

Role of Aspirin Anti-platelet Drug in Recurrent Pregnancy Related to Anti-phospholipid Anti-body Syndrome

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Abstract

In our day to day practice absence of viable issue due to recurrent history of pregnancy loss is not so uncommon. There are so many causes that are established as causative factors for recurrent pregnancy loss. We are first ruled out common abnormalities creating abortion by our available investigation procedure. Among recurrent pregnancy loss great significant cause is Antiphospholipid syndrome. Antiphospholipid syndrome causes recurrent pregnancy loss at any trimester of pregnancy which is pathetic for couple. Early diagnosis and preconceptional precaution for prevention of recurrent pregnancy loss is essential to deliver a healthy baby in a diagnosed case of Antiphospholipid syndrome. Antiplatelet drugs like Aspirin had a great play of role in reducing recurrent pregnancy loss due to Antiphospholipid syndrome.

Introduction

Recurrent pregnancy loss is a common problem now a day in our daily practice. Repeated pregnancy loss is a great burden for a couple as well as their surrounding circumstances. In our country this situation may breaks down the relationship between husband and wife and also from social circumstances. A tragedy arise when a couple has gone strong desire for a child but it is terminated as loss. Antiphospholipid Antibody plays like a great culprit in recurrent pregnancy loss. There are so many causes that are established as causative factor for recurrent pregnancy loss.¹⁰ Among them systemic causes includes uncontrolled Diabetes Mellitus, uncontrolled chronic hypertension, hypothyroidism and local causes includes uterine polyp, uterine fibroid cervical incompetency etc.¹ When there are no other common investigations failed to identify then cause of recurrent pregnancy loss is suspicious for Antiphospholipid Antibody syndrome. Sometimes where confirm diagnosis of Antiphospholipid syndrome is not possible due to lack of available investigations procedure we used empirically Aspirin gives a positive result. However, recurrent pregnancy loss needs an indication to screen for Antiphospholipid syndrome.

Incidence

Apparently among normal pregnancy approximately 10% to 30% terminated to spontaneous abortion. Among them recurrent pregnancy loss is 25 to 47 ACOG, 2001; (Dawood-Farqunaron & Queen by 2004). Antiphospholipid syndrome has a prevalence of 15% in women with 1st trimester recurrent miscarriage and this, as well as a single 2nd trimester miscarriage is one of the clinical component for diagnosis of the syndrome (Dewhurst's text book, 8th Edition, Page no-63).² 15% of future untreated pregnant women with Antiphospholipid syndrome miscarriage rate 90%.³

Pathophysiology of Antiphospholipid syndrome

Antiphospholipid syndrome is one example of an Autoimmune mediated pregnancy loss. In APS twenty auto antibodies detected against negatively charged phospholipids binding protein.⁴ The spectrum of antibodies found in women with pregnancy loss encompasses nonspecific antinuclear antibodies as well as antibodies against individual cellular components like phospholipids, histones and double or single stranded DNA.⁵

Antiphospholipid syndrome (APS) or Antiphospholipid Antibody Syndrome or Hughes Syndrome is an autoimmune; hypercoagulable state caused by Antiphospholipid Antibodies APS provokes blood clot (Thrombosis) in arteries and veins as well as pregnancy related complications such as miscarriage, preterm delivery, severe preeclampsia or still birth.¹ Its serological marker is the presence of Antiphospholipid Antibodies in the blood of these patients. The relation between the presence of Antibodies against anionic phospholipid and thromboembolic complications well established over the last 25 years but the pathophysiology of the syndrome is largely unclear.

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The primary antigenic determinant is β_2 glycoprotein which has an affinity for negatively charged phospholipids.⁶ The Antiphospholipid syndrome encompasses

- 1) Lupus Anticoagulant Antibody (LAG)
- 2) Anti Cardiolipin Antibody (ACL) or
- 3) Anti β_2 Glycoprotein.⁶

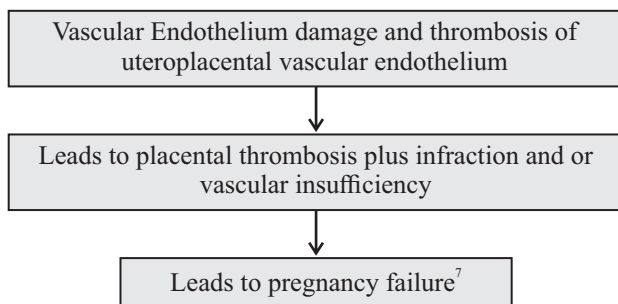
All antibodies play as culprit role in reproductive function. Maximum miscarriage occur in 1st trimester after establishment of fetal cardiac activity. Autoantibody act differently, possible and probable mechanism consist as follows.

1st Mechanism: The Antiphospholipid Antibody that are characteristic of APS are formed against normal plasma protein that are involved in the coagulation cascades and disrupt the phospholipid dependent anticoagulation process leading to a procoagulant state.⁷

2nd Mechanism: Antiphospholipid Antibodies (present in the serum of patients with APS) are known to induce platelet activation and the production of procoagulants such as Von Willebrand factor, thereby encouraging thrombosis. Antibodies have a direct toxic effect on trophoblasts tissue impeding uteroplacental blood flow.⁷

3rd Mechanism: Interfere prostacyclin plus thromboxane balance by interfering with prostacyclin production.⁷

Ultimate mechanism involved pregnancy loss: Clinical presentation



Antiphospholipid Syndrome is an autoimmune multi system disorder characterized by arterial, venous or small vesseles thromboembolic events and/or pregnancy morbidity in the presence of persistent Antiphospholipid Antibodies (APS). Primary Antiphospholipid syndrome is used when APS occurs in the absence of any other related disease and secondary APS is used when APS occurs in the context of other autoimmune diseases such as, SLE. In rare case APS leads to rapid organ failure due to generalized thrombosis this is termed catastrophic APS (CAPS) and is associated with a high risk of death in pregnant women affected by APS.¹

APS significantly increase pregnancy loss. It is estimated that 80% of women with APS experience at least one fetal loss (ACOG, 2005).⁷ The high loss rate of pregnancy

through recurrent spontaneous abortion. The presence of Antiphospholipid Antibodies does not produce symptom until a clot is precipitated. Primary symptom is 1st trimester pregnancy loss after establishment of fetal cardiac activity.⁴ APS may be suspected when a patient gives a strong family history has an unproven suspicious personal history or has repeated spontaneous abortion when other underlying conditions have been ruled out.

Others common secondary signs/symptoms are

- Superficial thrombophlebitis
- Deep vein thrombosis
- Thrombosis (Arterial or Venous)
- Pulmonary embolism
- Septic pelvic thrombophlebitis.⁷

Diagnostic criteria for APS is dependable on Clinical and Laboratory criteria. According to the American College of Obstetrics & Gynaecologist (ACOG, 2005). APS is defined by certain laboratory & clinical criteria. On clinical plus on laboratory criterion must be present to confirm diagnosis.⁷

Clinical criteria

Vascular thrombosis includes venous and arterial.

Fetal loss variable certainty like:

- I. One or more unexplained fetal death beyond 10 weeks gestation.
- ii. One or more premature birth before 34 weeks of gestation.
- iii. Three or more unexplained consecutive spontaneous abortion without hormonal or chromosomal abnormalities.⁸

Laboratory criteria:

Includes-

- I. Anticardiolipin Antibody (ACL)
- ii. Lupus Anticoagulant (LA)⁹

Role of Aspirin (Antiplatelet drug) in Antiphospholipid syndrome

Variants treatment options for APS including low dose Aspirin (LDA), Heparin, Prednisolone and Intravenous Immunoglobulin (IVIG) have been investigated.¹⁰ A systemic review showed that Prednisolone and Intravenous Immunoglobulin (IVIG) do not improve pregnancy outcomes and are associated with increased risk of diabettis and premature birth.¹¹ The same review concluded that LDA along was not of significant benefit but a combination of LDA and unfractionated heparin reduced subsequent pregnancy loss by 54%. Thus LDA and heparin are the recommended treatment for women with recurrent miscarriage and APS. In clinical practice low molecular weight heparins are preferred as they have reduced risk of thrombocytopenia.

Only need once daily administration and levels do not need to be monitored. However, low molecular weight may not have the same effect in reducing risk of miscarriage in APS.¹² Aspirin is an Antiplatelet drug which designated as Anticoagulation process mediated by Antibody detected in Antiphospholipid syndrome.

It acts against main culprit mechanism of abortion in APS like prevention of thrombosis in placental bed and consequence placental insufficiency and fetal loss. And we continue the concurrent pregnancy wellbeing by using Aspirin.

Aspirin (Antiplatelet drug) play role in following pathways:

1st- Prevention of thrombosis with low dose of Aspirin (81 mg).¹³ In our country circumstances dose is (75mg) giving throughout pregnancy and for (6-8) weeks postpartum.

2nd- Improvement of placental blood flow by decreasing thromboxane to prostacyclin ratio with low dose Aspirin.¹³

Conclusions

Although invention of Antiplatelet drug like Aspirin in Obstetrics practice have limited use but patients are beneficial suffering from Recurrent pregnancy loss. We can prevent the disaster from hazards of antibody mediated Recurrent pregnancy loss by using low dose Aspirin. Anticoagulation appears to prevent miscarriage in pregnant women. In pregnancy low molecular weight heparin and low dose aspirin are used instead of warfarin because of warfarin teratogenicity. Women with recurrent miscarriage are often advised to take aspirin and to start low molecular weight heparin treatment after missing a menstrual cycle. Thus aspirin play a great role the patients having Antiphospholipid Syndrome and as well as history of Recurrent pregnancy loss. APS is treated by giving Aspirin to inhibit platelet activation and/or Warfarin as an Anticoagulant. So, use of Aspirin greatly reduced Recurrent Pregnancy Loss. ith ill people or their environment, wearing mask etc.

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