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Original Research

Comparison of the Effect of Injection Enoxaparin Versus Conventional Treatment on Amniotic Fluid Index in Borderline Oligohydramnios in Third Trimester of Pregnancy: A Randomized Control Trial in a Tertiary Care Hospital

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Abstract

Background: Oligohydramnios is defined as amniotic fluid index (AFI) less than or equal to 5cm. A borderline AFI has been defined as an AFI of 5.1cm to 8cm. The incidence of borderline AFI compared with a normal AFI (8.1cm to 18cm) is 6% to 44% in different studies. A decrease in amniotic fluid leads to serious complications for the mother and fetus. The study objective was to evaluate if an injection of Enoxaparin improves the amount of liquor in oligohydramnios in the third trimester of pregnancy.

Methodology: A randomized controlled trial was conducted at a tertiary care obstetric center, involving a total of 130 participants. Inclusion criteria include participant in 3rd trimester of pregnancy, singleton pregnancy, intact amniotic membranes, and no known medical disorder. Patients with multiple pregnancies, ruptured amniotic membranes, anomalous fetuses, and known medical disorders were excluded. These participants were divided into two groups, each consisting of 65 participants. Group A received conventional treatment (intravenous fluid, tablet Aspirin, and rest in lateral position), while Group B received an injection of enoxaparin in addition to conventional treatment. AFI measurements were performed in the radiology department by radiologists using standard 4 quadrant measurements, twice weekly after the initiation of the treatment. The weight of the baby noted at birth and admission to neonatal intensive care was noted to assess the health of the neonate. Data was analyzed on SPSS (statistical package for social sciences) version 23.

Results: In group A, the AFI increased after treatment in 47(72.3%) patients, remained static in 6(9.2%) patients, and decreased in 12(18.4%) patients. Whereas in group B, AFI increased in 31(68.8%) patients and decreased in 14(31.3%) patients, p= 0.334.

Conclusion: The findings in the current study did not demonstrate any significant effect of the use of injection enoxaparin in improving borderline oligohydramnios. Further research is needed to apply this research to the general population

Keywords: Third Trimester of Pregnancy, Oligohydramnios, Injection Enoxaparin, Conventional Treatment, Mode of Delivery, AFI.

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Introduction

Oligohydramnios is defined as amniotic fluid index (AFI) less than or equal to 5 cm. [1,2,3] A borderline AFI has been defined as an AFI of 5.1 cm to 8 cm. [4] The incidence of borderline AFI compared with a normal AFI (8.1 cm to 18 cm) ranges from 6% to 44% in different studies, with the overall incidence being 12%.[4] Amniotic fluid is present from the formation of the gestational sac. In the first half of pregnancy, it is produced from maternal plasma and passes through the fetal membranes by hydrostatic and osmotic forces. When fetal kidneys begin to function around 16 weeks, fetal urine also contributes to the amniotic fluid.[5]

One of the most important components of a normal pregnancy is an appropriate amount of amniotic fluid. The effect of oligohydramnios on fetal and maternal outcomes is significant. It can cause fetal pulmonary hypoplasia, cord compression, fetal growth restriction, intrauterine fetal demise, low APGAR (appearance, pulse, grimace, activity, respiration) score, Neonatal Intensive care Unit (NICU) admission, and neonatal mortality. Maternal complications such as prolonged labour as well as increased incidence of caesarean sections can occur. [6,7]

Despite years of investigations, the regulation of amniotic fluid and its composition remains incompletely understood. Several maternal, fetal, and placental conditions are responsible for this condition. Many factors affect the amniotic fluid volume. The mother's blood volume plays an important role in maintaining the amniotic fluid volume [8].

Some studies have suggested that oligohydramnios can be linked to placental insufficiency leading to decreased blood flow to the fetal kidneys and decreased urine production which is the ultimate source of amniotic fluid in the third trimester. One of the major causes of this placental insufficiency is inappropriate coagulation activation. This forms the foundation for the effectiveness of anticoagulant therapy, such as enoxaparin, a type of low molecular-weight heparin. This treatment has demonstrated significant success in reducing the occurrence of these complications.[9] Researching improved management options for oligohydramnios is crucial due to its devastating effects on both maternal and fetal health.

This study was planned to evaluate the role of enoxaparin and conventional treatment (low-dose aspirin, intravenous fluid, and rest in lateral position) versus conventional treatment alone in improving the AFI in women with borderline oligohydramnios after 28 weeks of gestation in our population.

Material and Methods:

This randomized controlled trial (parallel group) was initiated following approval from the ethical committee of NESCOM (National Engineering and Scientific Commission) Hospital Islamabad. The sample size was calculated using the WHO sample calculator. The trial was conducted from August 01, 2021, to July 31, 2022. The study enrolled patients from the Obstetrics Outpatient Department. Inclusion criteria were, the participants who were at or after 28 weeks of gestation and exhibited borderline oligohydramnios in singleton pregnancies, intact membranes, and no known medical disorder. Exclusion criteria include, patients with multiple gestation, fetuses with anomalies, ruptured membranes, and known medical disorders at the time of enrollment were excluded from the study. Informed consent was obtained from all the participants. Comprehensive history-taking and examinations were conducted, and the amniotic fluid index (AFI) was measured by assessing amniotic fluid in four quadrants and aggregating the measurements. Ultrasonography was done in the Radiology Department by a radiologist. Two groups were established: Group "A" (control group) and Group "B" (interventional group). Group "A" received conventional treatment for oligohydramnios, which included a daily dose of 75 mg tablet loprin, intravenous hydration with 5% dextrose water (1000 ml daily), and increased oral fluid intake of up to 2000 ml daily. Each participant in Group "B" was administered enoxaparin 40 mg subcutaneously daily

in addition to the conventional treatment. The allocation of the patients was done by simple randomization of patients between Group "A" and Group "B." Patients were recruited in each group by simple random method. Randomization is done by a trained medical officer. Both groups were subjected to AFI monitoring twice weekly, until delivery. The mode of delivery was recorded. The weight of the neonate was noted. The neonate is shifted to the Neonatal Intensive Care Unit (NICU) or handed over to the mother also recorded to assess the health of the neonate.

Statistical analysis: The data was analyzed with Statistical Package for Social Sciences(SPSS) version 23. Continuous variables were expressed as mean ± standard deviation and categorical data was recorded as percentages. Student T-test and Chi-square test were applied to compare the results between the two groups. A p-value of ≤ 0.05 was considered statistically significant.

Results

During the study period, a total of 1030 deliveries were recorded. Among these, 130 (12.6%) patients were diagnosed with oligohydramnios. A total of 130 patients were included in the study, with 65 patients assigned to each group. In Group A, 65 patients received daily intravenous fluid along with 75 mg of tablet Aspirin and consumed 2000 ml of oral fluids. In Group B, patients received a daily subcutaneous injection of 40 mg enoxaparin, in addition to the conventional treatment administered to Group A. Both groups showed no bias in terms of amniotic fluid index (AFI) with p-value=0.261.
The average age of patients in group A was 29.79±4.3 years and in group B was 29.25±3.2 years, there was no statistically significant difference in age between the two groups. The average gestational age in group A was 34.4±2.52 weeks and in group B it was 32.09±2.70 weeks which was significantly low with a p-value <0.0001.

Out of 110 patients, regarding parity, 51(46.6%) patients were in their first ongoing pregnancy and 29(26.4%) were in their 3rd ongoing pregnancy. The maximum parity reported was 5. Patients with 2nd,3rd and 4th n going pregnancy were 15(13.6%),16(14.5%) and 17(15.5%) respectively. The maximum gravidity was reported as 8 in our study. The majority of cases, 78(70.9%), reported no miscarriage, while 17(15.45%) reported experiencing it once. The maximum number of miscarriages reported was 7. The important risk factors identified included anaemia which was present in 28(43%) women in group A and 19(42.2%) women in group B while gestational diabetes mellitus was present in 3(4.6%) women in group A and 1(2.2%)woman in group B. Other risk factors elicited included pregnancy-induced hypertension, anti-phospholipid syndrome, chronic hypertension, and intra-hepatic cholestasis. Idiopathic oligohydramnios were found in 29(44.6%) patients in Group A and 19(42.2%) patients in Group B.

Table 1. Risk factors in the study population.

Risk factors	Group A Frequency(%) N=65	Group B Frequency(%) N=45	Total
Idiopathic	29 (44.6%)	19 (42.2%)	48 (43.6%)
Anaemia	28 (43%)	19 (42.2%)	47 (42.7%)
GDM	3 (4.6%)	1 (2.2%)	4 (3.6%)
IHCS	1 (1.5%)	1 (2.2%)	2 (1.8%)
APS	0 (0%)	1 (2.2%)	1 (0.9%)
Ch. HTN	1 (1.5%)	1 (2.2%)	2 (1.8%)
PIH	3 (4.5%)	3 (6.6%)	6 (5.4%)

IV=intravenous, GDM=gestational diabetes mellitus, IHCS=intrahepatic cholestasis, APS=antiphospholipid syndrome, Ch.HTN=chronic hypertension, PIH=pregnancy induced hypertension.

The results shown in Table 2, upon admission 43(66.2%) patients in Group A had an AFI of 7-8 cm whereas in Group B, patients with an AFI of 7-8cm accounted for 25(55.6%), p-value=0.261 that is not statistically significant. The proportion of the patients having AFI greater than 7 cm at delivery was significantly different between the two groups, with a p-value of 0.026. In the present study, 48(73.8%) patients in group A had an AFI greater than 7cm at delivery, whereas in group B, only 23(53.3%) patients had an AFI greater than 7cm. However, in group A, an increase in AFI after treatment was observed in 47(72.3%) patients, the AFI remained static in 6(9.2%) patients and it decreased in 12(18.4%) patients. On the other hand, in group B, an increased AFI was noticed in 31(68.8%) patients, and a reduction was observed in 14(31.3%) patients. The P value for change in AFI after treatment is 0.334.

Table 2 - Comparison of AFI in Group A and Group B.

Variable		Group A Frequency (%)	Group B Frequency (%)	P value
AFI at admission	5- 7cm	22(33.8%)	20(44.4%)	0.261
	7-8cm	43(66.2%)	25(55.6%)	
AFI at delivery	5- 7 cm	17(26.2%)	21(46.7%)	0.026
	7-8 cm	48(73.8%)	24(53.3%)	
Change in AFI after treatment	decreased	12(18.4%)	14(31.1%)	0.334
	static	6(9.2 %)	0(0.00%)	
	increased	47(72.3%)	31(68.8%)	

AFI=amniotic fluid index

Table 3 explains that the average fetal weight in group A is slightly higher, measuring (2.67±0.357) kg, compared to group B where the average fetal weight is (2.58±0.54) kg, with a p-value of 0.288. However, the two groups did not show significant differences in terms of IUGR (intrauterine growth Restriction), mode of delivery, risk factors, and NICU (neonatal intensive care unit) admission.

Table 3. Post-treatment qualitative characteristics of the patients

Variable		Treatment		
		Group A Frequency (%)	Group B Frequency (%)	P value
IUGR	Absent	33(50.8%)	23(51.1%)	0.972
	Present	32(49.8%)	22(48.9%)	
Mode of delivery	LSCS	51(78.5%)	38(84.4%)	0.432
	SVD	14(21.5%)	7(15.6%)	
Risk factors	None	29(44.6%)	19(42.2%)	0.966
	Anaemia	28(43.15)	20(44.4%)	
	Others	8(12.3%)	6(13.3%)	
NICU Admission	No	44(67.7%)	32(71.1%)	0.703
	Yes	21(32.3%)	13(28.9%)	

IUGR=intrauterine growth restriction, NICU=neonatal intensive care unit, SVD= spontaneous vertex delivery, LSCS= lower segment caesarean section

Discussion

Healthcare professionals are always seeking innovations to improve patient management. The adequacy of amniotic fluid in the mother's womb, which nurtures the developing fetus, is of utmost importance. Its reduction critically affects fetal well-being. The use of injection enoxaparin in cases of oligohydramnios aims to prolong pregnancy by enhancing the AFI or preventing further deterioration.

Amniotic fluid plays a pivotal role in fetal development and serves as a determinant of fetal morbidity. This can manifest as prematurity, low birth weight, respiratory distress, NICU (neonatal intensive care unit) admission, and neonatal morbidity.

During the literature review, the author was unable to locate any research that directly compared the effects of the injection of enoxaparin with maternal hydration. Existing studies tend to focus solely on either maternal hydration or enoxaparin individually.

This study revealed that the improvement in the amniotic fluid index was more significant in group A who received conventional treatment alone, when compared to the patients who received Injection enoxaparin along with conventional treatment. However, this increase in AFI was not significant. It was noticed in this study that the use of injection enoxaparin did not help in improving AFI when compared to conventional treatment alone.

A study conducted in Iran,[10] yielded similar results to the present study. In their research, they exclusively utilized intravenous hydration for treating oligohydramnios, and they observed a significant improvement in amniotic fluid index (AFI) through hydration alone. Furthermore, several other studies conducted across various regions globally also reported a beneficial effect of maternal hydration in enhancing AFI. [11,12,13] This study further reinforces the notion that maternal hydration contributes to the improvement of AFI and, consequently, improves fetal outcomes.

In contrast to our findings, a study conducted in Faisalabad,[14] reported a significantly superior outcome with the use of injection. However, it is important to note that their primary variables were focused on intrauterine growth restriction (IUGR) and oligohydramnios, and they compared the effect of injection of enoxaparin with aspirin. Another study conducted in Lahore, Pakistan [15] also demonstrated the beneficial impact of enoxaparin on fetal outcomes. It's worth mentioning that their study initiated the injection of enoxaparin at 16 weeks of gestation. In comparison, our current study administered an injection of enoxaparin at 28 weeks or later, once the patient had already developed oligohydramnios..

In this study, around 80% of patients with oligohydramnios were delivered by lower-segment caesarean section. Similar results were obtained in a study done in China [16] and in India [17], they had (84%) and (81%) lower segment caesarean section rates in their study respectively.

In the present study, the admission into the NICU (neonatal intensive care unit) was 28% and 32% in the intervention group versus the control group respectively. This NICU admission rate was almost similar to a study conducted by Sandhyasri and colleagues [18] in India, where 24% were NICU (neonatal intensive care unit) admissions, and another study done in Bangladesh [19] had 34%, Nepal [20] had 39% NICU admission with oligohydramnios.

Conclusion

The findings of the current study indicate that the use of injection enoxaparin did not demonstrate significant improvement in the amniotic fluid index (AFI) compared to conventional treatment. Therefore based on the results obtained, it can be concluded that injection enoxaparin does not appear to be beneficial for enhancing AFI in the context of this study. Further research and exploration may be necessary to better understand the potential role of injection enoxaparin or other alternative treatments in managing AFI levels effectively.

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