Danaparoid is a low molecular weight heparinoid (6000 D) containing 84% heparan sulphate, 12% dermatan sulphate and 4% chondroitin sulphate. It catalyses the inactivation of factor Xa mediated by antithrombin and also exhibits some anti-factor II activity. With only a small percentage of cross-reactivity (7%) with heparin-induced antibodies, danaparoid plays its main role in the prevention or treatment of thromboembolic events in patients with HIT II. So far there are no data about the prolonged use of danaparoid during lactation and only a few case reports about its use in pregnancy (1-3).

We report on a 39-year-old Caucasian patient (weight 56 kg, height 165 cm) with a heterozygous factor-V-Leiden mutation (Arg506Gln in position 1691) who had developed a deep pelvic vein thrombosis during a previous pregnancy. Under treatment with unfractionated heparin, a heparin-induced thrombocytopenia (HIT) type II had occurred with a drop in the platelet count from 576000/µl to 151000/µl on day 25 of the heparin therapy. The clinical suspicion was finally proven by a repeatedly positive heparin-PF4-antibody-assay (ELISA) and a positive heparin-induced platelet aggregation assay (HIPA). Six years later, the patient reappeared in our department in her 6th week of pregnancy with a reoccurrence and an in vitro selected alternative regimen of anticoagulation in pregnancy and lactation.

We started a therapy in the 20th week of pregnancy with a dose of 3 x 750 anti-Xa units danaparoid (Orgaran®, Celltech, Germany) and increased it to 2 x 1500 anti-Xa units from the 25th week of pregnancy onwards, depending on the anti-Xa-level 5 hours after s.c. application (target level: 0.2-0.4 anti-Xa units/ml). The application was stopped 24 hours before spontaneous delivery (39th week of pregnancy), and restarted 12 hours thereafter with half of the dose (2 x 750 anti-Xa units), increasing to full dose (2 x 1500 anti-Xa units) another 12 hours later for the 6-week period of childbed. The patient gave birth to a healthy child in 39th week of pregnancy. No bleeding complications occurred during or after delivery.

Because of the patient’s wish to continue the use of danaparoid during lactation, we established a chromogenic anti-Xa assay for danaparoid measurement in human breast-milk according to Harrison et al (4). Calibration was performed with an untreated volunteer’s breast milk. This breast milk was used to dissolve lyophilized normal human plasma (Instrumentation Laboratory, Kirchheim, Germany). Danaparoid in increasing concentrations (0.2-1.0 units/ml) was added to these solutions. After centrifugation at 2000G for 2 min. and precipitation of the lipids in the milk, the concentration in the remaining clear solution could be determined using a chromogenic anti-Xa assay (Substrate S2222, FXa 71 nkat, antithrombin III 10U, Haemochrom Diagnostika, Essen, Germany). Even with an anti-Xa-activity of 0.38 units/ml in the maternal blood (measured 5 hours after s.c. application), danaparoid could not be detected in breast-milk (optical density = 1.092 = 0.04 U/ml danaparoid), so that finally the patient was allowed to breast-feed. No side effects were observed either in the mother or child.

We conclude that danaparoid is not detectable in breast-milk. It seems that breast-feeding can be continued safely under danaparoid treatment during lactation. Besides, danaparoid is unlikely to cause any anticoagulant effects in breast fed infants since it exhibits poor gastrointestinal absorption (5). The presented case strongly supports the few former reports that danaparoid seems to be the medication of choice for anticoagulation in pregnant women with a past history of HIT.

Marc Schindewolf, Gerlinde Mosch, Rupert M. Bauersachs, Edelgard Lindhoff-Last
Division of Vascular Medicine, I. Medical Department, Center of Internal Medicine, Johann Wolfgang Goethe-University Hospital, Frankfurt/Main, Germany

Correspondence to:
M. Schindewolf, MD
Division of Vascular Medicine, I. Medical Department
Centre of Internal Medicine
Johann-Wolfgang Goethe-University Hospital, Frankfurt/Main
Theodor-Stern-Kai 7
60590 Frankfurt am Main, Germany
E-mail: marc.schindewolf@kgu.de
Received January 19, 2004
Accepted after revision April 1, 2004
Presented at the XIXth Congress of the International Society on Thrombosis and Haemostasis, July 12-18, 2003

Thromb Haemost 2004; 92: 211

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