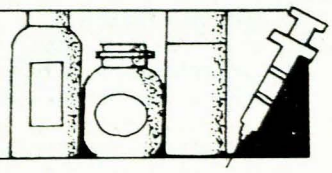
Medisyne in die Praktyk/Drugs in Practice



Anticoagulation during pregnancy

Anticoagulation therapy during pregnancy is essential in thrombo-embolic disease and for prophylaxis in patients with prosthetic heart valves. Any agent used to achieve this introduces a certain risk to mother and fetus. There is a definite, although low, incidence of teratogenesis associated with the use of warfarin in the first trimester of pregnancy.[1-4] Exposure at 6 - 9 weeks' gestation is reported to carry an approximately 8% incidence of warfarin embryopathy (the fetal warfarin syndrome), characterized by nasal hypoplasia and stippled epiphyses.[3] Warfarin administration during the second and third trimesters of pregnancy has been associated with an increased incidence of central nervous system defects such as microcephaly and mental retardation, and eye defects including blindness, optic atrophy and microphthalmia.[5-7] Late third-trimester exposure carries with it a clear danger of prenatal, perinatal or postnatal haemorrhage. In a series of 418 pregnant women treated with coumarin derivatives, one-sixth of the pregnancies resulted in abnormal liveborn infants, one-sixth ended in abortion or stillbirth, and two-thirds had a normal outcome.[3]

Heparin, on the other hand, is strongly polar and has certain advantages in pregnancy since it does not cross the placenta. However, although heparin is not known to be teratogenic its administration to pregnant women has been associated with an increased incidence of prematurity and stillbirth. Furthermore, significant maternal complications may occur, such as painful haematomas at injection sites and bone demineralization or osteopenia. Of particular concern is possible heparin-induced osteopenia in patients who receive more than 15 000 U daily for more than 6 months, and which has been associated with complications such as multiple vertebral compression fractures.[8-11] Even asymptomatic patients receiving prolonged subcutaneous heparin therapy have been shown to develop a degree of bone demineralization.[12]

Streptokinase has been used successfully to treat deep-vein thrombosis in 12 pregnant patients,[13] and there are several other case reports of streptokinase use in pregnancy.[14-16] Although little streptokinase crosses the placenta,[17] pregnancy is considered a minor contraindication to the use of thrombolytic therapy and subsequent delivery within 10 days a major contraindication.[18] At present there is insufficient experience documented to recommend the use of thrombolytic agents in pregnancy except under exceptional circumstances.

The most widely followed recommendations for anticoagulation in pregnancy are those of Hirsch *et al.*:[19] intravenous heparin during the first trimester followed by warfarin between 13 and 36 weeks, and reverting to heparin for the last weeks of pregnancy. It has been questioned whether oral anticoagulants should be used even after the first trimester[20] and some authors prefer subcutaneous, self-administered heparin throughout pregnancy.[4,21] It is not established whether subcutaneous heparin is as efficacious as warfarin, and because of the real risk of heparin-induced maternal osteopenia and the apparently low incidence of abnormalities induced by warfarin during the second and third trimester it would seem prudent to follow the recommendations of Hirsch *et al.*[19]

Because of the risks of anticoagulation therapy, venography is advisable to confirm the diagnosis in pregnant women considered to have deep-vein thrombosis. With adequate shielding of the uterus the direct radiation dose is small and venography of the femoral and more distal veins can be performed.[4]

Patients with prosthetic heart valves should be on effective contraception and need to be warned of the dangers of oral anticoagulants during the first trimester should they become pregnant. Those patients who require anticoagulation and who strongly desire to become pregnant should ideally attend a pre-conception clinic, be taking warfarin at the time of conception, and then be converted to heparin therapy as soon as pregnancy is diagnosed, following the protocol outlined by Hirsch *et al.*[19]

Not infrequently cardiac patients conceive inadvertently and present to their doctor only after 4-6 weeks, having continued to take warfarin. The most susceptible period of exposure for the development of warfarin embryopathy is the 6th - 9th week of pregnancy and it is therefore important to change to heparin for the remainder of the first trimester. However, patients should be advised of the potential risks to the fetus of exposure to warfarin and perhaps be offered the option of therapeutic abortion.

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