Comparative Study Between Effect of Sildenafil Citrate and Acetylsalicylic Acid and Clexane on Uteroplacental Perfusion in Intrauterine Growth Restriction

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Comparative Study Between Effect of Sildenafil Citrate and Acetylsalicylic Acid and Clexane on Uteroplacental Perfusion in Intrauterine Growth Restriction

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Abstract

Background: Numerous studies suggested that since sildenafil citrate enhances the endothelial function of myometrial arteries in these women, it may provide a viable treatment approach to increase uteroplacental blood flow in pregnancies complicated by FGR.

Aim and objectives: To compare how acetylsalicylic acid, clexane, and sildenafil citrate affect uteroplacental perfusion in intrauterine growth restriction.

Subjects and methods: Three pregnant woman groups were involved in the study, and a computer was randomly assigned to the groups. Group 1 consists of thirty pregnant women who will get treatment twice daily for six weeks with sildenafil citrate tab 20 mg (Respatio, MPI Company). Group 2 consists of thirty pregnant women who will receive treatment for six weeks with a 40 mg syringe of enoxaparin sodium (Clexane, Sanofi Comp.) administered subcutaneously once daily. Group 3: 30 expectant mothers will receive treatment with a 75 mg tab of acetylsalicylic acid (Aspirin, ID comp.) once a day for six weeks. Then, after the medicine was administered to each group and across groups, determine the primary endpoint Doppler changes (pulsatility index (PI), resistance index (RI), or systolic/diastolic (S/D) ratio) that happened in each of the vessels tested (uterine, umbilical, or MCA): delivery challenges, neonatal morbidity and death, further related abnormalities, and newborns' APGAR rating.

Result: Regarding estimated fetal weight (EFW) upon admission, there were no appreciable variations between the groups under study (P>0.05). After six weeks, the group taking sildenafil citrate experienced a more significant increase in EFW than the other groups. Additionally, among the three groups under study, EFW increased significantly after six weeks compared to admission (P<0.001).

Conclusion: Our findings indicate that the combination of sildenafil, heparin, and aspirin is more effective in treating growth-restricted fetuses than any medication alone, as seen by improvements in fetal growth indices and a decrease in NICU hospitalizations. While all treatment choices are determined to be equally effective, sildenafil has a more significant number of adverse effects even when it is tolerated.

Keywords: Comparative study; Sildenafil citrate; Acetylsalicylic acid; Clexane; Uteroplacental perfusion

1. Introduction

Uteroplacental blood flow plays a significant role in the transfer of nutrients from the mother to her fetus, and it rises significantly in the second and third trimesters of pregnancy. Seven to fifteen percent of pregnancies are complicated by fetal growth restriction (FGR), which increases the risk of neonatal morbidity and death when it appears early and in a severe form. The fetal growth rate (FGR) prediction and the identification of their reduction or alteration in impaired pregnancies can be achieved through an antenatal estimate of placental size, uteroplacental blood flows, and expression of angiogenic and vasoactive factors. Encouraged medical professionals to propose using therapeutic drugs that specifically targeted placental blood flow to lessen these harmful effects.
Several novel vasodilator medications have been proposed to improve blood flow to tissues. Among these is sildenafil citrate, a selective inhibitor of the phosphodiesterase specific to type V cyclic guanosine monophosphate (cGMP). Sildenafil increases the effects of nitric oxide by blocking the enzyme phosphodiesterase type 5, which breaks down cGMP. When sildenafil is taken, cGMP levels stay high, which causes vascular relaxation and increased uterine blood flow.3

PGI2 promotes vasodilation and decreases platelet adhesiveness, while TXA2 acts as a vasoconstrictor and enhances platelet aggregatation and adhesion to vascular walls. The PGI2/TXA2 ratio appears essential in pregnancy and the development of the functioning uteroplacental unit.3

Recently, antiplatelet treatment, such as low-dose aspirin therapy, has been effective in preventing the development of PIH and preeclampsia. TXA2 breaks down spontaneously into an inactive, stable substance, TXB2. Another stable, inactive metabolite, malondialdehyde (MDA), is formed via the same pathway. TXB2 and MDA are produced in approximately equimolar quantities.5

Oxyparin sodium is the active component of Clexane. Clexane is used to stop clots from growing larger or from developing again after medical procedures or illness. The usual method of administering clexane is by subcutaneous injection. Additionally, it can be injected intravenously or into the tubing of a dialysis machine.6

Clexane mainly acts by activating antithrombin through its mode of action. Clexane and antithrombin combine to generate a complex. This complex experiences a conformational shift; in its modified state, the primary mechanism of action is the inhibition of factor Xa (FXa).7

This study aims to compare trans-Jugular Access versus Transfemoral Access in Endovascular embolization in the Treatment of Pelvic Congestion Syndrome as regards complications, cannulation of right and left ovarian veins, and the most accessible access.

2. Patients and methods

This comparative study included 90 pregnant women diagnosed with IUGR who attended outpatient obstetrics and gynecology clinics of Al-Azhar University Hospitals from March 2021 to June 2022.

Samples of pregnant women were collected using a random systematic method without favoring one group over another. The included pregnant women were diagnosed with IUGR by a lag of 2 weeks or more between current biometric measures and documented pregnancy dating in the first trimester or estimated fetal weight less than the tenth percentile for gestational age.

Also, Pregnancy dating was calculated through one of the following: 1) sure accurate LMP preceded by three regular cycles or 2) documented 1st trimester ultrasound between 8 to 13 weeks.

Ethical consideration

Clexane mainly acts by activating antithrombin through its mode of action. Clexane and antithrombin combine to generate a complex. This complex experiences a conformational shift; in its modified state, the primary mechanism of action is the inhibition of factor Xa (FXa):

Educating patients about the significance of the study will increase their cooperation and level of interest. The privacy of the patient’s information was ensured. The patients were free to withdraw from the study at any time without having to give a reason and at the meeting whenever they chose. Their written consent was obtained after the patients were informed about the procedures.

After the study, all samples were disposed of and never again used in experiments or additional research. Every patient chosen by the inclusion and exclusion standards

Inclusion criteria: At 24 weeks gestation or more, Singleton gestation diagnosed IUGR with two weeks or more lag from documented dating and normal umbilical morphology (two arteries and one vein).

Exclusion criteria: Pregnant women who smoked or drank alcohol, multifetal pregnancies, and the existence of fetal congenital disabilities.

Sample size

The sample size for this study was determined based on research conducted by Mousa et al.8 The sample size was determined using Epi Info STATCALC with the following assumptions: 95% two-sided confidence level, 80% power, 5% error, and an odds ratio of 1.115 were computed. The final maximum sample size that could be obtained from the Epi-Info output was 82 cases. The sample size was raised to 90 pregnant women to account for potential dropout cases during follow-up.

All pregnant women in this study were randomized and divided by the computer into three groups: Group 1 included 30 pregnant women treated using acetylsalicylic acid (Aspirin, CID comp.) 75 mg tab once daily for six weeks. Group 2: included 30 pregnant women treated using enoxaparin sodium (Clexane, Sanofi comp.) 40 mg syringe by SC route once daily for six weeks. Group 3 included 30 pregnant women treated using sildenafil citrate tab 20 mg (Respatio, MPI Company) twice daily for six weeks.

Methods

Every expectant participant in this trial underwent a complete history taking, which includes the patient’s personal history, medical
history, surgical and medical history, family history, obstetric history, menstrual history, and any complaints. The complete physical examination comprised vital signs (heart rate, temperature, blood pressure, and respiration rate) and symptoms of jaundice, pallor, cyanosis, and enlarged lymph nodes.

Every pregnant woman was evaluated for gestational age. She was determined by calculating her last consistent menstrual cycle and verifying it with an ultrasound examination (by GE Voluson P6 Ultrasound) during the first trimester. She also had Hb level, CBC, hematocrit (Hct), and red blood cell (RBC) investigations in the lab.

Using a transabdominal probe operating at 3.5 MHz, an ultrasound examination that included measurements of the fetal anthropometrics was carried out. Using software supplied by the ultrasonography equipment, the cross-sectional area of the umbilical cord and umbilical vessels was measured in a free loop of the umbilical cord. The cross-sectional area of Wharton’s jelly was determined by deducting the ship’s location from the cord’s overall area. The woman’s bladder was complete when the transabdominal examination was performed to measure the uterine artery (Ut A) in the second trimester. The U/S beam was pointed toward the pelvis and the lateral side of the uterus, and the probe was positioned roughly 2-3 cm inside the iliac crests. Color flow mapping was used to identify each uterine artery at the point where it appeared to cross over with the external iliac artery.

Before the collateral branches emerged, at the main trunk of the uterine artery, a sample that was roughly 1 cm distilled to the crossover with the external iliac artery-Doppler velocities were measured. With the least amount of insonation angle feasible, the pulsed Doppler gate was positioned over the vessels and adjusted to 2 mm.9,10

The cord vessels were seen in a longitudinal segment in a free loop without fetal breathing or movement to acquire a UA Doppler. Only waveforms with a high signal-to-noise ratio were acceptable, and care was taken to prevent the waveform from becoming contaminated with extraneous signals, either above or below the baseline. At least three arterial waveforms were acquired in a row.11,12

To document the fetal MCA, Doppler acquired and magnified an axial portion of the brain, including the thalami and sphenoid bone wings. The proximal MCA and the circle of Willis were located using color flow mapping. The vessel and the U/S beam were oriented parallel. We did not measure when the fetus was breathing, hiccupping, or moving.

Next, the pulsed-wave Doppler gate was positioned near the origin of the internal carotid arteries in the proximal part of the MCA. As near to zero as feasible was maintained as the angle between the U/S beam and the blood flow direction. Every effort was made to prevent the fetal head from receiving needless pressure. Waveforms were captured for at least three and no more than ten consecutive times.13,14
Uterine artery doppler

Figure 1b. Ultrasound pictures of Doppler study on umbilical, MCA, and uterine artery

Primary outcome

Following drug administration in each group and between groups, Doppler alterations (pulsatility index (PI), resistance index (RI), or systolic/diastolic (S/D) ratio) occurred in each of the vessel tested (uterine, umbilical, or MCA).

Statistical analysis

The standard computer programs used to tabulate and statistically evaluate the results were MICROSOFT EXCEL 2019 and SPSS V.25 for MICROSOFT WINDOWS 10.

Descriptive statistics: This comprises: For quantitative data, the data was described using mean (±) SD, and for qualitative data, frequency and percentage. The total number of observations is the mean divided by the total number of observations. At the same time, the standard deviation measures the degree of dispersal of different types around their mean.

Analytical statistics: This comprises: For a normally distributed quantitative variable, the student’s t-test was employed to collectively indicate any significant difference between the two groups. To compare the same groups in terms of quantitative variables (mean ± SD), a paired t-test was employed. Chi-squared (χ²) is a statistical tool used to compare one or more groups concerning one qualitative characteristic. One method ANOVA in F For a normally distributed quantitative variable, a one-way analysis of variance (ANOVA) is a single test used to collectively indicate the presence of any significant difference between many groups. A difference was deemed necessary if the p-value was less than 0.05 and not crucial if the p-value was more substantial than 0.05. P-value < 0.001, however, was regarded as highly important.

3. Results

Table 1. Socio-demographic data among the studied groups.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>ACETYLsalicylic ACID (N=30)</th>
<th>ENOXAPARIN SODIUM (N=30)</th>
<th>SILDENAFIL CITRATE (N=30)</th>
<th>F</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE/YEAR</td>
<td>25.90±4.69 (20.00-33.00)</td>
<td>27.63±4.57 (24.00-35.00)</td>
<td>28.23±7.12 (17.00-39.00)</td>
<td>1.254</td>
<td>0.234</td>
</tr>
<tr>
<td>GESTATIONAL AGE (WKS.) AT ADMISSION</td>
<td>30.50±1.93 (28.00-33.00)</td>
<td>28.25±3.65 (25.00-33.00)</td>
<td>31.00±2.26 (28.00-34.00)</td>
<td>2.732</td>
<td>0.085</td>
</tr>
<tr>
<td>AFT 6 WEEKS</td>
<td>36.50±1.93 (34.00-39.00)</td>
<td>34.25±3.65 (31.00-39.00)</td>
<td>37.00±2.26 (34.00-40.00)</td>
<td>2.732</td>
<td>0.085</td>
</tr>
<tr>
<td>GRAVIDA</td>
<td>2.17±0.38 (2.00-3.00)</td>
<td>2.42±0.74 (1.00-4.00)</td>
<td>2.30±0.47 (2.00-3.00)</td>
<td>2.435</td>
<td>0.113</td>
</tr>
<tr>
<td>PARITY</td>
<td>1.17±0.38 (1.00-2.00)</td>
<td>1.81±0.81 (1.00-4.00)</td>
<td>1.30±0.47 (1.00-2.00)</td>
<td>2.541</td>
<td>0.102</td>
</tr>
<tr>
<td>MOOD OF DELIVERY N/V C/S</td>
<td>11 (36.67%)</td>
<td>15 (50.0%)</td>
<td>12 (40.0%)</td>
<td>χ²</td>
<td>0.553</td>
</tr>
</tbody>
</table>
| NVB: Normal Vaginal Birth. C.S: Caesarean section. F: ANOVA F test. *Significant. This table shows that, there were no significantly differences among the studied groups regarding age, gestational age, gravida, parity and mood of delivery (P>0.05).

Figure 2. Age, gravida and parity among the studied groups.
Table 2. Clinical data among the studied groups.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>ACETYLSAUCYLIC ACID (N=30)</th>
<th>ENOXAPARIN SODIUM (N=30)</th>
<th>SILDENAFIL CITRATE (N=30)</th>
<th>F</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEIGHT (KG) MEAN ±SD RANGE</td>
<td>74.23±7.39 (62.00-81.00)</td>
<td>76.30±1.70 (75.00-79.00)</td>
<td>74.96±11.21 (65.00-92.00)</td>
<td>0.539</td>
<td>0.585</td>
</tr>
<tr>
<td>HEIGHT (M) MEAN ±SD RANGE</td>
<td>1.65±0.13 (1.62-1.68)</td>
<td>1.62±0.14 (1.57-1.66)</td>
<td>1.68±0.16 (1.59-1.75)</td>
<td>1.325</td>
<td>0.234</td>
</tr>
<tr>
<td>BMI (KG/M²) MEAN ±SD RANGE</td>
<td>28.40±2.31 (23.05-30.39)</td>
<td>29.67±1.15 (26.23-31.22)</td>
<td>27.64±1.04 (22.86-32.74)</td>
<td>1.652</td>
<td>0.176</td>
</tr>
</tbody>
</table>


This table demonstrates that there were no appreciable variations in weight, height, or BMI across the groups under study (P>0.05).

Table 3. Bi-parietal diameter among the studied groups.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>ACETYLSAUCYLIC ACID (N=30)</th>
<th>ENOXAPARIN SODIUM (N=30)</th>
<th>SILDENAFIL CITRATE (N=30)</th>
<th>F</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPD (MM) US</td>
<td></td>
<td></td>
<td></td>
<td>2.490</td>
<td>0.103</td>
</tr>
<tr>
<td>AT ADMISSION MEAN ±SD RANGE</td>
<td>7.02±0.68 (6.20-7.70)</td>
<td>6.73±1.01 (5.80-7.90)</td>
<td>7.17±0.69 (6.40-8.20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AFTER 6 WEEKS MEAN ±SD RANGE</td>
<td>8.60±0.26 (8.20-8.80)</td>
<td>8.10±0.97 (7.20-9.20)</td>
<td>8.63±0.39 (8.20-9.20)</td>
<td>2.206</td>
<td>0.131</td>
</tr>
<tr>
<td>PAIRED T-TEST P-VALUE</td>
<td>19.799</td>
<td>18.984</td>
<td>11.726</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>


This table shows that, there were no significantly differences between the studied groups regarding Bi-parietal diameter (BPD) at admission and after 6 weeks (P>0.05). While, Bi-parietal diameter (BPD) was significantly increased after 6 weeks compared at admission among the three studied groups (P<0.001).

Table 4. Neonatal characteristics among the studied groups.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>ACETYLSAUCYLIC ACID (N=30)</th>
<th>ENOXAPARIN SODIUM (N=30)</th>
<th>SILDENAFIL CITRATE (N=30)</th>
<th>F</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEONATAL WEIGHT/G MEAN ±SD RANGE</td>
<td>2475±73 (2400-2550)</td>
<td>2525±70.8 (2450-2600)</td>
<td>2625±123.3 (2500-2750)</td>
<td>2.13</td>
<td>0.085</td>
</tr>
<tr>
<td>APGAR SCORE MEAN ±SD RANGE</td>
<td>5.5±0.3 (5-6)</td>
<td>6.5±0.4 (6-7)</td>
<td>6.5±0.1 (6-7)</td>
<td>0.77</td>
<td>0.401</td>
</tr>
<tr>
<td>MODE OF DELIVERY (NVD) (CS)</td>
<td>17 (56.67%)</td>
<td>16 (53.33%)</td>
<td>11 (36.67%)</td>
<td>X²=</td>
<td>0.119</td>
</tr>
<tr>
<td>NEONATAL ICU</td>
<td>4 (13.33%)</td>
<td>7 (23.33%)</td>
<td>3 (10%)</td>
<td>X²=0.250</td>
<td>0.702</td>
</tr>
<tr>
<td>NEONATAL DEATHS</td>
<td>1 (3.33%)</td>
<td>1 (3.33%)</td>
<td>0 (0%)</td>
<td>0.154</td>
<td>0.960</td>
</tr>
</tbody>
</table>

This table shows that, there were not significantly differences between the studied groups regarding Neonatal weight/g, APGAR score, Mode of delivery, Neonatal ICU and Neonatal deaths (P>0.05).
Table 5. Femur length among the studied groups.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>ACETYLSALICYLIC ACID (N=30)</th>
<th>ENOXAPARIN SODIUM (N=30)</th>
<th>SILDENAFIL CITRATE (N=30)</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT ADMISSION MEAN ±SD RANGE</td>
<td>FL (MM) US</td>
<td>5.25±0.54 (4.70-6.10)</td>
<td>4.85±0.88 (3.90-5.90)</td>
<td>5.20±0.46 (4.70-6.10)</td>
<td>2.393</td>
<td>0.112</td>
</tr>
<tr>
<td>AFTER 6 WEEKS MEAN ±SD RANGE</td>
<td>FL (MM) US</td>
<td>6.70±0.27 (6.30-7.00)</td>
<td>5.98±0.73 (5.20-6.80)</td>
<td>6.52±0.31 (5.90-6.80)</td>
<td>5.425</td>
<td>0.011*</td>
</tr>
<tr>
<td>PAIRED T-TEST P-VALUE</td>
<td>13.229</td>
<td>19.130</td>
<td>18.204</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>


According to this table, there were no discernible changes in femur length (FL) at admission between the groups under investigation (P=0.112). However, was considerably lower in the Enoxaparin sodium group after 6 weeks compared to the Acetylsalicylic acid group (P=0.008) and the Sildenafil citrate group (P=0.023). Conversely, femur length (FL) increased considerably in all groups after 6 weeks compared to entry (P<0.001).

Table 6. Head circumference (Hc) among the studied groups.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>ACETYLSALICYLIC ACID (N=30)</th>
<th>ENOXAPARIN SODIUM (N=30)</th>
<th>SILDENAFIL CITRATE (N=30)</th>
<th>F</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT ADMISSION MEAN ±SD RANGE</td>
<td>HC (MM) US</td>
<td>23.78±3.62 (18.70-28.00)</td>
<td>23.45±3.96 (19.80-28.00)</td>
<td>24.97±2.32 (24.20-29.60)</td>
<td>1.429</td>
</tr>
<tr>
<td>AFTER 6 WEEKS MEAN ±SD RANGE</td>
<td>HC (MM) US</td>
<td>31.43±0.80 (30.40-32.40)</td>
<td>28.90±3.45 (25.20-32.40)</td>
<td>31.00±1.64 (28.80-32.40)</td>
<td>3.224</td>
</tr>
<tr>
<td>PAIRED T-TEST P-VALUE</td>
<td>16.135</td>
<td>12.629</td>
<td>13.521</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>


The data indicates that there were no significant variations in head circumference (Hc) between the study groups when it came to femur length (Hc) upon admission (P=0.294) or six weeks later (P=0.057. W). Conversely, femur length (HC) increased considerably in all groups after 6 weeks compared to admission (P<0.001).

Table 7. Estimated fetal weight among the studied groups.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>ACETYLSALICYLIC ACID (N=30)</th>
<th>ENOXAPARIN SODIUM (N=30)</th>
<th>SILDENAFIL CITRATE (N=30)</th>
<th>F</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT ADMISSION MEAN ±SD RANGE</td>
<td>EFW (GM) US</td>
<td>1231.67±138.59</td>
<td>937.50±340.95</td>
<td>1060.0±122.6</td>
<td>3.913</td>
</tr>
<tr>
<td>AFTER 6 WEEKS MEAN ±SD RANGE</td>
<td>EFW (GM) US</td>
<td>2366.67±51.64</td>
<td>1712.50±860.54</td>
<td>2040.7±386.5</td>
<td>7.388</td>
</tr>
<tr>
<td>PAIRED T-TEST P-VALUE</td>
<td>14.789</td>
<td>5.757</td>
<td>11.99</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

There were not significantly differences between the studied groups regarding estimated fetal weight (EFW) at admission (P>0.05). While EFW was significantly increased after 6 weeks among Sildenafil citrate group more than other groups. Also, EFW was significantly increased after 6 weeks compared at admission among the studied three groups (P<0.001).

Table 8. Resistance index among the studied groups.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>ACETYLsalicylic Acid (N=30)</th>
<th>ENOXAPARIN Sodium (N=30)</th>
<th>SILENDAFIL CITRATE (N=30)</th>
<th>F</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADMISSION</td>
<td>0.62±0.043 (0.55-0.70)</td>
<td>0.60±0.02 (0.57-0.62)</td>
<td>0.59±0.01 (0.57-0.61)</td>
<td>8.472</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>AFTER 6 WEEKS</td>
<td>0.64±0.02 (0.63-0.67)</td>
<td>0.59±0.03 (0.54-0.62)</td>
<td>0.62±0.02 (0.60-0.65)</td>
<td>18.404</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>PAIRED T TEST</td>
<td>1.258</td>
<td>1.275</td>
<td>14.832</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>P-VALUE</td>
<td>0.170</td>
<td>0.222</td>
<td>&lt;0.001*</td>
<td>---</td>
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</tbody>
</table>


Resistance index at admission and after 6 weeks were significantly decreased among Acetylsalicylic acid group than Enoxaparin sodium and Sildenafil citrate groups (P>0.001). Also, resistance index was significantly decreased after 6 weeks compared at admission among Sildenafil citrate group (P<0.001).

4. Discussion

The present study showed that age was significantly increased among the sildenafil citrate group than in enoxaparin sodium and acetylsalicylic acid groups (P<0.001). Additionally, enoxaparin sodium group members had considerably higher gravida and parity than sildenafil citrate and acetylsalicylic acid group members (P<0.001). However, when it came to the mood of delivery and gestational age, there were no significant changes between the groups under study (p<0.05).

Our findings concurred with Shalaby’s investigation since they stated that the mother ages, pregnancy, parity, and pregnancy age did not differ significantly between the two study groups. The study comprised 50 patients receiving sildenafil therapy, 50 receiving heparin/low doses of aspirin, and 100 patients with fetal IUGR.

Also, Mousa et al. discovered no discernible difference between the heparin/low-dose aspirin B group and the Sildenafil A group. Based on parity, gestational age, gravidity, and mother age.

Our result revealed that the body mass index was considerably raised among the enoxaparin sodium group than in the Sildenafil citrate and Acetylsalicylic acid groups (P<0.001). However, there were no appreciable variations in Weight across the groups under investigation (P>0.05).

The current study found that after six weeks, the femur length of the Enoxaparin sodium group was considerably shorter than that of the acetylsalicylic acid and sildenafil citrate groups (P=0.011). However, there were no appreciable variations (P>0.05) in the study groups’ admission femur length, bi-parietal diameter, or bi-parietal diameter after six weeks. Conversely, there was a substantial increase in femur length and bi-parietal diameter at six weeks compared to admission (P<0.001).

This result, in agreement with the result obtained by Mohamed and Ali demonstrated that the difference in symphysis fundal height measurement between study groups is not statistically significant. Group A had an average estimated fetal weight of 1194.5 (±49.43 SD) with a range of 1117-1276, an average biparietal diameter of 5.82 (±0.61 SD) with a range of 5-7, and an average femur length of 4.81 (±0.96 SD) with a range of 3.2-6.7. The estimated fetal Weight in Group B was found to be 1190.5 (±46.23 SD) with a range of 1114-1271, the biparietal diameter was 5.9 (±0.66 SD) with a range of 5-7, and the femur length was 4.77 (±0.89 SD) with a range of 3.4-6.8. Between study groups, there is a non-significant change.

These results were consistent with Mousa et al. as they revealed that, in terms of fetal biometry (BPD, FL, AC, and EFW) by the US, there had been no discernible difference among the groups under study before the initiation of therapy. A non-significant difference was seen when comparing the two groups fetal biometry following the medication. Heparin/aspirin group (Group-B n=43; group-A n=40; Sildenafil.

After six weeks, the Enoxaparin sodium group in this study had a considerably smaller abdomen circumference than the Acetylsalicylic acid and sildenafil citrate groups (P<0.05). However, there were no appreciable variations in the groups under study’s admission abdominal circumference (P>0.05). Compared to admission, there was a substantial rise in abdominal circumference after six weeks (P<0.001).

There were no discernible changes in EFW upon admission between the groups under investigation in our study. However, after six weeks, the sildenafil citrate group experienced a much higher EFW than the other groups. Moreover, EFW increased significantly in all three of the tested groups after six weeks compared to admission.

Our results were close to those obtained by El-Shalakany et al.; there were no significant differences between the Sildenafil citrate and heparin groups regarding estimated fetal weight at
diagnosis. However, there was a substantial difference between the Sildenafil citrate and heparin groups regarding estimated fetal weight at delivery time. At the same time, the estimated fetal weight significantly increased at the delivery time compared to the time of diagnosis. Also, there was no significant difference between the Enoxaparin and the control groups regarding estimated fetal weight.

The present study shows that the resistance index at admission and after six weeks was significantly higher among the acetylsalicylic acid group than among the enoxaparin sodium and Sildenafil citrate groups. Also, the resistance index was considerably higher after six weeks than at admission among the sildenafil citrate group.

Similarly, Mohamed and Ali revealed significant changes among the two groups regarding RI and significant changes among studied groups regarding PI of UA. In the Sildenafil group, the mean RI Fetal middle cerebral artery was 0.73± 0.03 SD with a range of 0.68-0.78. In the aspirin group, the mean RI was 0.74± 0.03 SD with a range of 0.68-0.78. There is nonsignificant change among study groups. This result agrees with Dastjerdi et al., concluding that Doppler velocimetry index records mirror reduced placental bed vascular resistances after sildenafil administrations.

Another previous study by Singh and Saiyda reported that, Sildenafil, as a vasodilator, could be an alternative in the treatment of Intra Uterine Growth Retardation (IUGR) and preeclampsia by later normalization in velocimetric profile. Treatment with sildenafil citrate in the last third of gestation counteracts fetal growth retardation by favoring placental development and function and, thus, fetal growth. Administration of sildenafil citrate may have a potential benefit in pregnancies complicated by placental insufficiency and IUGR. Shirazi et al. concluded that enoxaparin had a good safety profile in our studied cases. Still, it didn't prolong pregnancy, increase fetal birth weight, or improve fetal outcomes, even in patients with impaired baseline Doppler findings. The heparin/Aspirin treatment group showed a longer duration of pregnancy than the sildenafil-treated group, also with significant side effects observed in the sildenafil-treated group.

5. Conclusion

Combining heparin and aspirin is more effective in treating growth-restricted fetuses than either drug alone, as evidenced by improved fetal growth metrics and a decrease in NICU admissions. While all treatment choices are determined to be equally effective, sildenafil has a more significant number of adverse effects even when it is tolerated and reduces neonatal morbidity and mortality caused by prematurity and low birth weight by neonatal weight improvement. When it comes to treating fetal limited growth, sildenafil is more beneficial than aspirin alone, improving the parameters related to the development of the fetus.

5.1 Recommendations

To determine whether comparable results are confirmed, more study is required. Ad hoc trials and more significant patient numbers should be designed for participants receiving treatment for uteroplacental perfusion in intrauterine growth restriction.

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Conflicts of interest

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References


SHALABY, H. Sildenafil Citrate versus Aspirin/Heparin Combination for Fetus growing Restriction: A Randomized Clinical Trial. Med. J. Cairo Univ. 2017;85(7), 2461-2467.


