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Solcoseryl versus Low Molecular Weighte Heparin for Intrauterine Fetal Growth Restriction

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: FETAL Growth Restriction (FGR) is a problem where the fetus fails to attain its normal growth potential and this affects nearly about 8% of all pregnancies Solcoseryl is a protein-free and antigen-free haemodialysate derived from calf blood. It is thought to activate the cellular respiratory chain leading to better oxygen utilisation by the tissues. Aim of the study was to compare between Solcoseryl and low molecular weight heparin in treatment of patients suffered from intrauterine growth restriction due to placental insufficiency.
Methods: The patients who included in this study were divided randomly via (computer-generated random numeric tables prepared by a statistician) into two groups with 35 cases in each group. Group (A) (Solcoseryl. Group): 35 women received Solcoseryl ampule 42.5 mg intravenous infusion (Misr Compony) Once daily for 3 weeks .Group (B) (LMWH (Clexan) Group): 35 women received single dose of LMWH subcutaneous (clexane 40 mg) once daily for 3 weeks.
Results: There is a significant decrease regarding umbilical artery RI in both groups but the significant decrease was better in group A compared to group B. Otherwise, there is no significant difference between the two groups umbilical artery RI at different time intervals. there is significant increase in Gestational age and birth weight in patients who receive solcoseryl and LMWH .There is an improvement in Doppler indices of both (UA and MCA) in both group but is better in solcoseryl than LMWH and significant increase in Apgar score at 1min and 5 min in both groups but is better in solcoseryl than LMWH.

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Conclusions: In this study, LMWH and Solcoseryl administration in IUGR fetuses enhance Doppler indices, promote significant increase in Gestational age so enhance neonatal birth weight.

Keywords: Solcoseryl; low molecular weighte heparin; intrauterine; growth restriction.

1. INTRODUCTION

FETAL Growth Restriction (FGR) is a problem where the fetus fails to attain its normal growth potential and this affects nearly about 8% of all pregnancies [1-2]. The growth restricted fetuses are almost suffering a poor pregnancy outcome being at increased risk of perinatal complications mainly, fetal distress, asphyxia, neonatal hypoglycemia as well as poor feeding [3].

Second; they are more prone to long-term neurological and developmental disorders, increased incidence of hypertension, diabetes mellitus and coronary heart disease in adulthood [3,4].

Abnormal formation and function of the placenta with subsequent placental insufficiency is considered as the main pathogenic mechanism involved in FGR. These pregnancies are commonly associated with elevated peripheral vascular resistance in the maternal arterial system as seen in pregnancies complicated with preeclampsia [5]. The trophoblastic production of nitric oxide in normal pregnancy plays an important role in vasodilatation at the feto-placental circulation, thus improving fetal oxygen and nutritional supply [6].

This effect, in fact, is attributed to its potent relaxing effect on arterial and venous smooth muscle and perhaps inhibiting platelets aggregation and adhesiveness [7].

To date no available therapy addressed with demonstrable effectiveness that makes monitoring and timely delivered growth restricted fetus to be an easy and optimistic clinical entity [8].

Solcoseryl is a protein-free and antigen-free haemodialysate derived from calf blood. It is thought to: (i) activate the cellular respiratory chain leading to better oxygen utilisation by the tissues, (ii) increase the energy reserves of the cells, (iii) decrease the total peripheral resistance of the arteries and (iv) stimulate the con-tractile heart force. The effects of sol- coseryl therapy in a comparative study of pregnancies with growth retardation diagnosed by ultrasound measurement of hPL in maternal serum and amniotic fluid, measurement of oestriol in maternal serum and urine, and cardiotocography. [9-11]. The aim of the study was to compare between Solcoseryl and low molecular weight heparin in treatment of patients suffered from intrauterine growth restriction due to placental insufficiency.

2. PATIENTS AND METHODS

The clinical prospective randomized study was conducted at Tanta university hospital. Patients were recruited from the high risk pregnancy unit in the period from januray 2020 to April 2021. The study group consisted of 70 patients diagnosed with Asymmetrical intrauterine growth restriction .

Inclusion criteria:

- Maternal age between 20-35 years.
- Gestational age 28-35wks.
- Singleton pregnancy.

Fetal growth restriction diagnosed by ultrasound with estimated fetal weight below the 10th percentile for gestational age

Exclusion criteria for the final analysis are:

- Chronic diseases with pregnancy e.g. chronic hypertension, diabetes type 1 or 2.
- Symmetrical IUGR due to fetal malformations, aneuploidy, infections or other etiologies.
- Suspected fetal compromise requiring emergency delivery.
- Any contraindication to the use of solcoseryl.

Any contraindication to the use of LMWH e.g. known bleeding disorder, active antenatal bleeding or at increased risk of major hemorrhage (e.g. placenta praevia), thrombocytopenia, severe renal or hepatic disease.

- Smokers.
- Patient refusied to participate in the study or unable to consent.
- Multiple gestation.

The patients who included in this study were divided randomly via(computer-generated random numeric tables prepared by a statistician.). into two groups with 35 cases in each group

Group (A) (Solcoseryl.Group): 35 women received Solcoseryl ampule 42.5 mg intravenous infusion (Misr Compony) Once daily for 3 weeks.

Group (B) (LMWH (Clexan) Group): 35 women received single dose of LMWH subcutaneous (clexane 40mg) once daily for 3 weeks.

All patients in the study underwent uniform antenatal assessment protocol that included, History taking, Clinical ,General and obstetric examination.and routine antenatal Investigations as (Complete blood picture, random blood sugar, liver, renal functions and coagulation profile).

Ultrasound study evaluation of gestation was done for each case at start of study before medications and after one, two & three weeks of medical treatment.

Ultrasound examination included (Fetal biometry (BPD, FL, AC), AFI, Doppler ultrasound studies of umbilical artery (UA), and fetal middle cerebral artery (MCA).

Ultrasound machine MINDRAY DC 30 with abdominal probe capable of high resolution gray-scale, pulsed wave and color Doppler modes was used . Pulsed wave Doppler measurements of UA, MCA were obtained using the pulsatility index (PI) and resistance index (RI) to quantify arterial Doppler waveforms.

All recordings were obtained in the absence of fetal breathing and fetal movements. For each vessel, an average of three consecutive Doppler velocity waveforms was used for statistical analysis.

The angle independent PI was calculated electronically from smooth curves fitted to good quality wave forms over three cardiac cycles according to the following formulae:

$$PI = (S-D) / A$$

The resistance index (RI) It also gave an angle-independent measure of pulsatility:

Where

(S) Represents the peak systolic and
(D) The end-diastolic frequency shift

2.1 Statistical Analysis

The sample size was calculated using Epi-Info software statistical package created by World Health organization and center for Disease Control and Prevention, Atlanta, Georgia, USA version 2002. The criteria used for sample size calculation (n>33) were 95% confidence limit, 80% power of the study, expected outcome in in treatment group 90% compared to 60% for control groups.

Analysis of data were performed by SPSS v25 (SPSS Inc., Chicago, IL, USA). Quantitative parametric variables (e.g. age) were presented as mean and standard deviation (SD). They were compared between the two groups by unpaired student's t- test and within the same group by paired T test. Quantitative non-parametric variables (e.g. VAS) were presented as median and range and compared between the two groups by Mann Whitney (U) test and within the same group by Wilcoxon test. P value < 0.05 was considered significant.

3. RESULTS

Table 1. Demographic characteristics and clinical data of the studied groups

	Group A (n=35)	Group B (n=35)	t	P
Age (years) Mean ± SD	24.9 ± 3.63	24.8 ± 2.76	.129	0.897
BMI (kg/m2) Mean ± SD	29.4 ± 4.1	28.35 ± 3.31	1.179	0.243
Parity Mean ± SD	1.5 ± 1.01	1.6 ± 0.940	MU 148	.659
GA (weeks) Mean ± SD	31.95 ± 2.82	32.3 ± 2.59	0.539	0.590

This table shows that there is no significant difference between the groups regarding maternal age, BMI, parity, and GA

Table 2. Umbilical artery RI of the two studied groups

	Umbilical artery resistance index Mean ± SD				Fr	P
	Pre treatment	Post treatment 1 week	Post treatment 2 weeks	Post treatment 3 weeks		
Group A (n=35)	0.871 ± 0.052	0.858 ± 0.053	0.852 ± 0.047	0.842 ± 0.036	16.857	0.001*
Group B (n=35)	0.845 ± 0.083	0.844 ± 0.077	0.840 ± 0.089	0.832 ± 0.077	5.319	0.028*
t	1.19	.453	.262	.500	--	
p	.244	.653	.795	.620		

** Significant p value < 0.05; This table shows: There is a significant decrease regarding umbilical artery RI in both groups but the significant decrease was better in group A compared to group B. Otherwise, there is no significant difference between the two groups umbilical artery RI at different time intervals.*

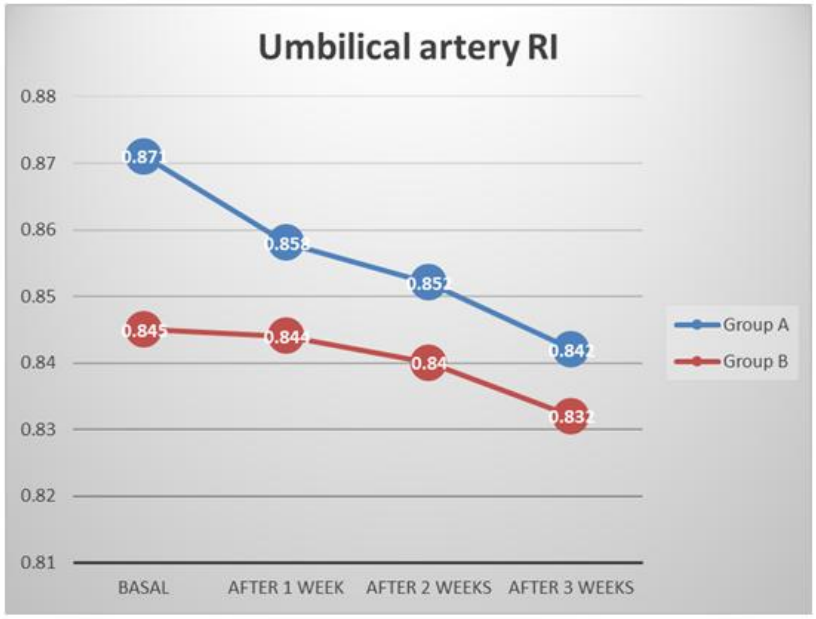

Fig. 1. A significant decrease regarding umbilical artery RI in both groups but the significant decrease was better in group A compared to group B. Otherwise, there is no significant difference between the two groups umbilical artery RI at different time intervals

Table 3. Umbilical artery PI of the two studied groups

	Umbilical artery pulsatility index Mean ± SD				Fr	P
	Pre treatment	Post treatment 1 week	Post treatment 2 weeks	Post treatment 3 weeks		
Group A (n=35)	1.343 ± 0.188	1.340 ± 0.189	1.338 ± 0.192	1.303 ± 0.184	27.531	0.001*
Group B (n=35)	1.241 ± 0.168	1.231 ± 0.162	1.226 ± 0.183	1.213 ± 0.155	5.937	0.026*
T	0.215	0.685	0.712	0.935	--	
P	0.624	0.527	0.416	0.219		

** Significant p value < 0.05; This table shows: There is a significant decrease regarding umbilical artery PI in both groups but the significant decrease was better in group A compared to group B. Otherwise, there is a non-significant difference between the two groups umbilical artery PI at all studied time intervals.*

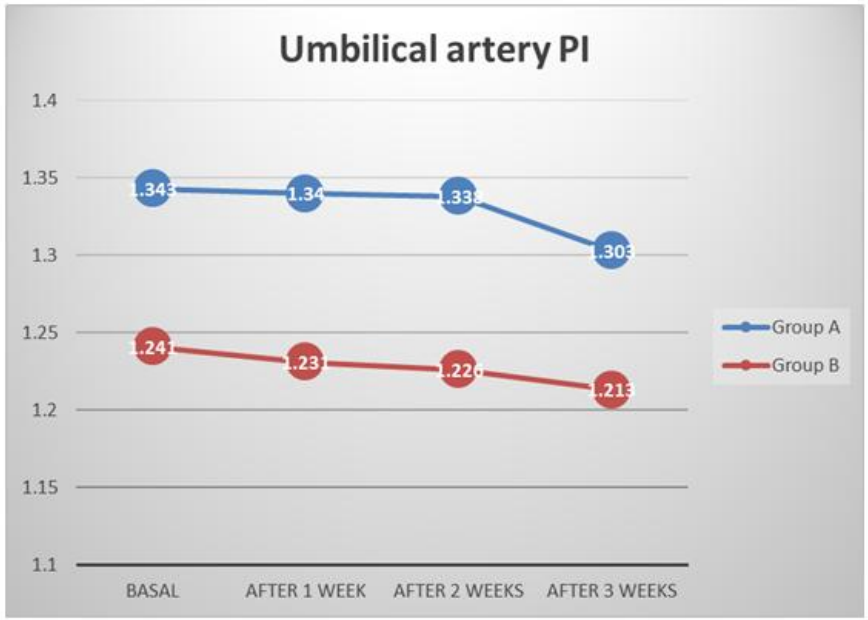

Fig. 2. A significant decrease regarding umbilical artery PI in both groups but the significant decrease was better in group A compared to group B. Otherwise, there is a non-significant difference between the two groups umbilical artery PI at all studied time intervals

Table 4. Middle cerebral artery RI of the two studied groups

	Middle cerebral artery resistance index Mean ± SD				Fr	P
	Pre treatment	Post treatment 1 week	Pos ttreatment 2 weeks	Post treatment 3 weeks		
Group A (n=35)	0.799 ± 0.141	0.819 ± 0.137	0.849 ± 0.135	0.892 ± 0.123	20.657	0.001*
Group B (n=35)	0.734 ± 0.136	0.764 ± 0.127	0.792 ± 0.125	0.851 ± 0.144	8.629	0.004*
T	1.49	1.46	1.53	1.27	--	
P	.146	.153	.135	.213		

** Significant p value < 0.05; This table shows: There is a significant increase regarding middle cerebral artery RI in both groups but the significant increase was better in group A compared to group B. Otherwise, there is no significant difference between the two groups middle cerebral artery RI at different time intervals.*

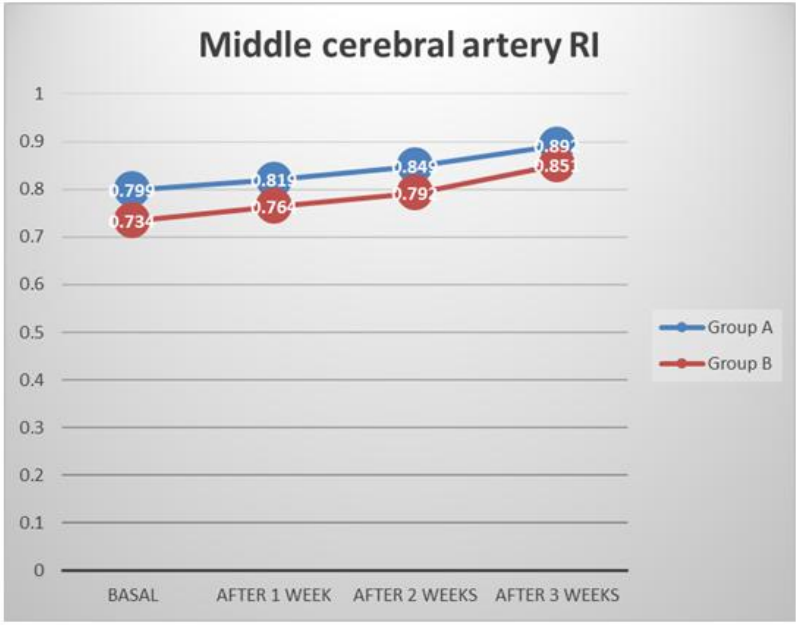

Fig. 3. A significant increase regarding middle cerebral artery RI in both groups but the significant increase was better in group A compared to group B. Otherwise, there is no significant difference between the two groups middle cerebral artery RI at different time intervals

Table 5. Middle cerebral artery PI of the two studied groups

	Middle cerebral artery pulsatility index Mean ± SD				Fr	P
	Pre treatment	Post treatment 1 week	Post treatment 2 weeks	Post treatment 3 weeks		
Group A (n=35)	1.443 ± 0.463	1.450 ± 0.468	1.475 ± 0.459	1.534 ± 0.443	15.831	0.001*
Group B (n=35)	1.394 ± 0.297	1.412 ± 0.319	1.449 ± 0.289	1.493 ± 0.277	7.315	0.010*
T	.756	.770	.812	.784	--	
P	.454	.446	.422	.438		

** Significant p value < 0.05. This table shows: There is a significant increase regarding middle cerebral artery PI in both groups but the significant increase was better in group A compared to group B. Otherwise, there is no significant difference between the two groups middle cerebral artery PI at different time intervals.*

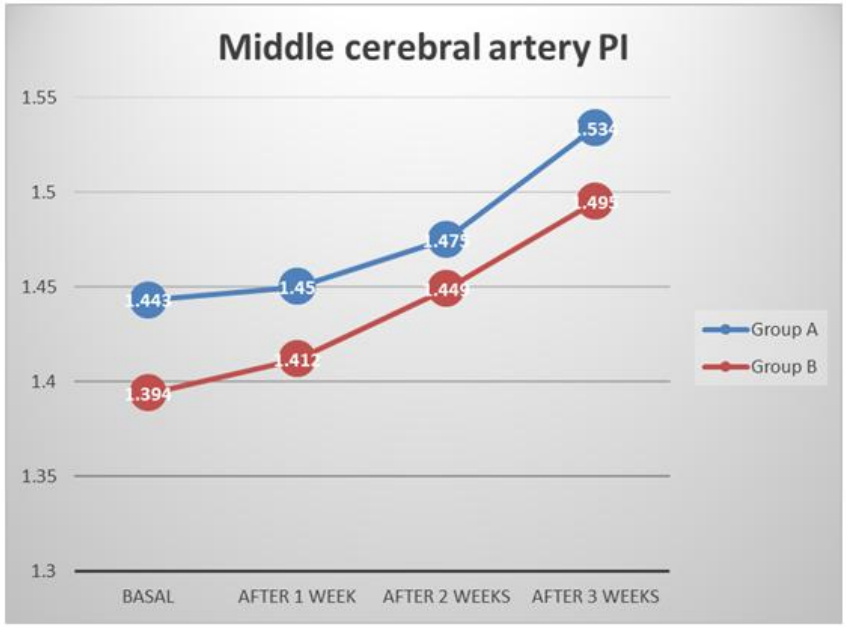

Fig. 4. A significant increase regarding middle cerebral artery PI in both groups but the significant increase was better in group A compared to group B. Otherwise, there is no significant difference between the two groups middle cerebral artery PI at different time intervals

Table 6. Umbilical artery within the group comparison of RI and PI in umblical artery UA in the studied groups

		Group A (n=35)	P value	Group B (n=35)	P value
RI	Pre treatment	0.871 ± 0.052	P1= 0.001*	0.845 ± 0.083	P1= 0.711
	Post treatment 1 week	0.858 ± 0.053	P2=.321	0.844 ± 0.077	P2= 0.814
	Post treatment 2 weeks	0.852 ± 0.047	P3=.001*	0.840 ± 0.089	P3= 0.013*
	Post treatment 3 weeks	0.842 ± 0.036	P4=.001*	0.832 ± 0.077	P4= 0.008*
PI	Pre treatment	1.343 ± 0.188	P1= 0.752	1.241 ± 0.168	P1= 0.329
	Post treatment 1 week	1.340 ± 0.189	P2=0.794	1.231 ± 0.162	P2= 0.458
	Post treatment 2 weeks	1.338 ± 0.192	P3=.029*	1.226 ± 0.183	P3= 0.106
	Post treatment 3 weeks	1.303 ± 0.184	P4=.003*	1.213 ± 0.155	P4= 0.019*

** Significant p value < 0.05; P1: Pretreatment –1-week post-treatment; P2: 1 week - 2 weeks post-treatment; P3: 2 weeks - 3 weeks post-treatment; P4: Pretreatment - 3 weeks post-treatment*

Table 7. Middle cerebral artery within the group comparison of (RI and PI) in middle cerebral artery MCA in the studied groups

		Group A (n=35)	P value	Group B (n=35)	P value
RI	Pre treatment	0.799 ± 0.141	P1= 0.235	0.734 ± 0.136	P1= 0.327
	Post treatment 1 week	0.819 ± 0.137	P2= 0.109	0.764 ± 0.127	P2= 0.194
	Post treatment 2 weeks	0.849 ± 0.135	P3= 0.024*	0.792 ± 0.125	P3= 0.031*
	Post treatment 3 weeks	0.892 ± 0.123	P4= 0.005*	0.851 ± 0.144	P4= 0.003*
PI	Pre treatment	1.443 ± 0.463	P1= 0.529	1.394 ± 0.297	P1= 0.431
	Post treatment 1 week	1.450 ± 0.468	P2=0.139	1.412 ± 0.319	P2= 0.109
	Post treatment 2 weeks	1.475 ± 0.459	P3=.019*	1.449 ± 0.289	P3= 0.021*
	Post treatment 3 weeks	1.534 ± 0.443	P4=.001*	1.493 ± 0.277	P4= 0.001*

** Significant p value < 0.05; P1: Pretreatment –1-week post-treatment; P2: 1 week - 2 weeks post-treatment; P3: 2 weeks - 3 weeks post-treatment; P4: Pretreatment - 3 weeks post-treatment*

Table 8. Pregnancy outcome between the two studied groups

		Group A (n=35)	Group B (n=35)	t/ χ2	P
GA (weeks) Mean ± SD		38.4 ± 2.96	37.5 ± 1.89	1.520	0.134
Birth weight (kg) Mean ± SD		3.16 ± 0.563	2.91 ± 0.709	1.629	0.107
Mode of delivery	CS	22 (62.9%)	20 (57.1%)	0.243	0.626
	VD	13 (37.1%)	15 (42.9%)		
Apgar at 1 min Mean ± SD		7.23 ± 1.27	6.82 ± 2.26	0.937	0.353
Apgar at 5 min Mean ± SD		9.7 ± 1.09	8.91 ± 2.83	1.542	0.128
Admitted to NICU		1 (2.9%)	5 (14.3%)	2.917	0.087
Duration of NICU (days) Mean ± SD		2	2.27 ± 0.462	0.531	0.622

There is Non significant difference between the groups in term of GA, birth weight, mode of delivery and NICU duration and NICU admition and Apgar score at 1 mint and 5 mint

3.1 Cases Presentations

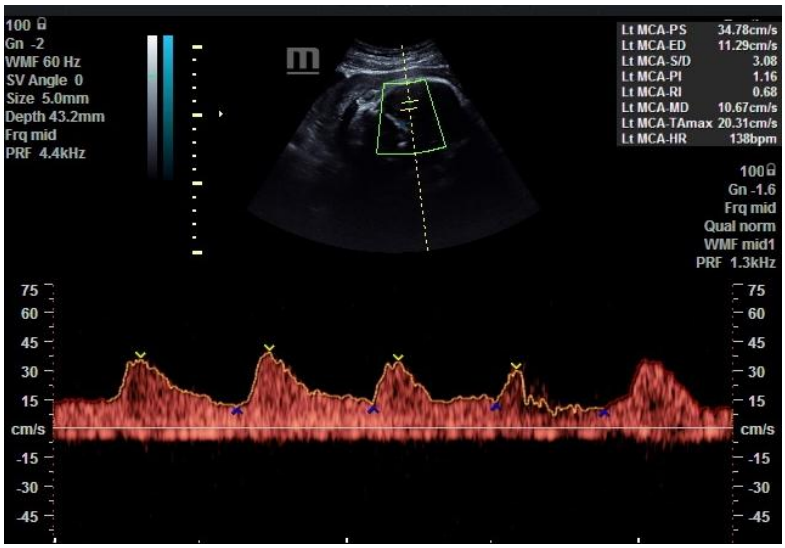

Fig 5. This figure shows MCA doppler study with measurement of decreased(PI, RI)before treatment with solcoseryl

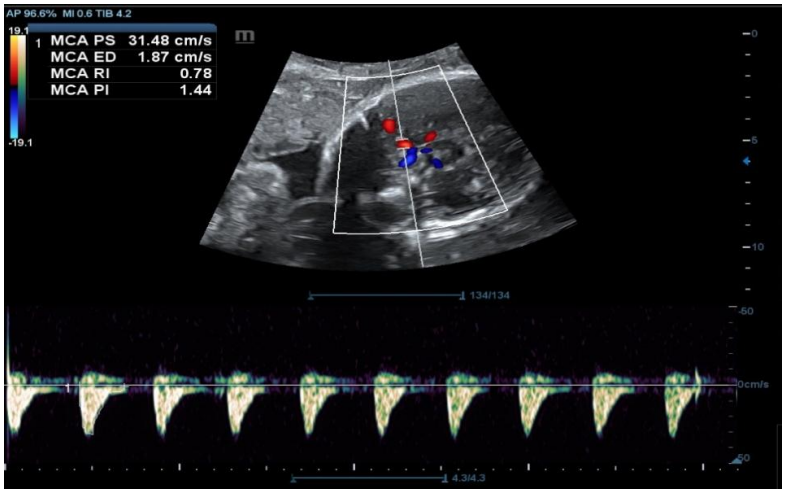

Fig 6. This figure shows MCA Doppler study with measurement of increased (PI, RI)After treatment with solcoseryl

4. DISCUSSION

During early pregnancy trophoblast invasion of the maternal spiral arteries remodels, creating a low-resistance and high-flow uteroplacental circulation capable of efficient gaseous. abnormal trophoblast invasion results in incomplete remodeling of the spiral arteries and persistence of a high-resistance and low-flow circulation [12].

To the best of our knowledge no study compared the effect of solcoseryl and heparin in the management of fetal growth restriction, hence the aim of our study was to compare between Solcoseryl and low molecular weight heparin in treatment of cases suffered from intrauterine growth restriction due to placental insufficienc.

Romero et al., [13]. There were 220 pregnant women with diagnosis of intrauterine growth restriction some of them receive solcoseryl administration. They carried out in these women Doppler study of umbilical artery and middle cerebral artery. It was followed the perinatal outcome of the newborns. The Doppler indices of

the umbilical artery and middle cerebral artery were improved in those who receive solcoseryl administration. There was significant increase in fetal birth weight in patients who receive solcoseryl administration .

Neena et al., [14]. studied 70 pregnant women with growth-restricted fetuses confirmed by ultrasound. These were followed up with Doppler studies of the umbilical artery. The study group consisted of 35 women who receive solcoseryl, The Doppler indices of the umbilical artery showed no significant changes in those who receive solcoseryl administration. There was no significant increase in fetal birth weight in patients who receive solcoseryl administration.

Schwarze et al., [15]. Seventy-four fetuses with intrauterine growth restriction (IUGR)(37 patient receive solcoseryl) and absent or reversed end-diastolic (ARED) flow in the UA at 24-34 weeks of gestation, which were delivered before 34 weeks' gestation, were examined. Absent or reversed flow during atrial contraction (a-wave) in the DV and pulsatile flow in the UV were examined to predict severe perinatal outcomes (stillbirth, neonatal death, perinatal death, acidemia, 5 min Apgar < 7, intraventricular hemorrhage and elevated nucleated red blood cell counts at delivery).There was significant improvement in those who receive solcoseryl .

Baschat et al., [16].studied 120 IUGR fetuses (60 patients receive solcoseryl). Doppler velocimetry of the umbilical artery (UA), middle cerebral artery (MCA), inferior vena cava (IVC), ductus venosus (DV) and free umbilical vein was performed with an UA pulsatility index (PI) > 2 SD above the gestational age mean and subsequent birth weight < 10th centile for gestational age. Groups based on the last Doppler exam were: 1 = abnormal UA-PI only (n = 42, 34.7%), 2 = MCA-PI > 2 SD below the gestational age mean (= 'brain sparing') in addition to abnormal UA-PI (n = 29, 24.0%), 3 = DV or IVC peak velocity index (PVIV) > 2 SD above the gestational age mean and/or pulsatile UV flow (n = 50, 41.3%). Perinatal mortality, respiratory distress (RDS), bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), circulatory failure and umbilical artery blood gases were recorded .

Also in the study of (Raja et al., [17]., they evaluated Use of Injection Solcoseryl for the treatment of oligohydramnios, doppler evaluation of uterine arteries resistance index (RI) improved significantly after Solcoseryl Administration in pregnant women with IUGR. They concluded that Solcoseryl is the drug of choice in pregnant women with IUGR, especially after twenty eight week of gestation. They also added The drug hemodialysate (solcoseryl) may be used confidently for the IUGR babies in mother during antenatal period. It improved APGAR score. It may help in fetal lung maturity but this needs further research.

Solcoseryl is a protein-free haemodialysate and contains a large number of low-molecular components of cells and serum of calf blood (dialysis/ultrafiltration, cut-off 5,000 Da), which until now have only partly been characterized chemically and pharmacologically (El-Mesallamy et al. [18].

They concluded that There was significant improvement in those who receive solcosery [19]. While in comparing sildenafil citrate versus LMWH, reported that, The neonatal BW in LMWH group was higher than SC group ($p < 0.000$) with a longer time from randomization till delivery, LMWH group had significant improvement in Ut A PI, UA PI, and MCA PI compared with SC treated group with p values 0.005, <0.000001, and 0.014, respectively.

In a controlled, open-labeled study done by [20], included 94 women with gestational hypertension and 30 healthy women enrolled at 24 to 26 weeks gestation. Doppler evaluation of uterine arteries resistance index (RI) was performed before and after a two-week course of LMWH (enoxaparin, 4000 IU/d, in 56 hypertensive patients) or no treatment (38 hypertensive women and 30 healthy controls). There was a significant decrease of uterine artery RI after LMWH ($p < 0.001$, paired Student's t-test), whereas the untreated hypertensive patients and the healthy control group showed no change between the two Doppler evaluations.

Abheiden et al., [21].The effect of heparin therapy on uteroplacental circulation is less clear. In a small open-label study of women with gestational hypertension, treatment with LMWH reduced the uterine artery resistance index. However, more sustained use of LMWH in a randomized control trial of LMWH and aspirin vs aspirin alone found no differences in uterine artery Doppler resistance index at 22-24 weeks or in umbilical artery Doppler pulsatility index at 22-24 weeks and later gestational ages.

They concluded that there was significant improvement in those who receive LMWH. In the study of [22]. They have investigated the effects of sol- coseryl therapy in a comparative study of pregnancies with growth retardation diagnosed by ultrasound measurement of hPL in maternal serum and amniotic fluid, measurement of oestriol in maternal serum and urine, and cardiotocography. Twenty-seven patients were treated with daily intravenous infusion of solcoseryl in addition to bedrest; 92% of the patients delivered infants with birthweights above the 10th centile. Twenty-five women were treated with bedrest alone; 30% delivered infants above the 10th centile.

DODD et al., [23]. The use of low molecular weight heparin improve maternal and perinatal outcomes in cases at risk for placental insufficiency has been extensively studied in the past years on the assumption that heparin prevent placental infarctions with subsequent increased placental perfusion heparin showed a significant increase in fetal AC, EFW as well as acceptable changes in Doppler indices (p-values <0.05). LMWH prophylactic role has been suggested. They concluded that there were significant improvement in birthweights with improvement in Doppler US.

The umbilical artery (UA) was the first vessel to be studied by Doppler ultrasonography. By about 15 weeks of gestation, diastolic flow can be identified in the UA. With advancing gestational age, the end-diastolic velocity increases secondary to the decrease in placental resistance. This is reflected in decreases in the S/D or PI. As the chorionic vascular bed undergoes an atherosclerotic-like process, local ischaemia and necrosis results. The Umbilical Artery shows increasing impedance that initially blunts forward flow during diastole, and ultimately reverses it at a later stage. These findings have been associated with adverse perinatal outcome. Once reversal of diastolic flow is identified, administration of steroids for fetal lung maturity in the premature fetus and delivery must be considered [24].

Middle cerebral artery (MCA) is another vessel well characterized by Doppler and has been shown to be affected by IUGR as well. MCA normally exhibits low amplitude of diastolic flow which increases in the presence of fetal hypoxia as a marker of cerebral vasodilation. This most commonly represents a later stage in the hypoxic process and typically occurs after changes in the uterine artery[25].

Dhand et al. [26] compared MCA Doppler indices with umbilical artery Doppler indices in a prospective study of 121 women of which 71 were high risk women with growth restricted fetuses and 50 women had healthy fetuses. The predictive value of Doppler PI for detecting abnormal fetal outcome was 94% in MCA as against 83% for umbilical artery. The sensitivity was 71% for MCA versus 44% for umbilical artery. Thus, the authors concluded that MCA Doppler indices were a better predictor for fetal outcome in IUGR when compared with umbilical artery in terms of sensitivity and predictive value.

Solcoseryl thus promotes the re-functionalization of hypoxia and/or lack of substrate of reversibly damaged tissue and speeds up as well as improves the quality of the healing of lesions [27].

Systemic administration calves' blood HD solcoseryl significantly accelerated the rate of diabetic wound healing and would open the possibility of their future use in regenerative medicine [28].

Unfractionated heparin and lowmolecular-weight heparin (LMWH) are commonly used in pregnancy for thromboprophylaxis and the treatment of venous thromboembolism. More recently LMWH is preferred to unfractionated heparin and appears safe and effective for these indications.28 Unfractionated heparin and LMWH do not cross the placenta29 and thus pose little direct risk to the fetus. Initial interest in heparins to prevent placental pathology centered on their anticoagulant properties and presumed ability to prevent placental thrombosis and subsequent infarction leading to miscarriage. In vitro and in vivo data suggest heparins have a variety of other biological properties including antiinflammatory,30 complement inhibition,31 and antitumor32 actions as well as being proangiogenic [29].

One of the challenging areas currently facing the obstetricians is management of IUGR. There is little doubt that these fetuses experience not only increase rates of perinatal morbidity and mortality but also higher complications in adult life. Some 30 per cent of sudden infant deaths syndrome (SIDS) cases were SGA at birth and the overall infant mortality of the infants suffering from IUGR is eight fold increase as the normal grown infant [30].

There are no proven treatments of FGR that will improve fetal growth or outcome once it is diagnosed. The only intervention clinicians can offer is iatrogenic preterm birth with timely administration of maternal corticosteroids and magnesium sulphate to improve neonatal outcome after early preterm birth. Several potential new therapies such as Solcoseryl and LMWH are on the horizon. It is important that clinicians wait for the results of appropriately designed and powered randomized controlled trials specific to FGR, which include information on meaningful longer-term outcomes before extrapolating positive preclinical and early clinical study findings into clinical practice [31].

From all the aforementioned data we can conclude that, The use of Solcoseryl and LMWH in pregnancies with IUGR is associated with a significant increase in neonatal BW, gestional age at delivery, and improvement in fetoplacental blood flow, with less maternal and neonatal complications. Further studies should be done on the role of Solcoseryl and LMWH in IUGR fetuses as regarding Doppler and clinical out comes.

5. CONCLUSIONS

In this study, solcosery and LMWH I administration in IUGR fetuses enhance Doppler indices, promote significant increase in Gestational age so increase neonatal birth weight.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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