EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 1
400-402
Year: 2020

ROLE OF LOW DOSE ASPIRIN AND LOW MOLECULAR WEIGHT HEPARIN IN UNEXPLAINED CASES OF RECURRENT PREGNANCY LOSS

***Dr. S. Bhanu Rekha, M.D**

Associate Prof., Dept. of Obstetrics & Gynaecology, SVS Medical College, Mahabubnagar, Telangana, India.

***Corresponding Author: Dr. S. Bhanu Rekha**
Associate Prof., Dept. of Obstetrics & Gynaecology, SVS Medical College, Mahabubnagar, Telangana, India.

Article Received on 30/10/2019 **Article Revised on 20/11/2019** **Article Accepted on 10/12/2019**

ABSTRACT

Objective: To assess the effectiveness of low dose Aspirin and low molecular weight Heparin in unexplained cases of recurrent pregnancy loss. **Materials and Methods:** This study was conducted in a private hospital in mahabubnagar from June 2017 to May 2019. A total of 40 pregnant ladies who had previous 2 and or more pregnancy losses in the early (before 20 weeks) or late (after 20weeks) pregnancy period were included in the study. These pregnant women were properly evaluated in regard to the history of previous period of gestation of loss, previous scans in regard to documentation of fetal pole and gestation, cardiac activity, anomaly scan and growth scan and any special investigations in previous pregnancies and present pregnancy. **Results:** 40 pregnant women with previous 2 and more unexplained pregnancy losses who were evaluated and found negative with major causes of pregnancy losses were treated with low dose aspirin and low molecular weight heparin till term. This could give us a 92% live birth rate which is quite satisfactory. **Conclusions:** Use of low dose aspirin and low molecular weight heparin seems to be a good choice of drugs in treating the unexplained recurrent pregnancy losses.

KEYWORDS: Recurrent pregnancy loss, low dose aspirin, Low molecular weight heparin.

BACKGROUND

Pregnancy is a boon to women, when they have an uneventful outcome and end up with a healthy neonate at the end of term pregnancy. This is not true in case of all pregnancies as few of the pregnancies do end up as abortions or preterm labours or stillbirths. This leads to mental agony to the aspiring mother to be as well as the entire family. After such recurring pregnancy losses for 2 and or more times, there is lot of anxiety to regarding to the entire family as well as expectations from the treating doctors. Women with such previous pregnancy losses should be evaluated properly with the history of pregnancy loss in respect to the gestational age, previous scans showing viable fetus, any infections in the past pregnancies and present, Hormonal evaluations like thyroid levels, Gestational Diabetes screening, Anti Phospholipid syndrome and Protein C and Protein S deficiencies, karyotyping of both Partners as well as previous Products of Conception was subjected to Karyotyping or Microarray, MRI of the Uterus to rule out any Uterine anomaly, preeclampsia, eclampsia apart from the routine antenatal investigations. In a town like Mahabubnagar with its feeding districts, many a times our patients can't afford beyond Microarray and any further analysis in respect to evaluation of recurrent pregnancy losses (RPL) so as to guide them during the next pregnancy. Hence there arises a need for managing these set of patients with minimum special investigations along with the routine antenatal tests to rule out the cause and start safe and empirical treatment to lessen the recurrence and anxiety associated with the current ongoing pregnancy.

AIMS AND OBJECTIVES

1. To identify, investigate and categorise the patients presenting with bad obstetric outcomes recurrently over a period of 2 years and pool up unexplained RPL.
2. To manage the patients with RPL and after evaluating with major identifiable causes and if found negative with common causes of RPL to start treatment as early as pregnancy confirmation with low dose Aspirin (75mg) daily once till 36 weeks and Lowest possible dose of Low Molecular weight Heparin (20mg) daily till term.

MATERIALS AND METHODS

This study was conducted in a private hospital from June 2017 to May 2019 over a period of 2 years. The patients who had 2 and or more pregnancy losses in the previous antenatal period were grouped as Early pregnancy losses (before 20 weeks gestation) and late pregnancy losses and who were presently pregnant and have registered in our antenatal clinic in 1st trimester were properly

evaluated and after finding negative for maternal infections, Gestational Diabetes, thyroid problems, uterine malformations, any karyotype or microarray assay, APLA syndrome, Protein C or S deficiency, previous medical disorders or preeclampsia, eclampsia were pooled up and started with low dose aspirin(75mg) daily once till 36 weeks and Low molecular weight Heparin (20mg) daily till term as soon as pregnancy was confirmed.

The data was pooled and results were formed and arrived at conclusion regarding the benefit of these two drugs for the unknown etiology of RPL.

Present study was carried out in a private hospital in Mahbubnagar, Telangana, India from June 2017 to May 2019. Over an average of 500 antenatal OPD monthly and 4500 annual OPD, 40 pregnant women were included in the present study who fitted into the following criteria.

1. These women had previous 2 and or more pregnancy losses varying from gestational age of 6 and more week gestation.
2. Most of these women had early fetal viability scans of their previous pregnancies.
3. These women were also negative for uterine malformations, Genetic analysis, Gestational Diabetes, APLA, protein C & S deficiency, Thyroid abnormalities, Medical causes, Preeclampsia or eclampsia in relevance to history and investigations.
4. Most of these women could get karyotyping barring 3 women and all the others had normal karyotyping except 1 who had banding in 18^{th} chromosome.
5. All the 40 patients were enrolled in present pregnancy and were investigated and treated with 75 mg of Aspirin daily once till 36 weeks of gestation and Low molecular weight Heparin 20mg on daily till term(1).

RESULTS

Out of 40 pregnant women with 2 and or more previous pregnancy losses who were fitting all the inclusion criteria of unexplained recurrent pregnancy losses of 4500 Antenatal OPD the incidence was accounting to 0.8%. Age group of majorities of women were in the group 18 -36 years. Around 30 pregnant women presented with previous early gestation loss (before 20 weeks) with history of spotting, loss of fetal cardiac activity or spontaneous abortions accounting to 75% and only 7 pregnant women had previous late pregnancy (more than 20 weeks) losses with sudden fetal death, acute oligo amnios sudden onset of abruption, preterm labour without any major etiology diagnosed(17.5%). 3 patients presented with both types of losses, early abortions and late pregnancy losses without any particular pattern (2.5%). All the 40 pregnant ladies in their first antenatal visit were asked in detail about the previous antenatal losses and investigations past and present to rule out the major etiology of recurrent pregnancy losses like Gestational Diabetes, APLA, Thyroid disorders, Karyotyping or rarely Protein C or Protein S deficiency or uterine malformation. The patients were counselled regarding the use of Low dose Aspirin (75mg) daily and Low Molecular weight Heparin (20mg) regarding the safety profile of the drugs and unpredictable outcome in spite of the best monitoring. Low molecular weight heparin was given 20 mg (2) daily for the normal weight women and 40 mg for the obese patients as there was no substantial gross evidence of any microthrombi or any such vascular lesion leading to fetal demise in both early and late pregnancy losses in previous pregnancies. Consent was obtained and the patients were duly registered for the combination treatment along with the routine antenatal supplements. These patients were monitored routinely and on nearing 36 weeks, low dose Aspirin was discontinued and low molecular weight Heparin was continued till term or onset of delivery. Out of 40 pregnant women with previous pregnancy losses, 37 patients had continued pregnancy till term and had a good outcome i.e a healthy mother who had delivered a healthy neonate by either vaginal route or abdominal route for obstetric indications alone. 1(2.5%) patient lost follow up, 1 patient (2.5%) had spontaneous abortion at 14weeks gestation despite on drugs and 1 patient (2.5%) had sudden IUD as the patient lost follow up and also discontinued drugs.

DISCUSSION

Recurrent pregnancy loss occurs in about 1% of couples. Many a times after ruling out all the major causes, there comes a time when there would be not much options in spite of the best of the available treatments except for the empirical treatments. This study used 75mg of ASA and 20mg LMWH (3) and monitoring their pregnancy outcomes. The most common assumption being an undetectable low grade inflammation or a micro thrombi responsible for these pregnancy losses (4). Many Cochrane studies like APRIL was done to study the role of LDA in prevention of recurrent spontaneous pregnancy losses.

This study was conducted on H/O pregnant ladies over a period of 2 years who had recurrent pregnant loss either early or late and were treated with LDA till 36 weeks and daily 20 mg LMWH(5) continued till term. Out of pregnant women in study group, 37 women continued till term. 2 pregnant women landed with abortions at 11 weeks and 16 weeks, 1 woman landed up with Intrauterine fetal death at 30 weeks and was found to have stopped treatment for the last 6 days before landing up with IUFD. This gives us 92% live birth rate which is similar to the study by Enrique et al (2014) which showed a higher birth rate too.

Combination of LDA along with LMWH proved superior in our cases as done by Mak. A. et al (6) who too had better outcomes of Heparin and aspirin which included APLA positive cases.

Though this study has very small inconspicuous data for coming to any conclusions, but has given a good scope for large multicentric trial of using low dose Aspirin(75mg) daily (7) and Low molecular weight heparin (20mg) daily till term in patients who have recurrent pregnancy losses with no detectable etiology and hence as treated empirically as unexplained RPL.

CONCLUSION

Recurrent pregnancy loss both early and late continues to be an unpleasant worry some issue for both the patient and the treating doctor, especially those cases whom have diagnosed negative with the major known detectable causes. Despite trying the best to investigate, there comes a time with no major detectable etiology. LDA and LMWH still gives an optimistic plausible result in unexplained RPL though large multicentric trials globally is needed to substantiate the use of the same in unexplained RPL.

REFERENCES

1. Ian A Greer, Low molecular weight heparin for pregnancy complications. The Lancet., 2016 nov 26; 2570-2.
2. Halide Yuksel et al, Low Molecular weight heparin use in unexplained recurrent miscarriage. Pak J Med Sci., 2014 Nov- Dec; 30(6): 1232 -1237.
3. Elisabeth Pasquier et al. Enoxaparin for prevention of unexplained recurrent miscarriage: a multicentre randomised double – blind placebo controlled trial. Blood, 2015 Apr 2; 125(14): 2200 -2205.
4. Bose P, Black S, Kadyrov M, et al. Heaprin and aspirin attenuate placental apoptosis in vitro: implications for early pregnancy failure. Am J obstet Gynecol, 2005; 192(1): 23-30.
5. Badawy Am et al. Low molecular weight heparin in patients with recurrent early miscarraiges of unknown etiology. J Obstet gynaecol, 2008; (3): 280-284.
6. Mac A et al. combination of heparin and aspirin is superior to aspirin alone in enhancing live births in patients with recurrent pregnancy loss and positive anti phospholipid antibodies: a meta analysis of randomised controlled trials and meta regression. Rheumatology, 2010; 49(2): 281-288.
7. Suzanne Demers et al., The use of aspirin durimg pregnancy. Am J obstet Gynecol, 2013; 208(2): 161-162.