The Thrombo-embolic Disease in Pre-eclampsia

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Towards the end of a normal pregnancy the concentration of a number of the blood coagulation factors is higher than in non-pregnants. Fibrinogen, prothrombin and especially the prothrombin accelerators are reported to occur in increasing amounts. Besides there is a remarkable potential of thromboplastic substances bound in the placenta and the fetal membranes. This latent hypercoaguability of the blood reaches a maximum at the term of the pregnancy and the days after the delivery. Additional thrombosis promoting factors as aggregation of the blood corpuscles (sedimentation rate always increased in pregnancy!), retardation of the venous flow from the legs, traumatic injury to the endothelium in pelvic veins during labor, and possible toxic influence from traumatized tissue, then easely changes the hypercoaguable state of the blood into a thrombotic process.

Because of administrative, economic, and pediatric reasons a general prophylaxis with anticoagulants which interferes with the coagulation mechanism is very difficult to obtain. Early mobilization, which means first, rising from the bed within twenty four hours after a normal delivery prevents, more than the half of the thromboses in the leg, which otherwise arise if the patient is kept in bed three days or more after the delivery. Through active excercise the rate of the venous flow from the lower extremity is increased which prevents an intravascular sedimentation of aggregated erythrocytes and hypercoagulable blood. Through these measures the frequency of obstetrical thrombosis (superficial and deep together) stays around 1 per cent. T u r u n e n and V a r a in 1954 thus reported a total frequency of obstetrical thrombosis at the University Hospital for Women in Helsinki of 1.42 per cent. In this hospital early mobilization has been used since 1939 which covers the time of the statistic cited. In opposition to earlier belief, the early mobilization also in other respects aids the recovery of the physical condition and gynecological status of the patient.

When one analyses the about 1 per cent of thrombotic cases in obstetrics which occurs despite the early ambulation it is found that about a third of these cases arises in patients which show symptoms of pre-eclampsia whereas two thirds of the thrombotic cases are found as single complication or in conjunction with some obstetric diagnosis other than pre-eclampsia.

Among 19 756 obstetrical cases treated during the years 1951—1955 at the I. University Hospital for Women in Helsinki late toxemia of pregnancy was diagnosed in 2077 cases. Of these patients with symptomes of pre-eclampsia there were 95 cases of thrombosis of the lower limb (58 in superficial and 37 in deep veins). This means a frequency of 4.6 per cent thrombosis in pre-eclampsia. The total number of thrombosis among the 19 756 obstetrical cases recorded was 241 (165 in superficial and 76 in deep veins) which means a total frequency of thrombosis of 1.2 per cent. If the cases of pre-eclampsia are excluded a frequency of 0.9 per cent thrombosis remains (table 1).

Table 1: The frequency of thrombosis and late toxemia of pregnancy in 19 756 obstetrical cases

	Number	Per cent
Obstetrical cases, total	19 756	
Cases of late toxemia of pregnancy	2 077	
Cases of thrombosis, total	241	1.2
Cases of thrombosis among 2077 toxemic cases	95	4.6 (of toxemic cases)
Non-toxemic cases of thrombosis	146	0.9

The frequency of different symptoms of pre-eclampsia in the thrombotic cases are shown in table 2.

Table 2: Distribution of symptoms of late toxemia of pregnancy in relation to the type of thrombosis

Type of thrombosis in the leg	Hypertension	Albumin	Pre-eclamps.	Eclampsism.	Eclamps.	Total
Superficial	26	20	8	4		58
Deep	16	8	6	6	1	37

It is thus evident that a thrombosis in the leg is about four times more frequent in late toxemia of pregnancy than in non-toxemic obstetrical conditions.

One is perhaps justified to correlate the high frequency of thrombosis in pre-eclampsia with the occurrence of multiple thromboses and infarcts in capillaries and small vessels in different organs in pre-eclampsia and eclampsia. Histologically observed tissue damage in liver, kidneys, brain, and placenta

caused by such microthrombotic processes was the reason when anticoagulants were tried as therapy in severe pre-eclampsia (Maeck and Zilliacus, Turunen and Kinnunen, Løvset, Knutsen and Jakobsen).

A number of factors which contribute to a thrombotic state in pre-eclampsia are known. The concentration of fibrinogen, which at the end of a normal pregnancy is about 300 mg % reaches values of 500—600 mg% in late toxemia. The intravascular aggregation of erythrocytes is remarkably pronounced in pre-eclampsia (Zilliacus) and the relatively high platelet count also indicates a thrombotic tendency (Vara and Kotsalo).

It is very likely, too, that the pool of thromboplastic substances in the placenta contributes to the formation of thrombotic processes in pre-eclampsia. In premature separation of the placenta, when considerable amounts of thromboplastic substances pass over to the maternal bloodstream, a precipitation occurs. Excepting the hemorrhagic tendency, which follows the hypofibrinogenemia, vital organs are damaged through the thromboplastic precipitation of fibrinogen. Capillaries in kidneys, brain, and liver have been found to contain multiple foci of fibrin deposits (Schneider). This type of premature placental separation is typical in pre-eclampsia and is believed to occur subsequent to the development of small thromboses and infarcts in the uteroplacental surface. It is, however, very suggestive to think that it is quite possible that small quantities of thromboplastic substances are liberated from the placenta as a consequence of uterine contractions in labor or when the placenta is separating during the third stage of a normal delivery.

Together with other pre-existing thrombosis promoting factors especially in pre-eclampsia, as earlier mentioned, these thromboplastic substances may form the cause, which starts a thromboplastic process in a vein in which a retarded venous flow forms the dynamic premises for the thrombotic process to start. In late toxemia permanent stay in bed, one of the main therapeutic measures, can hardly be avoided. The premises for a thrombotic process to start in a vein in the inferior extremity are thus evident.

In pre-eclampsia there is thus plenty of reason to stay on guard against different complications caused by the hypercoagulable state of the blood: premature separation of the placenta on the basis of small thromboses and infarcts in the utero-placentar surface; when premature separation occurs: a bleeding tendency due to afibrinogenemia induced by thromboplastins liberated from the placenta and organic lesions from disseminated fibrin deposits, and post partum thrombo-embolic complications due to the hypercoagulability of the blood and thrombosis promoting dynamic factors in conjunction with the possible occurrence of small quantities of thromboplastic substances in the blood deliberated from the placenta during labor.

Because of relatively common occurrence of puerperal thrombo-embolism in pre-eclampsia a prophylaxis with anticoagulants seems to be indicated in cases of late toxemia of pregnancy. Of the two principally different types of anticoagulants, heparin and dicumarols, heparin seems to be the agent of choice in these cases, because of its specific selectivity to bind thromboplastins. In late toxemia of pregnancy the condition of the liver may not be suitable for additional stress like the action of dicumarols on the formation of prothrombin.

Summary

On the basis von 19756 obstetrical cases reviewed with regard to the frequency of thrombo-embolism it was found that post partal thrombo-embolism occurs about four times more frequently in late toxemia of pregnancy than in non pre-eclamptic obstetrical cases. There were 95 cases of puerperal thrombo-embolism (58 in superficial and 37 in deep seated veins of the leg) among the 2077 cases of late toxemia of pregnancy, which means a frequency of 4.6 per cent against a total frequency of thrombo-embolism of 1.2 per cent among all the obstetrical cases reviewed. Possible causes for a thrombotic process in pre-eclampsia are dicussed: placental thromboplastins, high concentration of plasma fibrinogen and other coagulation factors, aggregation and sedimentation of erythrocytes, retardation of the venous flow.

Of the anticoagulants heparin is recommended as the most suitable agent in prophylactic treatment of thrombosis in late toxemia of pregnancy.

Résumé

Etudiant la fréquence des thromboembolies sur 19 756 cas d'obstétrique on a trouvé que la thrombo-embolie post partum est environ quatre fois plus fréquente dans les cas de toxémie tardive de la grossesse que dans les cas non préeclamptiques.

Sur 2077 cas de toxémie tardive, il y avait 95 cas de thrombo-embolie puérpuerale (58 veines superficielles, 37 veines profondes des jambes), ce qui représente une fréquence de 4,6%, alors que la fréquence globale des troubles thrombo-emboliques est de 1,2%. Les causes possibles d'une thrombose dans les cas de préeclampsie sont passées en revue et discutées: thromboplastine placentaire, concentration élevée du fibrinogène et d'autres facteurs de coagulation, agglomération et sédimentation des érythrocytes, ralentissement du courant sanguin.

De tous les anticoagulants l'héparine est recommandée comme l'agent convenant le mieux pour la thérapie prophylactique des thromboses dans la toxémie tardive de la grossesse.

Zusammenfassung

Bei 19 756 Fällen einer geburtshilflichen Klinik wurde die Thromboembolie-frequenz nachgeprüft. Dabei ergab sich, daß bei Spätgestose die postpartalen Thromboembolien ungefähr viermal häufiger sind als bei nicht präeklamptischen Fällen. Unter 2077 Fällen mit Spätgestose waren 95 Fälle mit Thromboembolien im Wochenbett (58 der oberflächlichen und 37 der tiefen Beinvenen), was einer Frequenz von 4,6% entspricht, gegenüber einer totalen Frequenz von 1,2% aller untersuchten geburtshilflichen Fälle. Die möglichen Ursachen eines thrombotischen Prozesses bei Präeklampsie werden geprüft und diskutiert: Thromboplastine der Plazenta, erhöhte Konzentration von Fibrinogen und anderen Gerinnungsfaktoren, Zusammenballung und Sedimentation der Erythrozyten, Verlangsamung des venösen Rückflusses.

Von den Antikoagulantien wird Heparin zur Thromboseprophylaxe bei Spätgestose empfohlen.

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