

Evaluation of prophylaxis using low doses of heparin associated with aspirin in pregnancy with multiple miscarriages and high antiphospholipid antibody levels - preliminary report

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Abstract

Introduction: Gestation constitutes a state of acquired hypercoagulability and the success of a pregnancy depends on an adequate placental blood circulation. The objective of this study was to evaluate the evolution of pregnant women suffering from antiphospholipid antibody syndrome and repetitive miscarriages treated with low doses of heparin and aspirin.

Material and methods: The patient report cards of 27 patients with histories of multiple miscarriages (2 or more events) and who suffered from antiphospholipid antibody syndrome were reviewed over 32 gestations. The ages of the gravidas were between 17 and 41 years old with a mean age of 26.6 years. Inclusion criteria included positive tests for lupus anticoagulant and anticardiolipin antibodies. The use of subcutaneous heparin at 5000 IU was recommended twice daily in these cases, as was the oral administration of 100 mg of aspirin.

Results: Of the 32 gestations studied 84.4% were successful and 15.6% miscarried. Gestational ages at delivery varied from 34 to 41 weeks, with a mean of 37 weeks. Gestational ages for the foetal losses varied from 7 to 26 weeks with an average of 15.2 weeks.

Conclusions: The association of heparin at the recommended dosage with aspirin was efficient in preventing miscarriages in patients with histories of repetitive foetal loss.

Key words: repetitive miscarriage, antiphospholipid antibodies, treatment, heparin, aspirin.

Introduction

Gestation constitutes a state of acquired hypercoagulability and the success of a pregnancy depends on an adequate placental blood circulation. Abnormalities of placental vascularization can result in a pathologic gestation, including miscarriage, intrauterine foetal death, intrauterine foetal growth restriction, premature separation of the placenta and pre-eclampsia [1]. Repetitive foetal loss is a problem that affects 5% of women of reproductive age.

Extensive infarcts, necrosis and thrombosis have been identified in the placentas of miscarried fetuses of women suffering from antiphospholipid

Table I. Characteristics of 27 patients included in the study

Patient	Age	Gestation	Live births	Foetal loss
1	23	1	1	0
2	25	1	1	0
3	25	1	1	0
4	32	1	1	0
5	30	1	1	0
6	26	1	1	0
7	27	1	1	0
8	28	1	1	0
9	30	1	1	0
10	17	1	1	0
11	29	1	1	0
12	32	2	2	0
13	26	1	0	1
14	24	3	1	2
15	27	1	1	0
16	22	1	1	0
17	41	1	1	0
18	23	2	1	1
19	28	2	2	0
20	19	1	1	0
21	32	1	1	0
22	33	1	1	0
23	21	1	0	1
24	23	1	1	0
25	23	1		0
26	32	1	1	0
27	21	1	1	0
Mean age	Gestation	27 (84.4%)	5 (15.6%)	
26.6	32			

antibody syndrome. A vasculopathy of the spiral arteriole of the decidua has also been linked to antiphospholipid antibodies related to foetal death [2].

The term antiphospholipid antibody syndrome refers to a varied group of autoantibodies including lupus anticoagulants and anticardiolipin antibodies. These are frequently associated with a history of repetitive foetal deaths in women, who may or may not be suffering from systemic lupus erythematosus. The predictive value of the antiphospholipid test for foetal death or thrombosis in groups of women is as high as 48% to 76% [3].

The pathogenic mechanism and the physiopathology of these antibodies remain controversial. However, the interference of the main components

of the coagulation system is postulated as a probable thrombotic mechanism of the syndrome [4].

Several therapeutic regimes have been recommended to reduce the foetal deaths of these women, including treatment using an association of prednisone and aspirin. Additionally, therapy using steroids was associated with side effects such as premature rupture of the membranes, premature births, foetal growth restriction, infection, pre-eclampsia, diabetes, osteopenia and avascular necrosis [5, 6]. Other studies demonstrated that low doses of aspirin in isolation are associated with successful gestations. Additionally, for the antiplatelet effect, low doses of aspirin increase the number of leukocytes derived from the production of interleukin [3], which stimulates the growth of thromboplasts and normal hormone function [5, 7]. Heparin associated with aspirin gives a result with fewer side effects than the association of aspirin with corticoids, and it gives a higher gestational success rate when compared with aspirin in isolation.

The aim of this study was to evaluate the evolution of [5, 7, 8] gestations of women suffering from antiphospholipid antibody syndrome treated with low doses of subcutaneous heparin and aspirin.

Material and methods

In an observational study the patient report cards of 27 pregnant women who suffered from antiphospholipid antibodies (anticardiolipin antibodies and lupus anticoagulant) and had a history of at least two miscarriages were reviewed. The ages of the patients at the time of the consultations varied from 17 to 41 years with a mean of 26.6 years (Table I). A total of 32 gestations of these patients (3 patients had two and 1 patient had three gestations) were evaluated. During all these pregnancies the women underwent prophylaxis using 5.000 IU of subcutaneous heparin twice daily and 100 mg of aspirin daily.

Evaluation of the anticardiolipin antibodies was achieved by enzyme-linked immunoabsorbent assay (ELISA) and tests of lupus anticoagulants were made by T.T.P.A. correction with normal plasma.

Statistical analysis was conducted using percentages.

Results

There was a good evolution with live births in 84.4% of the gestations but 5 women (15.6%) suffered fetal losses.

The deliveries occurred between 30 and 41 weeks of gestation, with an average of 37 weeks. One patient evolved with an extremely premature delivery (less than 34 weeks), 14 gestations evolved with preterm births and 12 with full-term births. Table I shows detailed patient characteristics - their age and evolution with the use of treatment after 2 or more pregnancy losses.

Discussion

Previous publications associate high levels of antiphospholipid antibodies with a bad prognosis in the evolution of gestations in about 80% of cases [1, 9]. The mechanism of pregnancy loss is probably decidual and placental insufficiency due to the thrombotic tendency. Several therapeutic schemes have been employed to prevent miscarriages: however, no consensus has been reached yet. This study evaluated the efficacy of prophylaxis using low doses of heparin associated with aspirin to prevent miscarriages in women suffering from antiphospholipid antibody syndrome giving similar results to those previously published [5, 10, 11]. Other schemes of prophylaxis such as the association of prednisone with aspirin gave a rate of 75% of live births, although there was a high incidence of premature births owing to pre-eclampsia or early rupture of the amniotic membranes with this association [3]. Aspirin in isolation presented a low efficiency of 42% successful births [12]. The association of heparin with aspirin has been one of the most recommended options [5, 10, 11]. The optimal dose of heparin to maximize benefit and minimize harm is unknown [13]. Higher doses of heparin increase the risk of bleeding and of complications caused by heparinization. An important aspect to be analyzed is the cost of treatment specifically in poorer countries, in relation to compliance with treatment when economic aspects are involved.

Another aspect that should be analyzed, and one that has not been stressed, is whether or not there is a greater risk of pulmonary thromboembolism in mothers [14, 15]. This serves as a warning of this possibility.

Due to the small number of patients included in the investigations, the study is of a preliminary nature. Further research should be continued to confirm our observations.

Conclusions

In conclusion, the association of heparin at the suggested dose with aspirin was efficient in the prevention of miscarriages in patients with histories of multiple foetal losses.

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