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Randomized Controlled Trial of Low-Dose Aspirin in Reducing Pregnancy Loss in Women with Antiphospholipid Syndrome

Neena jamil, Rashida Kousar,Fareeha Faryal. Aneeza Sikander,Wajiha, Sania Ali, Farah Naz Tahir

[1]MBBS, MCPS, FCPS obstetrics and gynecology, Integrated Medical centre phase 5 Lahore , njjamil1974@gmail.com

[2]MBBS, LMCC, Canada, MRCOG, Uk (Part 1 & 2), Sahiwal teaching hospital Sahiwal , rashidakousar25@yahoo.com

[3]MBBS, House Officer at CMH Lahore, CMH Lahore Medical College, fareehafaryal6@gmail.com

[4]MBBS. FCPS obs and gyane, Senior medical officer, Central park teaching hospital ane104892@gmail.com

[5]FCPS, Associate professor, Sialkot medical college, piffers2121@gmail.com

[6]MBBS, Woman Medical Officer THQ Hospital Kot Addu, saniaaliqureshi@gmail.com

[7]MBBS, MPhil, PhD, Associate Professor of Biochemistry, Central Park Medical College, Lahore Pakistan, tahirnazfarah@gmail.com

Abstract

Antiphospholipid syndrome (APS) is a significant contributor to recurrent pregnancy loss (RPL), primarily due to its prothrombotic effects. This randomized controlled trial aimed to evaluate the efficacy of low-dose aspirin (LDA) in reducing pregnancy loss among women diagnosed with APS. A total of 150 women with confirmed APS and a history of RPL were randomized into two groups: one receiving LDA (81 mg daily) and the other receiving a placebo. The primary outcome

measured was the live birth rate, while secondary outcomes included rates of miscarriage, preterm birth, and obstetric complications.

The LDA group demonstrated a statistically significant increase in live birth rates compared to the placebo group (85% vs. 60%, p=0.01). Additionally, the LDA group exhibited lower rates of miscarriage (10% vs. 30%, p=0.02) and preterm birth (5% vs. 15%, p=0.04). No significant differences were observed in the incidence of obstetric complications between the two groups.

These findings underscore the potential of LDA as a monotherapy in improving pregnancy outcomes for women with APS, offering a cost-effective and accessible intervention. The study fills a critical gap in the literature by providing robust evidence supporting LDA's role in managing APS-related pregnancy loss.

Keywords: Antiphospholipid Syndrome, Low-Dose Aspirin, Recurrent Pregnancy Loss

Introduction

Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by the presence of antiphospholipid antibodies (aPL), including lupus anticoagulant, anticardiolipin, and anti-β2 glycoprotein I antibodies. These antibodies increase the risk of thrombosis and are associated with adverse pregnancy outcomes, notably recurrent pregnancy loss (RPL). APS can occur as a primary condition or secondary to other autoimmune diseases, such as systemic lupus erythematosus. The pathophysiology involves the formation of thrombi in placental vasculature, leading to fetal loss and other obstetric complications.[1-3]

The management of APS in pregnancy aims to prevent thrombotic events and improve pregnancy outcomes. Low-dose aspirin (LDA) has been proposed as a potential treatment due to its antiplatelet properties, which may mitigate the hypercoagulable state induced by aPL. Several observational studies have suggested improved pregnancy outcomes with LDA therapy in APS patients. However, randomized controlled trials (RCTs) assessing its efficacy as a standalone treatment remain limited.[4-7]

Recent studies have explored the combination of LDA with low-molecular-weight heparin (LMWH) to enhance therapeutic efficacy. A systematic review and network meta-analysis indicated that combining LDA with LMWH significantly increased live birth rates in women with APS compared to LDA alone. However, the addition of LMWH may not be feasible in all settings due to cost and accessibility concerns. Therefore, evaluating the efficacy of LDA monotherapy remains clinically relevant.[8-10]

The current study aims to address this gap by conducting a randomized controlled trial to evaluate the effectiveness of LDA in reducing pregnancy loss among women with APS. By focusing on LDA monotherapy, the study seeks to determine its standalone efficacy, providing clarity on its role in managing APS-related RPL. This research is particularly pertinent for resource-limited settings where access to LMWH may be restricted.

Furthermore, understanding the immunomodulatory effects of LDA is essential. Studies have shown that LDA can influence T-cell phenotypes, shifting the balance from a Th1-dominant response, associated with pregnancy loss, to a Th2-dominant response, which supports pregnancy maintenance. This immunological shift may contribute to improved pregnancy outcomes in women with APS.

In summary, this study investigates the role of LDA monotherapy in improving pregnancy outcomes in women with APS. By providing robust evidence through a randomized controlled trial, the research aims to inform clinical practice, particularly in settings where combination therapy with LMWH is not feasible. The findings have the potential to impact treatment guidelines and improve the management of APS-related pregnancy complications.

Methodology

This double-blind, placebo-controlled trial was conducted at a tertiary care center Sahiwal teaching hospital Sahiwal over 24 months. Women aged 20-40 years with a confirmed diagnosis of APS, based on the revised Sapporo criteria, and a history of at least two consecutive pregnancy losses before 20 weeks of gestation were eligible. Exclusion criteria included concurrent autoimmune disorders, known thrombophilias other than APS, and contraindications to aspirin therapy.

Sample size calculation was performed using Epi Info software, considering a 25% difference in live birth rates between groups, with a power of 80% and a significance level of 0.05, resulting in a required sample size of 150 participants.

Participants were randomized into two groups: the intervention group received LDA (81 mg daily), and the control group received a placebo. Treatment commenced upon confirmation of pregnancy and continued until 36 weeks of gestation. All participants provided verbal and written informed consent, and the study was approved by the institutional ethics committee.

Regular follow-ups were scheduled every four weeks, with assessments including ultrasonography, laboratory evaluations, and monitoring for adverse events. Compliance was ensured through pill counts and patient diaries.

Results

Table 1: Demographic Characteristics

Variable	**LDA Group (n=75)**	**Placebo Group (n=75)**	**p-value**
Mean Age (years)	29.5 ± 4.2	30.1 ± 4.5	0.35
BMI (kg/m²)	24.8 ± 2.5	25.1 ± 2.7	0.48
Previous Miscarriages	2.3 ± 0.6	2.4 ± 0.7	0.60

Table 2: Pregnancy Outcomes

Outcome	**LDA Group (n=75)**	**Placebo Group (n=75)**	**p-value**
Live Births	64 (85%)	45 (60%)	0.01

Outcome	**LDA Group (n=75)**	**Placebo Group (n=75)**	**p-value**
Miscarriages	8 (10%)	22 (30%)	0.02
Preterm Births	3 (5%)	11 (15%)	0.04

Table 3: Obstetric Complications

Complication	**LDA Group (n=75)**	**Placebo Group (n=75)**	**p-value**
Preeclampsia	5 (6.7%)	7 (9.3%)	0.54
Gestational Diabetes	4 (5.3%)	6 (8%)	0.52
Placental Abruption	2 (2.7%)	3 (4%)	0.65

The LDA group showed a statistically significant improvement in live birth rates and reductions in miscarriage and preterm birth rates compared to the placebo group. No significant differences were observed in obstetric complications.

Discussion

The findings of this study demonstrate the efficacy of low-dose aspirin (LDA) in improving pregnancy outcomes among women with antiphospholipid syndrome (APS). The significant increase in live birth rates and reduction in miscarriage and preterm birth rates in the LDA group align with previous observational studies suggesting the beneficial effects of antiplatelet therapy in APS-related pregnancy complications.[11-14]

The mechanism by which LDA exerts its effects is primarily through the inhibition of thromboxane A2, reducing platelet aggregation and subsequent thrombus formation in placental vasculature.

This antithrombotic effect is crucial in mitigating the hypercoagulable state induced by antiphospholipid antibodies, thereby improving placental perfusion and fetal outcomes.[15-17]

While combination therapies involving LDA and heparin have been explored, the current study's focus on LDA monotherapy provides valuable insights into its standalone efficacy. The results suggest that LDA alone may suffice in managing APS-related RPL, offering a more accessible and cost-effective treatment option, especially in resource-limited settings.[18-20]

The study's strengths include its randomized controlled design, adequate sample size, and rigorous monitoring protocols. However, limitations such as the exclusion of women with concurrent autoimmune disorders and the short follow-up period postpartum warrant consideration. Future studies should explore the long-term outcomes of LDA therapy and its efficacy in diverse populations.[21-25]

Conclusion

Low-dose aspirin significantly improves pregnancy outcomes in women with antiphospholipid syndrome, reducing rates of miscarriage and preterm birth. This study fills a critical gap by providing robust evidence

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