Original Article

Pregnancy Outcome after Mechanical Mitral Valve Replacement: A Prospective Study

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Abstract

Background: *Pregnant patients with mechanical heart valves require anticoagulation. The risk of bleeding and embryopathy associated with oral anticoagulants must be weighed against the risk of valve thrombosis.*

Methods: *In this prospective study, undertaken between 1999 and 2009, 53 pregnancies (47 women with mechanical mitral valves; 29.8 ± 4.8 years old) were studied. Patients were divided into two groups: group I (n = 43) received Warfarin throughout the pregnancy, while group II (n = 10) received Heparin in the first trimester and then Warfarin until the 36th week.*

Results: *Thirty-two (60.4%) pregnancies resulted in live births, whereas 18 (34%) abortions, 2 (3.8%) stillbirths, and one (1.9%) maternal death occurred. In group I, there were 26 (60.5%) live births, one (2.3%) stillbirth, and 15 (34.9%) abortions. In group II, there were 6 (60%) live births, one (10%) stillbirth, and 3 (30%) abortions. There were no significant differences between the two groups in terms of fetal outcome. Thirty-nine (90.7%) of the pregnancies in group I and 50% of those in group II (p value = 0.001) were without complications. There were no congenital malformations in the two groups.*

Conclusion: *Fetal outcome was almost the same between the Warfarin and Heparin regimens. In maternal outcome, the Warfarin regimen is safer than Heparin.*

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Introduction

The management of a pregnant woman with a prosthetic heart valve requires important considerations, especially when it comes to maintaining anticoagulation. Because there is a paucity of prospective data, one cannot make definitive recommendations for each patient.[1] The treatment of women in child bearing age with a mechanical heart valve is a real challenge for the medical staff .Warfarin is considered to be a safe and effective anticoagulant for patients with prosthetic

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heart valves. However, treatment during pregnancy poses many difficulties, not least during the first trimester, due to its ability to cross the placenta and its associated fetotoxicity. Treatment with Heparin during the first trimester decreases the rate of embryopathy, but increases maternal morbidity and mortality.[2]

In general, the risk of thromboembolism is grater for older-generation prosthetic valves in the mitral position, such as the Bjork-Shiley tilting-disc prosthesis as compared with the St. Jude valve.[3] The risk of thromboembolism, miscarriage, and premature birth is felt to be higher in patients who have prosthetic heart valves requiring anticoagulation.[4] Thus, pregnancy in women with prosthetic mechanical heart valve replacement is problematic and troublesome even now. In this study, we evaluated our experience with the use of oral Warfarin and subcutaneous Heparin in the first trimester of pregnancy in women with mechanical mitral valves.

Methods

The study protocol, which complies with the Declaration of Helsinki, was approved by the institutional Ethics Committee. The institutional Review Board approved a grant, and written informed consent was obtained from all the participants. All pregnant women with prosthetic heart valves managed between 1999 and 2009 at the Department of Cardiac Surgery, Rajaie Cardiovascular, Medical, and Research Center, Tehran, Iran were enrolled in this study. Fifty-three pregnancies in 47 women with prosthetic mechanical mitral heart valve replacement were followed up.

Information on maternal age, parity, anticoagulation regimen, mode of delivery, and obstetric complications (abortion, stillbirth, preterm delivery, intrauterine growth restriction (IUGR), and hemorrhagic complications), congenital malformation, and thromboembolic complications (valve thrombosis) was extracted from the maternity records.

Spontaneous abortion was defined as any spontaneous fetal loss before 20 weeks of gestation. Therapeutic abortions included all medically indicated terminations before 20 weeks of gestation. Still birth referred to fetal loss after 20 weeks of gestation.

Preterm delivery was defined as birth before 37 weeks of gestation. IUGR was defined as birth weight less than the 10th percentile for gestational age.

In accordance with the policy of our department to fully inform each pregnant woman with a prosthetic heart valve of the potential fetal and maternal risks associated with any of the prescribed anticoagulant regimens, the participants were furnished with information of the fetal risks associated with Warfarin, i.e. congenital malformation and fetal loss rate, as well as the maternal risks associated with Heparin, including thrombocytopenia, osteoporosis and thromboembolism. All the patients who were referred in the first trimester had the following options discussed. The patients were divided into two groups. Group I received Warfarin throughout pregnancy and group II was treated with unfractionated Heparin during the first trimester of pregnancy, switching to Warfarin in the second trimester.

Unfractionated Heparin is usually given subcutaneously twice daily at a starting total dose of 35000 U to attain a target activated prothrombin time (aPTT) two to three times higher than the control. Warfarin was adjusted to attain a target international normalized ratio (INR) of 2.5 to 3. Patients on Warfarin treatment are usually shifted to Heparin at around 37 weeks of gestation.

Statistical methods

For the statistical analyses, the SPSS statistical software version 13.0 for Windows (SPSS Inc., Chicago, IL) was used. The outcome variables were compared via the chi-square test or the two-tailed Fisher exact test if the expected cell frequencies were small. A p value less than 0.05 was considered statistically significant.

Results

Over a ten-year period, we followed up 53 pregnancies in 47 women with mitral prosthetic valves. Seventy-nine percent (79.3%) of the women had St. Jude valve prostheses. The maternal characteristics of the study population are summarized in Table 1.

Table1. Maternal characteristics*

Age (y)	29.8±4.8 (21, 41)
Age at surgery (y)	22.7±6.6 (10, 38)
Gravidity	2.0±1.03 (1,5)
Parity	0.5±0.8 (0,3)
Abortion	0.4±0.8 (0,3)

*Data are presented as mean±SD (minimum, maximum)

All the women were in New York Heart Association class I or II, and 71% were in sinus rhythm in their first antenatal visit.

Overall, only 60.4% (n = 32) of the pregnancies resulted in live births. Eighteen (34%) women had abortions, 12 (3.8%) had stillbirths, and one (1.9%) had maternal death during delivery. The fetal outcomes are demonstrated in Table 2.

In group I, there were 26 (60.5%) live births, 15 (34%) abortions (7 abortions were therapeutic), and one (2.3%) stillbirth. In group II, there were 6 (60%) live births, 3 (30%) abortions, and one (11%) stillbirth. There were no significant differences with respect to the fetal outcome between the two groups.

Delivery was vaginal in 9 (33.3%) patients and Cesarean section in 18 (66.7%) in group I and the numbers were respectively 2 (28.6%) and 5 (71.4%) in group II. There was no case of embryopathy in this study. The mean weight of the newborns was 2784.3 ± 579.3 g (min = 1250, max = 4000). The maternal complications are depicted in Table 3.

Thirty-nine (90.7%) pregnancies in group I and 5 (50%) in group II (p value = 0.001) had no complications. In group I, 2 (4.7%) patients had valvular malfunction due to change of Warfarin to Heparin at the 36th week of gestational age versus one (10%) patient in group II. Three patients in group II had valvular malfunction during the change of Warfarin to Heparin in the first trimester and also one patient had an embolic event in this group.

Table 2. Fetal outcomes*

Variable	Warfarin group (n=43)	Heparin group (n=10)	P value
Ab	15 (34.9)	3 (30)	0.54
Live birth	26 (60.5)	6 (60)	0.62
NVD	9 (34.6)	2 (33.3)	0.95
CS	17 (65.4)	4 (66.7)	0.95
Stillbirth	1 (2.3)	1 (10)	0.34
Preterm	3 (7)	1 (10)	0.57

*Data are presented as n (%)
Ab, Abortion; CS, Caesarian section; NVD, Normal vaginal delivery

Table 3. Maternal complications*

Variable	Warfarin group (n=43)	Heparin group (n=10)	P value
No complication	39 (90.7)	5 (50)	< 0.01
Maternal death	1 (2.3)	-	0.81
Prosthetic valve dysfunction in first trimester	1 (2.3)	3 (30)	0.01
Prosthetic valve dysfunction in third trimester or after delivery	2 (4.7)	1 (10)	0.47
Embolic event	(0)	1 (10)	0.18

*Data are presented as n (%)

Discussion

All mechanical prosthetic valves are thrombogenic and require life-long anticoagulation to prevent thromboembolic complications.[5] In addition, pregnancy is a hypercoagulable state. Choosing which type of anticoagulation to use during pregnancy is problematic, as there is no perfect choice from the available data. Therefore, the major concerns associated with pregnant women with mechanical heart valves are thromboembolic complications, maternal bleeding, and increased fetal events.

The use of Warfarin in pregnant women during the first trimester resulted in a high rate of abortion (34.9%). A similar incidence of abortion was found by Salazar and associates (37.5%) and Shannon et al., who reported a 37% rate of abortion.[6, 7] In contrast, in the Akhtar et al. study, spontaneous abortion occurred more frequently in the Heparin group, whereas Geelani and colleagues reported a similar incidence of abortion in Warfarin and Heparin groups.[8, 9] In our study, the rate of live births was 60.5%, which is similar to that in the Akhtar et al. (70%) and Nassar et al. (65.8%) studies. In contrast, Shannon et al. reported a rate of 30%.[7, 8, 10]

Many articles have shown that the use of Warfarin between 6 and 12 weeks' gestational age results in a 6% to 10% risk of embryopathy.[11-13] In the present study, however, there was no embryopathy detected, which chimes in with the findings of the Akhtar and colleagues study.[8] The risk is probably lower if ≤ 5 mg of Warfarin is prescribed.[14, 15] Our previous study confirmed that a low dose of Warfarin during pregnancy is almost safe, with minimal feto-maternal complications.[16]

A large number of studies have reported that the risk of thromboembolic events during pregnancy in patients treated with Heparin is approximately 10%, compared with a 3.9% risk with the use of Warfarin throughout pregnancy. Unfortunately, the incidence of valvular thrombosis was 30% in our Heparin group, compared with 2.3% in the Warfarin group during the first trimester.

The use of unfractionated Heparin during pregnancy can be problematic, with an attenuated response of activated partial thromboplastin time, variable sensitivities of aPPT reagents, and wide peaks or troughs with the use of subcutaneous unfractionated heparin.[17] The reason for valvular thrombosis in our Heparin group must have been poor compliance, irregular dosing, and inadequate monitoring of aPTT.[8]

Most studies have found that the risk of thromboembolic complications is greater with prosthetic valves in the mitral valve position than with those in the aortic position.[13]

In the current study, the fetal outcome was almost identical between the Warfarin and Heparin regimens. As regards the maternal outcome, it is deserving of note that the Warfarin regimen is safer than Heparin.

Conclusion

Women who have prosthetic heart valves and are of a child-bearing age should be counseled (ideally before conception) about the potential issues that might arise during pregnancy.

Having a prosthetic heart valve puts both the mother and fetus at risk; therefore, the management of these women is required throughout pregnancy in a specialized program for high-risk patients by a multi-disciplinary team.

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