COAGULATION DISORDERS IN PREGNANCY A NEW THERAPEUTIC APPROACH — APROTININ

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Introduction

Often the treatment of coagulation disorders in pregnancy is empirical as the very etiological process is poorly understood. To combat this physiological aberration, we used a new therapeutic approach - Aprotinin.

Aprotinin is a basic polypeptide which inactivates most of the important proteinases in plasma and blood cells and inhibits their formation from their proenzymes. It affects the catalytic interactions between individual clotting factors and fibrinolysis through its inhibitory effect on a host of enzymes. Its main therapeutic value lies in the inhibition of plasminogen activation by endogenous activators and the blocking of plasmin.

Aprotinin is available as 200,000 K.I. (Kallekrein Inhibition) units ampoules. It has been recomended in various obstetric problems associated with hypofibrinogenic states, excess fibrinolytic activity and the initial states of consumptive coagulopathy. We used the drug in the following manner - a loading dose of 200,000 K.I. units to 300,000 K.I. units given slowly intravenously over 10 minutes. This was followed by a maintenance dose of 50,000 units per hour infusion in isotonic glucose.

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Case Summaries

The following case summaries are described to highlight our experiences with the drug in three different aspects of coagulation problems in obstetrics.

Case 1

A 29 year old primigravida came in early labour with a history of prolonged infertility. (She had voluntarily avoided pregnancy due to the loss of both her sisters who had died during the process of delivery because of post-partum haemorrhage).

Antenatally the blood studies showed a clotting of 5 minutes, bleeding time of 2 1/2 min and a serum fibrinogen of 330 mg%. On admission, she had a full term viable pregnancy with a ripe cervix. The clotting time 3 hours later was a 14 min good clot. which in another 3 hours become

18 min good clot. Aprotinin returned to normal 6 min good clot. A caesarean was done to deliver a 2.8 kg male baby. The surgery was uneventful, no excess bleeding was encountered and the post operative convalescence was smooth. Aprotinin was continued 12 hours after delivery.

The same patient conceived again after a 1 1/2 year gap. Her antenatal period was uneventful and her clotting profile was normal. A semi elective caesarean section was done when she came in early labour. She had a delayed clotting time of 16 minutes. Aprotinin was administered and the clotting time controlled under 14 min before the surgery was performed, which was eneventful. Aprotinin was stopped 12 hours post surgery.

Case 2

A 38 year second gravida came with a confirmed diagnosis of Intra uterine fetal death. The clotting time on admission was 10 min., serum fibrinogen was 250 mg% and the platelets on smear were adequate. Two days later the clotting time increased to 15 min. and laminaria tents were introduced. The tents were removed 24 hours later and membranes ruptured to augment labour. At this stage her clotting time became 22 mins and active induction with oxytocin with aprotinin therapy was commenced. The clotting time returned to 12 min within 45 minutes of starting Aprotinin, she delivered a macerated still birth by breech presentation. The post delivery blood loss was merely 80 ml and placental delivery followed almost immediately after delivery of the baby.

Case 3

A 31 year old second gravida gave a history of prolonged bleeding after tonsillectomy, and easy bruising after injuries. She had also suffered from moderate post partum haemorrhage after the first delivery a full term vaccum extraction delivery 4 years ago. The reports indicated that the clotting time at the time was 13 mins. Antenatally in this pregnancy she had the following clotting profile, at 36 weeks gestation: clotting time 8 min. bleeding time 5 min. At full term she came in labor with a clotting time of 10 min., a soft poorly retracted clot. Aprotinin was instituted and the labor accelerated with pitocin. She delivered 2 hours after and the clotting time returned to 6 minutes within 20 minutes.

Impressions

In India, due to various pressures mainly social and religious, blood and blood fractions are difficult to obtain, if at all they are available. The use of Aprotinin can easily preempt or rather prevent the onset of coagulation defects in pregnancy and delivery. The drug has minimal side effects and exercises its action within minutes of I V administration. Thus it is highly recommended for short term prophylaxis and acute conditions. The drug although no substitute for blood can buy time till blood is made available or at times may obviate the need of blood.

Obstetrically it also seems to have benefits. The separation and delivery of the placenta is faster, blood loss is reduced and the uterine contractions seem to be augmented, the last point can make it act synergistically with utero-tonics. In our patients we did not have any adverse reactions to the drug. However, occasionally nausea, vomiting, local thrombophlebitis or rarely anaphylaxis can occur.

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