

# Pregnancy Outcome with Intracytoplasmic Sperm Injection Method in a Woman with Prosthetic Heart Valves

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## Abstract

There is an increased risk of thromboembolism, anticoagulant-related hemorrhage, fetal-wastage and congestive cardiac failure in pregnant women with mechanical heart valves. In order to have a good outcome, the care of such patients must necessarily be multidisciplinary and in a well-equipped centre with adequate support services. One such patient who had mechanical mitral and aortic valves replacement in 2000 receiving warfarin anticoagulant therapy, presented with a first trimester pregnancy by ICSI method in 2006. She remained in stable homodynamic state and went through pregnancy without event. Delivery was done by caesarian section at 37 weeks gestation age.

With considering use of warfarin during pregnancy, use of stimulation protocol during ICSI and delivering normal neonate ultimately, this interesting case is presented herein.

**Keywords:** Pregnancy, Anticoagulant, Prosthetic Heart Valve, Intra Cytoplasmic Sperm Injection

## Introduction

In patients with mechanical prosthetic heart valves, long-term anticoagulant therapy is mandatory to prevent thromboembolic events. Additionally, the risk of maternal thromboembolic events is elevated during pregnancy because of the patient's hypercoagulable state, which is characterized by increased levels of certain clotting factors and fibrinogen and platelet adhesiveness (1). Also, Thromboembolic phenomena are serious consequences of assisted reproductive technology (ART) (2). Ovarian stimulation cycles accompanying high serum estradiol levels, haemoconcentration or ovarian hyperstimulation syndrome (OHSS) carry a potential risk of thromboembolism (3). Definitive recommendations on anticoagulation strategy in pregnant women who have prosthetic heart valves are lacking

because of the paucity of prospectively collected data. The use of warfarin, unfractionated heparin, low molecular weight heparin, or any other combination of these choices has potentially adverse effects for the mother and fetus. Although there is no treatment option, proven to be completely satisfactory, there is agreement that failures are most often due to under dosing and lack of intensive monitoring of anticoagulation (4). Our Patient was successfully treated by warfarin throughout pregnancy achieved by (ICSI) with special monitoring. We discuss the rational of different anticoagulation regimes with regards to maternal and fetal outcome in women with mechanical heart valves.

## Case Report

A 39 years old woman, who had undergone

Received: 5 May 2007, Accepted: 20 June 2007

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Royan Institute  
Iranian Journal of Fertility and Sterility  
Vol 1, No 2, Summer 2007, Pages: 89-91

Mitral valve replacement (M.V.R.) and Aortic valve replacement (A.V.R.) operation with St. Jude prosthetic mitral valve 27mm and aortic valve 23mm in Shaheed Rajarei Heart Center, married at 38 years old with a man who had undergone Vasectomy after having 3 children in his previous marriage. They were consulted about the risk of pregnancy with prosthetic heart valves. Persisting to have a child, the man underwent vasovasostomy operation but it failed, and finally ICSI was done in Royan institute. Before doing ICSI, transthoracic echocardiography study of the woman showed good function of prosthetic valves. Long standard GnRH agonist protocol was used to ovarian stimulation. In this protocol, the woman had first been down-regulated with GnRH analogue (Buserline, Hoechst, Germany) which was administered 500 µg/day subcutaneously from 21<sup>st</sup> day of previous menstrual cycle. When pituitary suppression was achieved (on second day of menstrual cycle, FSH≤5 IU/ml, LH≤5IU/ml, progesterone≤1ng/ml, Estradiol≤50pg/ml), Buserline was reduced to 200µg/day and 150-225 IU human Menopausal Gonadotrophin(Menopur, Ferring, Germany) was administered intramuscularly from 2<sup>nd</sup> day of menstrual cycle daily. After 3 or more follicles had reached 18mm in diameter, 10000 IU human Chorionic gonadotropins (hCG, Organon, Holland) was used to induce oocyte maturation. Oocytes were aspirated transvaginally with ultrasound guidance 34-36 hour later. After that, ICSI was done. Throughout the ovarian stimulation, PT was kept at 17'' and International Normalized Ratio (I.N.R.) at 2-2.2. Pregnancy occurred after ICSI. Precise observations were performed by Cardiologist, Cardiac surgeon and Gynecologist as a multidisciplinary team mainly because of warfarin therapy during pregnancy. The patient was receiving her prescribed warfarin along with PT control because of low dose warfarin regimen(less than 5mg per day). The pregnancy period completed with no complications and

terminated on 37<sup>w</sup> with C/S, bearing a 1900gr normal baby. Bleeding was not too much and there was no complication after delivery. Transthoracic echocardiography study showed normal function of prosthetic valves after delivery.

## Discussion

An optimal anticoagulation regimen for pregnant women with mechanical heart valves has not been determined yet. However, controversy exists about the most efficient and safest anticoagulation regimen in women with mechanical heart valves during pregnancy. Three different anticoagulation regimens have been recommended in the literature: (i) administration of warfarin derivatives throughout pregnancy and subcutaneous unfractionated heparin (UFH) near term; (ii) substitution of warfarin derivatives with subcutaneous UFH in the first trimester and near term, and (iii) subcutaneous UFH application throughout pregnancy (1).

Each of these three standard anticoagulative approaches imposes mother and fetus different thrombotic-hemorrhagic related complications.

Use of warfarin may be associated with embryopathy, spontaneous abortions, stillbirths and less commonly, central nervous system defects and fetal bleeding with exposure beyond the first trimester (5).

Recent publications however reported an increased incidence of valve thrombosis in patients with mechanical prosthesis treated with subcutaneous heparin during pregnancy (1).

Vital et al demonstrated dose – dependent fetal complications of warfarin in pregnant women with mechanical heart valves and they concluded that daily dose less than 5mg of warfarin does not have a major impact on the fetus (6).

Geelani et al also reported warfarin safe and convenient to be used during pregnancy. They believed that teratogenic effects

overstated, and switching to heparin is not mandatory (7).

Kim et al reported that warfarin use from the second trimester in combination anticoagulation regimens would increase the risk of adverse perinatal outcome (8).

In Kawamata et al study that reported 16 pregnancies in 12 women with prosthetic heart valve, warfarin was changed to heparin in these patients at 6-13 weeks of gestational age. The rate of healthy babies born to these mothers was 37.5% that is lower than the reports from western countries. Also in this study in 4 cases, valve thrombosis occurred (9). According to different studies, there is no completely safe anticoagulant regimen for women with prosthetic heart valve during pregnancy but warfarin therapy can be used throughout pregnancy except near term if the dose of daily warfarin is less than 5 mg.

Achieving pregnancy in elderly patients by aid of ART methods which both (pregnancy and ART treatment) are hypercoagulable state, existence of two prosthetic heart valves that makes the patient sensitive to thromboembolic events, and ultimately anticoagulant therapy with warfarin during pregnancy without any complications made a special item of this case reported herein.

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