

Maternal outcomes of pregnancy in women with mechanical heart valves prostheses — a single-center experience

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INTRODUCTION

A growing population of women with a mechanical heart valve (MHV) requiring anticoagulation reach childbearing age [1]. The aim of anticoagulation during pregnancy is to balance maternal risks, both thromboembolic and hemorrhagic, against the safety of the fetus [2]. Literature data suggest that vitamin K antagonists (VKA) are the safest treatment for the mother but are associated with higher rates of fetal anomalies [1, 2]. Not crossing placenta low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) are used as an alternative to VKA. Unfortunately, this management is associated with higher rates of maternal complications, mainly thromboembolic events. The current guidelines of the European Society of Cardiology on the management of cardiovascular diseases during pregnancy allow the use of different anticoagulation regimens in the discussed population [3].

We aimed to assess the pregnancy course and the incidence of maternal complications in different anticoagulation regimens in women with MHV followed up in a single tertiary cardiological center.

METHODS

We analyzed 23 pregnancies in women with a mean (standard deviation) age of 28.7 years (± 5.8 years) and MHV who were followed up in our center between 2003 and 2018. The data retrieved from medical records included, among others, the type and position of a mechanical valve and an anticoagulation regimen. Four types of anticoagulation therapy were applied: VKA throughout pregnancy, LMWH throughout pregnancy, sequential

regimens, i.e., UFH subcutaneously or LMWH from 6th to 12th weeks, VKA in the 2nd and 3rd trimester, and UFH or LMWH from the 36th week.

Maternal outcomes included: maternal death during pregnancy, mechanical valve thrombosis (MVT), a need for urgent valve reoperation, ischemic stroke, and postpartum hemorrhage. MVT diagnosis required echocardiographic confirmation. Ischemic stroke was defined as an acute neurological deficit persisting over 24 hours and verified with brain imaging. Postpartum hemorrhage was defined as loss of over 1000 ml of blood within 24 hours after the cesarean section [2].

As approved by our Institutional Ethics Committee, the study protocol conformed to the ethical guidelines set forth by the 1975 Declaration of Helsinki.

Statistical analysis

For descriptive analysis, data were expressed as a mean with standard deviation for continuous variables and percentages for categorical variables. Analysis was performed using PQStat v.1.8.2.

RESULTS AND DISCUSSION

Study population

We obtained data from nineteen patients who underwent 23 pregnancies. Moreover, we excluded five (18%) cases with spontaneous miscarriages in the first trimester from our analysis. The demographic and clinical data are presented in Table 1.

Type and position of MHV

Ten (43%) pregnancies occurred in women with the following aortic MHV: 7 ONX type,

Table 1. Baseline characteristics of pregnant patients with mechanical heart valves

No	Age, years	Prosthesis type	Time from valve surgery, years	Pregnancy sequence	Anticoagulation regimen in pregnancy	Week and mode of delivery	Maternal complications
1	39	AVR	5	1	UFH/VKA/UFH	35/cs	0
2	23	AVR	13	1	VKA	37/cs	0
3	22	AVR ^c	17	1	LMWH	27/cs	Valve thrombosis Urgent valve surgery Maternal death
4	21	AVR	10	2	UFH/VKA/UFH	37/cs	0
5	30	AVR	4	1	UFH/VKA/UFH	35/cs	0
6 ^a	22	AVR	15	1	UFH/VKA/UFH	37/cs	0
6 ^b	33	AVR	26	3	UFH/VKA/UFH	38/cs	Valve thrombosis
7	29	AVR	12	1	UFH/VKA/UFH	37/cs	0
8 ^a	30	AVR	10	1	UFH/VKA/UFH	37/cs	0
8 ^b	37	AVR	17	2	UFH/VKA/UFH	37/cs	0
9	27	MVR	21	1	UFH/VKA/UFH	38/cs	Valve thrombosis
10	25	MVR	18	1	LMWH/VKA/ LMWH/UFH	38/cs	Stroke
11	19	MVR	7	1	VKA	37/cs	0
12	25	MVR	15	1	VKA	37/cs	Post-delivery hemorrhage
13	27	MVR	18	1	UFH/VKA/UFH	37/cs	Valve thrombosis
14	34	MVR	19	1	UFH/VKA	25/cs	Valve thrombosis Urgent valve surgery
15 ^a	31	MVR	2	1	UFH/VKA/UFH	37/cs	Valve thrombosis
15 ^b	41	MVR	12	3	UFH/VKA/UFH	37/cs	0
16	24	MVR	8	3	UFH/VKA/UFH	37/cs	0
17	31	AVR + MVR	4	1	VKA	37/cs	0
18 ^a	28	AVR + MVR	6	1	UFH	9	Stroke
18 ^b	32	AVR + MVR	10	2	UFH	Termination 10 Termination	—
19	29	TVR	16	1	UFH/VKA/UFH	32/cs	Valve thrombosis

^aFirst pregnancy; ^bNext pregnancy from the same patient that was included in the analysis; ^cTilting AVR

Abbreviations: AVR, 2-disc mechanical aortic valve prosthesis; cs, cesarean section; LMWH, low-molecular-weight heparin; MVR, 2-disc mechanical mitral valve prosthesis; TVR, 2-disc mechanical tricuspid valve prosthesis; UFH, unfractionated heparin; VKA, vitamin K antagonists

2 St. Jude type, and 1 Bjork-Shiley. Nine (39%) pregnancies occurred in patients with the following mitral MHV: 7 St. Jude and 2 Sorin Bicarbon. Women with both aortic and mitral MHV ONX type had three (13%) pregnancies. One (4%) pregnancy was followed in a patient with tricuspid MHV (Saint Jude).

Anticoagulation regimen

Four pregnancies (17.4%) were managed with VKA before delivery. Most women during pregnancies ($n = 17$; 74%) received sequential anticoagulant therapy with subcutaneous UFH, and in the case of one pregnancy (4%), sequential anticoagulant therapy was followed with the use of LMWH. One patient (4%) was managed with the use of LMWH only.

Maternal outcomes

There was one (4%) maternal death occurred during urgent prosthesis reoperation. It was related to aortic MVT in a patient treated in another healthcare center and receiving LMWH throughout the pregnancy without anti-Xa monitoring. We observed MVT in 7 (30%) patients: one in the mentioned-above patient, and other six in women followed on sequential anticoagulation therapy with subcutaneous UFH. Two (9%) patients required urgent valve surgery. Two

(9%) patients suffered from ischemic stroke. In the first trimester, one neurological incident occurred in a patient managed with a sequential therapy with subcutaneous UFH. The other stroke was observed in a patient followed on a sequential therapy using LMWH 12 hours after a cesarean section. Post-delivery hemorrhage was observed in one (4%) patient followed on VKA throughout the pregnancy.

Thromboembolic complications

In our study, thromboembolic complications occurred in 43% of pregnancies. MVT is the most feared complication with even a 20% risk of death [2]. We observed one maternal death due to MVT. Additionally, in our study, we found seven (30%) MVT cases at every stage of pregnancy, but most of them ($n = 4$; 57%) occurred post-delivery. At that time, the risk of hypercoagulability is the highest, and patients are under-anticoagulated due to the fear of hemorrhagic complications. The MVT risk amounts to 5%–16% in the available literature and is mainly observed in the first trimester while switching to heparin-based therapy [1, 2]. Our study also shows that most MVT cases (86%) occurred in women followed on a sequential therapy using subcutaneous UFH. Due to the low bioavailability and anticoagulation strength of UFH, its administering subcutaneously

throughout pregnancy may be associated with a high thromboembolic risk amounting to 11.2%–33% [4, 5]. According to the recent American and European guidelines [3, 6], UFH given subcutaneously is no longer recommended in the discussed population and, in our center, was replaced by subcutaneous LMWH that characterizes a more predictable mode of action and a lower rate of thromboembolic complications [5]. However, our observation, i.e., the death of a patient using LMWH without anti-Xa activity control, confirms the necessity of strict anti-Xa activity monitoring. Literature data suggest that pregnant women with MHV require much higher doses of LMWH than non-pregnant patients [1]. It results not only from a weight gain but also from an increase in the glomerular filtration rate and the blood volume during pregnancy.

Thromboembolic complications are very rarely observed in pregnant women treated with VKA due to their strong anticoagulant effect. In our study, no patient taking VKA through the whole pregnancy presented with MVT. This is in accordance with the available literature data [6]. As a result, the recent European and American cardiologic guidelines accept the use of VKA throughout pregnancy, especially when low doses of warfarin (<5 mg/day) or acenocoumarol (<2 mg/day) are required to achieve therapeutic INR values [3, 6]. When higher doses of VKA are needed, sequential therapy is suggested to prevent fetal complications. We observed MVT in 35% of pregnancies treated with a sequential therapy using subcutaneous UFH. This group included four pregnancies with a mechanical mitral valve and one pregnancy with a mechanical tricuspid valve. It is well known that these prostheses, due to a low-velocity blood flow, are associated with high-risk thromboembolic complications in comparison to aortic prostheses, whatever anticoagulation regimen is used [7]. In the meta-analysis, Chan et al. [4] reported 9.2% of MVT cases in pregnant women treated with sequential therapy.

Stroke results from the thrombotic material that forms on prosthesis discs while subtherapeutic anticoagulation is used. We observed 2 (9%) cases of a stroke while using UFH. In the available literature, this complication occurred in 1.4%–7% of pregnancies [1, 2].

Hemorrhagic complications

Our study identified one case (4%) of post-delivery hemorrhage that required obstetrical intervention and blood transfusion. The incidence of hemorrhagic complications in the available literature is much higher and amounts to 1.3%–29% of pregnancies [1, 2, 4, 5]. The applied anticoagulation regimen has a significant impact on the bleeding frequency, with the lowest risk in the subgroup treated exclusively with VKA (1.3%) and the highest risk in patients managed with heparin (both LMWH or UFH) (11.5% of pregnancies) [5].

Study limitations

This is a single cardiologic tertiary center experience. A small number of patients impeded proper statistical

analysis. Another limitation is a low number of patients using different regimens, essentially VKA alone and LMWH in the sequential regimen.

CONCLUSIONS

There is no safe anticoagulation regimen in pregnant women with mechanical heart valves. The impressive rate of complications in this high-risk group advocates for the centralization of their care. Only experienced centers, where close cooperation between cardiologists and obstetricians is possible, can guarantee the highest rate of event-free pregnancies.

Article information

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