Pregnancy in Mothers with Prosthetic Heart Valves

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Abstract: Prosthetic mechanical valves have a high risk condition for patients in pregnancy. The aim of this study was to evaluate the safety of pregnancy in mothers with prosthetic heart valves. In this cross sectional study, we compared incidence of thromboembolic attacks abortion and maternal and fetal complications in 19 patients with prosthetic heart valves. We reviewed medical records, also office visit and follow up of these women for 10 years. Between 10 years we studied 19 patients, 13 had mechanical heart valves with mean ages of 28.2±5.43, 4 cases with bioprosthetic valves with mean age of 25.4±4.12 and 2 cases of valve repaired. 7.07. Seven women were uniparous 8 cases were in second pregnancy, one had 3rd and another one were gravid 4th. There was a mean interval between valve surgery and pregnancy of 7.65±6.07(1-23) years. Dominant underlying disease for valve replacement was rheumatic. In conclusion bridge anticoagulation during pregnancy is safe for mother and fetus in women with mechanical heart valves.

Key words: Pregnancy, prosthetic heart valves, fetal outcomes

INTRODUCTION

Prosthetic mechanical valves which require anticoagulation during pregnancy have a high risk condition for patient (Roeder et al., 2011). Using of oral anticoagulants during pregnancy is controversial and many studies didn’t show any agreement on the most suitable form of treatment for pregnant women, with mechanical prosthetic heart valves, who have a high risk of thromboembolism (Goldust et al., 2013a; Lotti et al., 2013; Suri et al., 2011). Warfarin derivatives carry the risk of embryopathy when given between the sixth and the 12th week of pregnancy but this complication can be prevented when heparin is substituted for oral anticoagulants in this period (Goldust et al., 2013b; Mohebbipour et al., 2012; Sim’kov et al., 2011). The risk of warfarin embryopathy with oral anticoagulation when used throughout pregnancy is approximately 6% but the frequency of warfarin embryopathy effect of decrease after replaced by heparin between 6 and 12 weeks (Goldust et al., 2013c, d; McLintock, 2011). Using of heparin in all trimesters without warfarin has a risk of thrombotic attacks for mothers (Walfisch and Koren, 2010). Although, warfarin derivatives are relatively safe for the mother with a lower incidence of valve thrombosis than un-fractionated and low-molecular-weight heparin but carries the risk of embryopathy which is probably dose-dependent (Huisman, 2010; Sadghi et al., 2011; Vafee et al., 2012). In the face of valve thrombosis during pregnancy, thrombolysis is the preferable therapeutic option. Bioprostheses and valve repair have a more favorable pregnancy outcome than mechanical prostheses but have high re-operation rate in young women and they do not an ideal alternative (Goldust et al., 2012; Milan et al., 2011; Saeed et al., 2011). Other risks of prosthetic valves in pregnancy are included with a variety of complications, such as structural failure of the valve, infection, heart failure and bleeding due to anticoagulation (Quinn et al., 2009). Valve thrombosis with the procoagulant state of pregnancy increases the risk of thrombus formation especially among women with first generations of mechanical valves. This risk is potentially a life-threatening complication event and depends upon the type and location of the prosthetic valve, as well as a number of other risk factors. Likes history of a prior thromboembolic event, atrial fibrillation, prosthesis in the mitral position and multiple prosthetic valves (Golfarashan et al., 2011; McLintock et al., 2009; Sadeghpour et al., 2011). The patient should be informed about the risk of life threatening thromboembolic events and a thrombotic stroke exists regardless of the anticoagulant regimen utilized and although risks of fetal loss, bleedings and other complications (Goldust et al., 2011; Martinez-Diaz, 2008). While warfarin seems to offer the best protection against thromboembolic events in women with mechanical heart valves during pregnancy but its freely passes the placenta and so associated with characteristic embryopathy and an increase in late fetal

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deaths and hemorrhagic sequelae (Jeejeebhoy, 2009). Un Fractionated Heparin (UFH) and Low Molecular Weight Heparin (LMWH) do not cross the placenta but require twice daily subcutaneous injections and are associated with higher rates of maternal valve thrombosis and thromboembolism (Mohammed, 2009). Other confound problem with heparin are the use of sub-therapeutic dose regimens or poor compliance in many (but not all) reported cases of valve thromboses or thromboembolism (Montavon et al., 2008). The aim of this study was to assess the rate of maternal thrombolytic and hemorrhagic complications and pregnancy outcomes and fetal complications in women with prosthetic heart valves in high risk pregnancy who received treatment with enoxaparin during 6 up to 12 of gestational ages week of pregnancy and then on 36 up to 37.

MATERIALS AND METHODS

In this cross sectional study that was conducted from June 2001 till June 2012 in Tabriz Madani hospital, we analyzed all medical records, also monthly office visit of cardiologist, gynecologist (fellowship of high risk pregnancy) and follow up of the women with prosthetic heart valves during pregnancy and also full echocardiography study in each trimester. This study was approved by ethic committee, Tabriz University of medical sciences; Written consent was obtained from all the patients. For 10 years maternal outcomes included thrombo embolic and hemorrhagic complications, fertility history include parity gravidity and abortion and bridge anticoagulation. Pregnancy and fetal outcomes included miscarriage, still birth, type of delivery, mod of anticoagulation, comorbidities, abortion and live birth, low birth weight, type of prosthetic valve and warfarin embryopathy. Data are expressed as mean values±SD or proportions. A paired t test was used to investigate the time-dependent variables and Student t test to compare 2 groups. A p-value<0.05 was accepted as significant. SPSS 16 software (SPSS, Chicago, Illinois) was used for statistical analysis.

RESULTS

Between 10 years, we studied 19 patients, 13 had mechanical heart valves with mean ages of 28.30±5.43 (19-38), 4 cases with bioprosthetic valves with mean age of 25.4±12.12 (20-50) and 2 cases of valve repaired 27.00±7.07 (22-32). Seven women were uniparous 8 cases were in second pregnancy, one had 3rd and another one were gravid 4th. There was a mean interval between valve surgery and pregnancy of 7.65±6.07(1-23) years. In mechanical heart valves cases, 10 cases from 13 had one valve replacement and 2 cases had double valve replacement. Bioprosthetic valves were only in four patients. The majority of patients had undergone isolated mitral valve replacement (11 cases) and also aortic valve replacement were in 2 cases. Most of the valves were bileaflet type (12/13) and one had cage and ball valve. Sinus rhythm was more common and atrial fibrillation was only in one case. The mean INR for bileaf let valves were 2.5-3.5 and 3-3.5 for cage and ball valve. Dominant underling disease for valve replacement was rheumatic (Table 1, Fig. 1).

Table 1. Analysis of type of valve

<table>
<thead>
<tr>
<th>Type of valve</th>
<th>Bileaflet</th>
<th>Cage</th>
<th>Av</th>
<th>Age=SD (Range)</th>
<th>Doble</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioprosthetic</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>25.40±8.12 (20-38)</td>
<td></td>
</tr>
<tr>
<td>Mechanical</td>
<td>13</td>
<td>1</td>
<td>3</td>
<td>28.30±5.43 (19-38)</td>
<td>2</td>
</tr>
<tr>
<td>Repair</td>
<td>2</td>
<td></td>
<td></td>
<td>27.00±7.07 (22-32)</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

The management of anticoagulation during pregnancy is controversial and there is no ideal clear cut treatment option (Koch, 2008). Patients with prosthetic heart valve have highest risk of thromboembolism and pregnancy itself is a factor of hypercoagulability (pregnancy-induced hypercoagulability) as a physiologically adaptive mechanism to prevent postpartum hemorrhage, hence increases risk of embolization (Curtis et al., 2008). Thromboembolic events are lower with modern valve as compared with older generation, because of improvement in design and materials. The prevalence decreased but not disappeared. There is general agreement about discontinuation of oral anticoagulant during first trimester of pregnancy to avoid the warfarin embryopathy (Khamooshi et al., 2007). According to ACC/AHA guide lines in 2008 anticoagulant during pregnancy in women with prosthetic heart valve must ensure continuous, monitored, therapeutic anticoagulation. Women who elect to stop warfarin between 6-12 weeks of gestation to reduce the risk of fetal defect should receive continuous IV or dose adjusted subcutaneous (SQ) UFH or dose adjusted subcutaneous LMWH (Mischke, 2007). Adjusted- dose of LMWH is twice daily to maintain anti-Xa level between 0.7-1.24 mL^-1 4 h after administration. Unfractionated heparin (UFH, initiated in high doses 17,500-20,000 IU every 12 hours to achieve 6 hours post dose of a PTT at least twice control. Warfarin to achieve INR goals of 3 (ranges = 2.5-3) (Roos-Hesselinke et al., 2007). Thromboembolic event rate of mechanical heart valves
Fig. 1: Demographic diagram of study population

is 7.5-23% even with anticoagulation and mortality rate of 40% (8-11,14). As we pointed earlier older mechanical valves and mitral valve position, have highest thromboembolic risk (Trzeciak et al., 2006). Warfarin embryopathy seems to be dose related and warfarin should be safely used during pregnancy. Our study showed excellent results of bridge anticoagulation for mothers and even good outcome for fetus. These are in complete agreement with results of other studies (Varadarajan et al., 2006). Salazar et al. (1996) used subcutaneous LMWH from 6-12 weeks and again in the last 2 weeks of pregnancy in 37 women with prosthetic heart valves, 2 died of fatal valve thrombosis of tilting disc mitral valve during pregnancy and another one died of anticoagulation-related gastrointestinal bleeding. (Salazar et al., 1996). Fetal complications included 15 spontaneous abortion of first trimester with no incidence of warfarin induced embryopathy. In our study we hadn't mother's death due to thrombotic event or bleeding complication. This is may be due to close monitoring of patients with frequent visits and telephone call. Also giving of more information to the patients before and
during pregnancy was important in reducing complication rate. Maximum doses of warfarin in our study were between 5-7.5 mg day⁻¹ which is relatively low dose and absence of warfarin embryopathy in this study could be explained. Geelani et al. (2005) from India reported 250 pregnancies in 245 women. In one group oral warfarin and in another group subcutaneous heparin used in first trimester. The incidences of spontaneous abortion were the same in both groups (Geelani et al., 2005). We had not valve thrombosis in our study but in other studies thromboembolic rate was high in heparin group. The explanation may be related to poor compliance of patients to frequent heparin injection. In availability of measurement of anti-Xa in every centers or inadequate monitoring of aPTT maybe the cause of increase thrombosis in heparin group (Greer, 2005). Final dates of our study revealed no complication with bioprosthetic or repaired valves. This recommendation for women with childbearing age is choice of repair valve or bioprosthetic valve replacement.

CONCLUSION

According to this data, anticoagulation during pregnancy is safe for mother and fetus in women with mechanical heart valves.

REFERENCE


