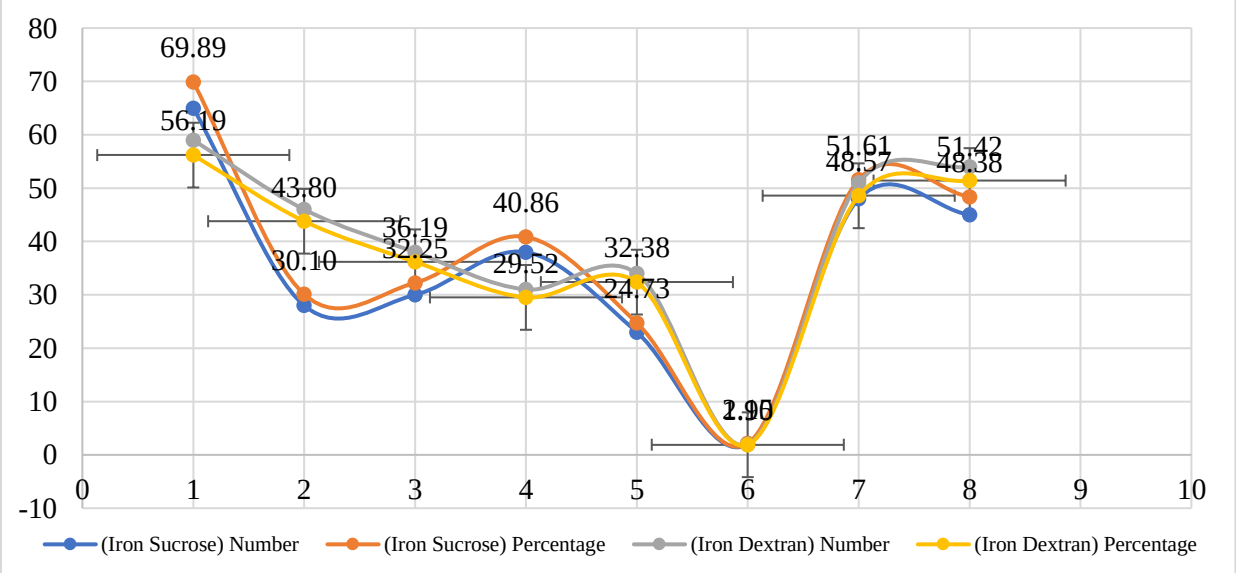
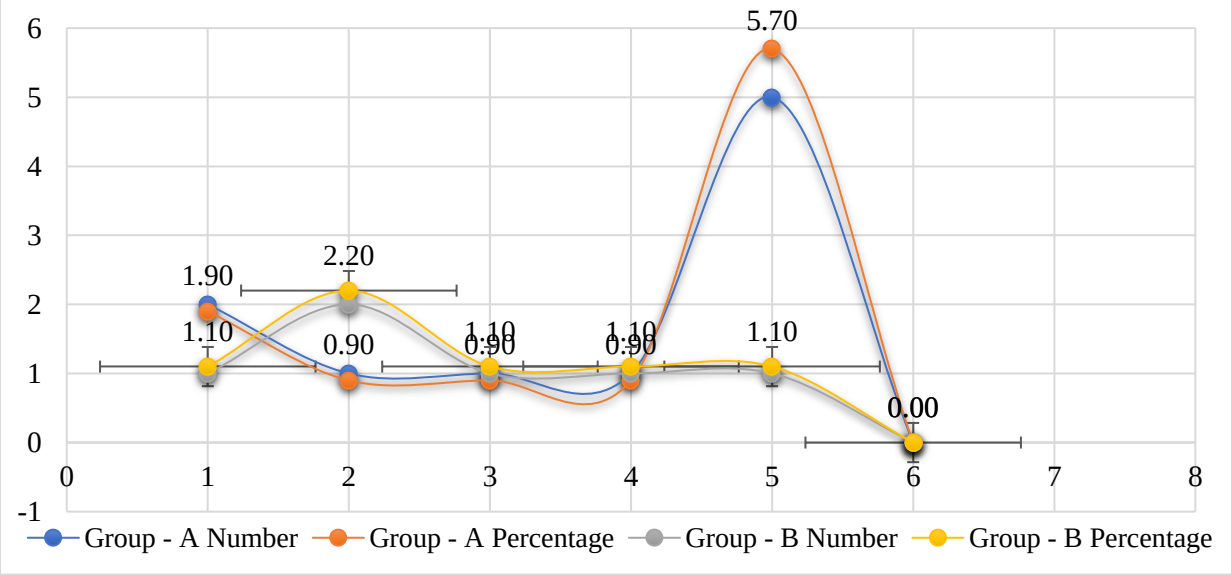


Table – II: Group-Wise Mean, SD, Minimum and Maximum Values

Details		(Iron Sucrose)	(Iron Dextran)
		93 (47%)	**105 (53%)**
Pre-infusion Hb	Mean	9.0 gm/dl	8.7 gm/dl
	SD	0.83	0.95
	Min - Max	6.6 - 10.4	6.1 - 10.5
Pre-infusion Hb at 4 weeks	Mean	10.7 gm/dl	10.6 gm/dl
	SD	1.04	1.22
	Min - Max	8 to 14	8.5 - 14
	P-value	< 0.001*	< 0.001*
Pre-infusion Hb at delivery	Mean	11.06 gm/dl	10.8 gm/dl
	SD	0.86	1.11
	Min - Max	7.7 - 13	7 - 13.5
	P-value	< 0.001**	< 0.001**

Table – III: Group-Wise Side Effects

Side Effects	Group – A		Group – B	
	Number	**Percentage**	**Number**	**Percentage**
Palpitation	2	1.90	1	1.10
Shivering	1	0.90	2	2.20
Low blood pressure	1	0.90	1	1.10
Heat intolerance	1	0.90	1	1.10
Small joint stiffness	5	5.70	1	1.10
Adverse drug event	0	0.00	0	0.00



DISCUSSION:

IDA attributes in substantial economic burden along with decreased productivity, impaired performance at school and poor pregnancy outcomes in underdeveloped countries [4]. Among the pregnant women of third world countries, about 30% were affected from nutritional status during first pregnancy which is also seconded by other authors due to low and middle socioeconomic status among fifty percent of the pregnant women [15]. IDA incidence advances with advancing gestational age. Habib also reported a shift from 29.6% to 34% respectively from first to third trimester [16]. Similarly, Ayyub, Dreyfuss and Morasso also reported constant fall in the mean value of Hb from first to third trimester [11, 17, 18].

Complications are faced during labour if the disease is left untreated which can increase neonatal and maternal mortality and morbidity [4, 5]. A country with already scarce medical facilities the situation is even worst. We reported severely depleted iron stores among 66% pregnant women as the level of serum ferritin was under 6 µg/l which indicated poor nutritional intake. Another local research reported higher IDA occurrence even in the presence of iron prophylaxis therapy [19].

Both parenteral iron therapies were equally effective but more iron depleted patients were significantly raised. Ayyub also reported similar outcomes among iron stores depleted pregnant patients [20]. Anaemia recovery was achieved before delivery in both groups; Perewusnyk also documented the same as no patient required blood transfusion [10]. Iron dextran TDI is cost effective as it requires a single dose; whereas, iron sucrose requires multiple doses. Compliance is another issue in Pakistani healthcare setup as healthcare facilities are not in the reach of every patient along with the development of gastrointestinal signs. TDI is cost effective due to various cultural barriers, healthcare access, poverty etc. Safety can be assured with iron infusion in daycare in the availability of cardiopulmonary resuscitation equipment. Peripheral veins are good for infusion spot along with avoidance of the formation of chemical phlebitis at the site of infusion. Slow intravenous management of iron sucrose or iron dextran in the course of infusion has no association with increased inflammation/ oxidation markers [21] iron dextran.

Both therapies did not give any outcomes like anaphylaxis. Ayyub reported the same outcomes and recommended it as IDA management therapy during pregnancies [20]. Similarly, Sinha also concluded iron dextran TDI as effective and safe without any adverse outcomes than iron sucrose [22]. LMW Plasma half-life is three to four days, this slow release and stability of iron results in reduced oxidative stress; however, it is more common in non-dextran iron [23].

Our outcomes report hypotension with iron dextran and iron sucrose respectively as (0.9%) and (1.1%). Which is in corresponding with the information of manufacturer of the product as LMW iron dextran is less involved in the production of hypotension (<0.1%) in comparison to the iron sucrose (<1.00%) with same adverse outcomes occurrences.

CONCLUSION:

Both iron sucrose and iron dextran (LMW) were equally effective for the management of IDA among pregnant women; however, the later has an advantage that there is no need for the second visit for the treatment of IDA as it manages the onset of IDA at the first visit.

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