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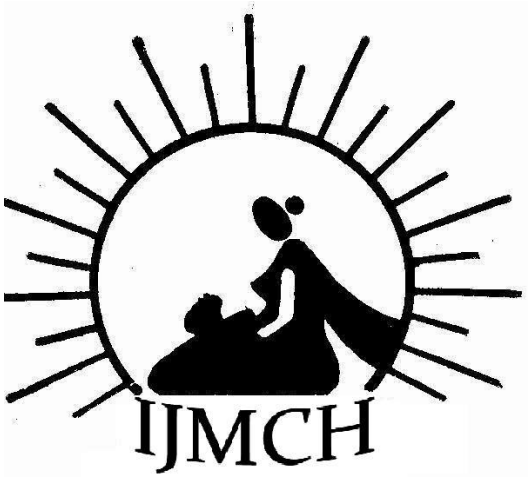

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Patients with mechanical heart valves require anticoagulation which is associated with significant maternal mortality (1-4%) and fetal complications (31%) in pregnancy.

Successful maternal and fetal outcome of pregnancy following heart valve replacement using a sequential anti coagulation regime

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ABSTRACT

Patients with mechanical heart valves require anticoagulation which is associated with significant maternal mortality (1-4%) and fetal complications (31%) in pregnancy. We present two years of experience during which we had seven cases of successful pregnancy outcome following heart valve replacement with anticoagulant regime consisting of warfarin and low molecular weight heparin.

Key words: Heart valve replacement, pregnancy, anticoagulant

INTRODUCTION

The management of anti coagulation during pregnancy in women with mechanical heart valves is associated with an increased risk of maternal and fetal complications. During pregnancy their thrombotic risk increases (estimated to be as high as 29%)[1]. With a 2.9% maternal mortality rate.[2]

Thus the need for effective anticoagulation is greater. Oral anticoagulation offer the best maternal protection against thrombosis[2,3]. But their use is associated with higher fetal loss rate (as high as 59%) and can have damaging effects on the fetus.[2].

Heparin derivatives are associated with reduced risk of fetal damage, but increased risk of valve thrombosis in mother.

The risk of prosthetic valve thrombosis is higher with mechanical valves than with biological valves and is increased by the hyper coagulable state of pregnancy and any interruption to anticoagulation therapy.[3]

Pre conception counseling to enable early discussion of the additional risks that pregnancy may place on the heart should be seriously considered in women with known cardiac disease. The counseling is difficult due to the paucity of good data relating to maternal or fetal outcomes. Recommendations from various expert groups have suggested that since there is no ideal anticoagulant regime, women should be given the information and encouraged to choose their therapy.[4]

The aim of this study is to produce the peri-partum management of a woman with prosthetic heart valve so as to obtain the best outcomes for mother and baby.

MATERIAL AND METHODS

We included eleven women with artificial mechanical prosthetic heart valves became pregnant during the study period (August 2011 to June 2013), irrespective of the outcome of the pregnancy.

We studied the management and outcomes of these women.Anticoagulation was achieved using oral anticoagulants Acitrom / Warfarin, low molecular weight heparin during various stages of pregnancy.

The risk of valve thrombosis due to inadequate anticoagulation was balanced against the risk of direct harm to the fetus by the anticoagulation used, along with the risk of hemorrhage to both the mother and fetus.

To prevent the risk of warfarin / acitrom embryopathy the oral anticoagulant were used during the first trimester as soon as her pregnancy was confirmed. Low molecular weight heparin was started and warfarin or acitrom recommended at 16 weeks gestation and stopped at 36 weeks at which time she was restarted on low molecular weight heparin. The dose of LMWH was calculated on the basis of weight of the patient. INR was monitored while the patients were on oral anticoagulants and target INR was set as per the position of the valve.

RESULTS

The majority of women were in the age group of 21 to 25 years (7 out of 11), three women (27.2%) were in the age between 26 to 30 years. There were six (54.5%) primigravidas in their study. All patients had an uncomplicated ante-natal period. Three (27.2%) had pre term delivery beyond 35 weeks and the rest delivered at term. One women aborted her fetus during the first trimester itself. Four patients (36.3% patients underwent a lower segment caesarean section for fetal distress. All the babies cried immediately post delivery and were shifted to mothers. One required re-laparatomy on day 3 for pelvic hematoma drainage and another patient had post partum hemorrhage after instrumental delivery which was managed medically.

Table 1 : Distribution according to Age

Age in Years	No. of Patients	%
21-25	7	64.6%
26-30	3	27.2%
31-35	1	9%
Total	11	

Table 2 : Distribution according to Gravidity

Gravidity	No. of Patients	%
1	06	54.5%
2	03	27.2%
3 or more	01	9.1%
Total	10	

Table 3 : Distribution according to Mode of Delivery

Mode of Delivery	No. of Patients	%
Vaginal	3	30%
Instrumental	3	30%
LSCS	4	40%
Total	10	100

Table 4 : Distribution according to Period of Gestation at Delivery

Period of Gestation	No. of Patients	%
Pre Term	03	30%
Term	07	70%
Post term	00	
Total	10	100

DISCUSSION

Prosthetic heart valves are associated with thrombo-embolism, bleeding secondary to anticoagulation, structural failure and infection.

Thrombo-embolism rates in pregnant women vary between 7 to 23% per patient per year and half of these episodes arise from valve thrombosis with increase in risk upto 25% in the absence of adequate anticoagulation.[5]

Women with older generation prosthetic valves (e.g. Starr Edwards and Bjork Shiley valves) in the middle position, especially with atrial fibrillation are at higher risk of thrombo-embolic complications.[6] other patients in this category include those with multiple prosthetic valves or a history of thrombo-embolic events. Women in normal sinus rhythm with prosthetic aortic valves (e.g. St. Jude Medical, ATS & Sorin Bileaflet valves) and those with bioprosthetic valves are at a relatively low risk of thrombo-embolic complications.[7]

Bio prosthetic valves undergo accelerated deterioration during pregnancy. Anil et al[7] conducted a 5 years prospective follow up of 48 patients with prosthetic valves who became pregnant and 37 comparable women who did not and found a comparable rate of SVD (27% and 30% respectively) and reoperation (8% in both groups). Although most available data might support an accelerated SVD of bio prosthetic valves during pregnancy, this could simply reflect the well established deterioration of tissue valves in young individuals.

Anticoagulation can be achieved using warfarin, unfractioned heparin (UFH), low molecular weight heparin (LMWH) or a combination of above.

The risk of valve thrombosis due to inadequate anticoagulation has to be balanced against the risk of direct harm to the fetus by the anticoagulation used, along with the risk of haemorrhage to both the mother and fetus.

The major difference between the two anticoagulants is that warfarin crosses the placenta while heparin does not.

There is overwhelming evidence that warfarin offer the best protection against prosthetic valve thrombosis. Warfarin embryopathy is characterized mainly by skeletal abnormalities and primarily contraindicated during at least the first trimester of pregnancy (6^{th} and 12^{th} week of gestation) because of their teratogenic effects. In one survey of European cardiologists (and their uncontrolled practices) found no congenital abnormalities in 46 women with prosthetic valves who took warfarin during the first trimester [8]. In contrast, other studies have not found such benign outcome, primarily in patients taking warfarin between 6^{th} and 12^{th} week of gestation. The incidence has been quoted as low as 1.6% of live births however skeletal deformity and nasal hypoplasia have been reported in up to 10% of babies exposed to watrfarin[6,7]. Warfarin can also result in fetal and neonatal hemorrhage and maternal administration at the time of delivery significantly increases the risk. [(8-10)]

Vitale et al [(10)] reported 58 pregnancies in 43 women with mechanical heart valves who were treated with warfarin. There were 27 foetal complications, including 22 spontaneous abortions, 2 warfarin embryopathies and one each ventricular septal defect, still birth and growth retardation.

There were 22 fetal complications among women on a warfarin dose requiring more than 5 mgm/day of warfarin throughout pregnancy to maintain an INR of 2.5 to 3.5 compared with 5 complications in those taking 5mgm/day or less.

Heparin derivatives,ie, unfractionated heparin (UFH) or low molecular weight heparin (LMWH) does not cross the placenta and thus it does not carry the same risk of

teratogenicity as oral anticoagulants. However, heparin of either type appear to provide less protection against prosthetic valve thrombosis[9].

A review of 81 pregnancies in 75 women with mechanical prosthetic heart valve treated with LMWH during pregnancy reported a high 8.6% rate of valve thrombosis prompting one LMWH manufacturer to issue a warning regarding the use of product for this purpose[11]. However this was subsequently thought to be due to inadequate dose and monitoring rather than the drug itself. Heparin does causes have loss and there are many case reports and series of pregnant women with osteoporotic fractures during and after prolonged use of heparin[12].

Recommendations from an American consensus conference on anti-thrombotic therapy for patients with mechanical heart valves recommended anticoagulation management choices which are as follow[13].

- High dose (e.g. 17500 to 20,000 units) subcutaneous UFH throughout pregnancy given twice daily, with monitoring to guide dosing (arising for a 6 hour post dose activated partial thrombo-plastin time (APTT) of twice the control level or anti X-a level maintained at 0.35 -0.70 IU/ml).
- LMWH (e.g. deltaparin 100 units/Kg) subcutaneous throughout pregnancy with anti Xa monitoring to guide dosing (aiming for a 4 hour post dosing anti-Xa level of about 1.0 IU/ml).
- UFH or LMWH therapy as above until the 13th week of gestation followed by warfarin until the middle of third trimester, then restart UFH or LMWH therapy until delivery.

We followed the third regimen and had good outcomes with no fetal malformation in majority of the patients.

As soon as the pregnancy was confirmed, patients were commenced on LMWH (twice daily) and her warfarin stopped. Warfarin was recommended at 16 weeks gestation and stopped at 36 weeks at which time she is restarted as LMWH. We encountered hemorrhagic complications in two patients that were dealt with uttering artery embolization and the patients were discharged in satisfactory condition. Overall in our study there was no major complications observed and all patients have successful outcome of their pregnancies. Both mother and babies remained safe.

CONCLUSIONS

The rational approach to anticoagulation therapy in pregnant patients with mechanical prosthetic heart valves should include patients risk factors, including the type and location of the valve as well as cardiac function, patients symptoms and functional capacity.

Preconception counseling to enable early discussion of the additional risks that pregnancy may place on the heart should be seriously considered in women with known cardiac disease. Because clinical deterioration often occurs during pregnancy, patients with marked impairment of left ventricular or valvular function that are moderately or severely symptomatic (Class III-IV) should be advised against pregnancy.

Anticoagulation is necessary in pregnant patients with mechanical prosthetic valves, but each of the therapeutic approaches carries its own risk.

The following recommendations should be followed in the peripartum management of a women with prosthetic heart valve.

- Warfarin should be avoided between 6 and 12 weeks of gestation and close to term.
- Heparin should be administered every 6 to 12 hours in divided doses to achieve a mid internal PTT that is 2 to 3 times control. After a stable dose is achieved, the PTT should be measured at least weekly.
- After 12 weeks, All patients should be treated with warfarin with a goal INR of 2.5 to 3.0. during the last two weeks of gestation, in preparation for delivery, intravenous heparin is used in place of warfarin, the switch to heparin should be performed no later than 35 or 36 weeks of gestation. Heparin is then discontinued during labor and restarted after delivery.
- An alternative to this approach is to perform an elective caesarean section during the last two weeks of gestation.
- For patients or clinicians who prefer to avoid warfarin at all times during pregnancy, the use of continuous intravenous heparin throughout the entire pregnancy or subcutaneous heparin administered every 6 to 12 hours are alternatives.

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