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STUDYING THE EFFECT OF SPINAL ANESTHESIA ON PLATELET FUNCTION UNDERGOING CESAREAN SECTION

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ABSTRACT

In clinical practice, the only tests of platelet function are bleeding time and platelet number. Bleeding time lacks sensitivity and specificity but the PFA-100, an in vitro analyser of platelet function may be of value. This study aimed to evaluate any correlation between platelet number and function using the PFA-100 in pregnant women. During a 21-month period, platelet function was evaluated in whole blood as part of the pre-anaesthetic coagulation testing screen with the PFA-100 using collagen and epinephrine (PFA-EPI) or ADP (PFA-ADP) as platelet agonists. Thrombocytopenia was defined as a platelet number less than 150 G litre–1. The patients were divided into four groups. The increased PFA values and the correlation between PFA-ADP and platelet number in hypertensive thrombocytopenic women confirm that platelet function may be decreased in such patients. In patients with pregnancy-induced thrombocytopenia, platelet function may be preserved when the platelet count is as low as 60 G litre–1.

KEYWORDS: Spinal anesthesia, platelet function, casarean section.

INTRODUCTION

Until recently, only two tests could be performed to evaluate platelet function in a routine clinical setting. Bleeding time, which is highly operator-dependent, lacks sensitivity and specificity and has a poor diagnostic value even when platelet function is altered.[1]

Platelet aggregation tests cannot be used in usual practice and as the bleeding time, cannot predict the risk of haemorrhage. However, during pregnancy, knowledge of platelet function may be of critical importance before performing epidural anaesthesia. Indeed, platelet count may be decreased at the end of the third term of normal pregnancy in about 0.3% of women despite an increased platelet aggregability.3 In contrast, 28% of women with pre-eclampsia may have platelet counts of less than 150 G litre–1.[2]

Thrombocytopenia less than 100 G litre–1 is only observed in severe pre-eclampsia. In such patients, regional anaesthesia has been performed without any subsequent neurological complications,[3] even when decreased platelet function has been documented from both platelet aggregation tests and bleeding times. In pre-eclampsia patients, the platelet count above which epidural anaesthesia may be performed safely is not known. This may explain why there is still controversy regarding the value of measuring the platelet count at the end of pregnancy. The recent report of a spinal haematoma following epidural anaesthesia in an eclamptic woman with thrombocytopenia reinforces the need for a reproducible and accurate test to evaluate platelet function in this clinical setting.[4]

The PFA-100 platelet function analyser may be of value in such circumstances. The PFA-100 evaluates in vitro primary haemostasis by measuring the time required for whole blood to occlude an aperture in the membrane of a test cartridge, which is coated with platelet agonists. A sample (500 µl) of citrated blood is placed in the reservoir of the test cartridge, which is maintained at 37°C. It is aspirated under steady vacuum into the stainless steel capillaries, through which there is a central aperture cut into the membrane covered with collagen and the platelet agonist, epinephrine (PFA-EPI), or adenosine diphosphate (PFA-ADP). Platelet activation and aggregation occurs on the membrane leading to occlusion of the aperture and the interruption of blood flow.[5] This test is easy to perform and gives reproducible results, measured in seconds and similar to in vitro aggregation tests, within a few minutes.13 Moreover, as this test is performed on whole blood, it can evaluate platelet function in its natural environment.

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In such patients, regional anaesthesia has been performed without any subsequent neurological complications, 5–8 even when decreased platelet function has been documented from both platelet aggregation tests and bleeding times. 910 In pre-eclampsia patients, the platelet counts above which epidural anaesthesia may be performed safely is not known. This may explain why there is still controversy regarding the value of measuring the platelet count at the end of pregnancy.

REVIEW OF LITERATURE

Effects of anesthesia on coagulation

One of the physiological functions of platelets is to aggregate and, thus, to participate in hemostasis. There are chemical compounds such as adenosine diphosphate (ADP), adrenaline, collagen, and ristocetin that induce platelet aggregation.[6] There has been some interest in the interaction between inhaled anesthetics and platelet function. Several studies of the effects of inhalational anesthetic agents on platelet function have been reported since Ueda[7] demonstrated in 1971 that clinical concentrations of halothane inhibited (ADP)-induced platelet aggregation. Although some reported findings remain controversial halothane is considered to inhibit platelet aggregation[8], whereas isoflurane is not.

Sevoflurane in particular has been recently the subject of several investigations, however, the results remain contradictory. Skillful surgery combined with blood saving methods and careful management of blood coagulation will all help in reducing unnecessary blood loss and transfusion requirements. Excessive surgical bleeding causes hypovolemia, hemodynamic instability, anemia and reduced oxygen delivery to tissues with a subsequent increase in postoperative morbidity and mortality.[9] The role of anesthetists in managing

surgical blood loss has grown greatly in the last decade. Intraoperative blood loss varies according to the anesthetic agent used and with the type of anesthesia.[10]

Maintaining normothermia reduces blood loss, because of the deleterious effects of hypothermia on platelet function.[11] Moreover, anesthetists are increasingly confronted with subgroups of patients who refuse blood transfusion or who are likely to lose more blood in the perioperative period (e.g. patients on antiplatelet agents or anticoagulants, patients with hepatic cirrhosis, and those with chronic renal failure). The aim of this study is to assess the effects of sevoflurane and isoflurane on the coagulation system.

Platelet count

The expansion of the circulation associated with pregnancy reduces the platelets count. Thresholds for thrombocytopenia vary from 150 x109 g/dL to 100 x109 g/dL and counts between these thresholds are common in mothers at delivery.[12] Very low platelet counts are a concern to obstetric anaesthetists because of the risk of haemorrhage within the bony confines of the spine leading to paraplegia as a result of cord compression from a spinal haematoma following regional blockade.[13]

This is a rare complication in any surgical population, and in obstetric practice it is too rare to give a clear incidence. There is a single report of an epidural haematoma in a pregnant woman occurring in the presence of thrombocytopenia (71x109 g/dL). The debate regarding the safety of neuraxial blockade in women with thrombocytopenia is never going to be addressed by a clinical trial. For the foreseeable future, clinical practice will be guided by expert consensus opinion.[14]

Tests of platelet function

Potentially available tests of platelet function include the gold standard but expensive and time-consuming platelet aggregation studies conducted by some coagulation laboratories; the point of care assessments are provided by the platelet function analyser and different forms of thromboelastography. Paradoxically, the more sophisticated and sensitive the test, the less value it has for the obstetric anaesthetist in an immediate situation. Platelet aggregation studies are regarded by many as the best and most sophisticated tests of platelet function. In their attempt to isolate all compounding variables a laboratory protocol is used to standardise platelet count.[15]

They are of value in thrombocytopenia but take too long to organise and complete in an urgent clinical situation. The platelet function analyser is less sophisticated, but it does isolate other influences at work on coagulation. The impact of platelet count is unlikely to be seen unless counts are low.[16] Devices that assess the visco-elastic forces at play during whole blood coagulation, like the Thromboelastogram, are of value, although not affected by aspirin without a special protocol. It reflects most changes in haemostasis including prothrombin and bleeding states. The assessment of platelet function is in terms of clot strength, and as this is an in vivo assessment, it is dependent on fibrinogen levels, which are usually very high at term. The overall effects of the normal hypercoagulable state of pregnancy and deficits in the coagulation process can be evaluated together in a single trace. If the question asked by the obstetric anaesthetist is 'Will this blood clot?', then at present this is most likely to answer the question. Critics of the point of care coagulation monitoring point out that the reliability and safety of these devices when used to guide clinical decisions has never been established. Given the nature of the problem, this is unlikely to change.[17]

METHODS

After local ethical committee approval and informed consent, platelet function was assessed at the end of pregnancy during the anaesthetic visit on the first 99 normal pregnant patients studied and each time a patient presented with thrombocytopenia or pregnancy-induced hypertension (PIH) over a 21-month period.

Platelet count, activated partial thromboplastin times (APTT), prothrombin times (PT) and fibrinogen levels were also performed. PFA-100s, Patients were defined as normal (Group I) when they had no thrombocytopenia, hypertension, or past history of clinical bleeding, and clinical examination revealed no bleeding tendency. The other patients were divided into three groups according to the presence of thrombocytopenia (platelet count <150 G litre–1) and/or PIH: Group II, normal pregnancy with thrombocytopenia; Group III, hypertension of pregnancy without thrombocytopenia; and Group IV, hypertension with thrombocytopenia.

RESULTS

The results show that, there were no statistically significant differences between both groups regarding the demographic characteristics ($P > 0.05$). and shows the changes in pH and temperature in both studied groups.

There were no statistically significant differences between both groups at all times of measurements (P>0.05%). And shows the changes in Red blood cells count (RBCs), hemoglobin concentration (HB) and platelets count in both studied groups.

There were no statistically significant differences between both groups at all times of measurements. (P>0.05%), shows the changes in bleeding time, prothrombin time and prothrombin activity in both studied groups. There were no statistically significant differences between both groups at all times of measurements. (P>0.05) and the results show the changes in activated partial thromboplastine time (aPTT) and palteletes aggregation ratio in both studied groups.

There were statistically non-significant differences in (aPTT) between both groups at all times of measurements (P>0.05). While there was a statistically significant decrease in platelets aggregation ratios in the group(S) compared with the ratios in the group (I) during both intra and post operative periods (P).

None of the patients were in labour at the time of sampling. In Group II (40 women), the platelet count was less than 100 G litre–1 in 21 samples, and between 100 and 125 G litre–1 in 24 samples. In the 19 patients in Group IV, platelet count was less than 100 G litre–1 in 22 samples, less than 125 G litre–1 in four patients, and less than 150 G litre–1 in four patients. This distribution was not statistically different between Groups II and IV using Barnet Woolf tests (P>0.05).

PFA-EPI was statistically increased in Groups II, III, and IV compared with Group I whereas PFA-ADP was only increased in Group II compared with Group I (Table 2). When looking at individual results, PFA-ADP levels were within normal limits in all the patients from Groups I and III but higher in four patients from Group II and two from Group IV (P<0.01 by Barnet Woolf test). PFA-EPI was slightly increased above normal values in six samples from Group I, three samples from Group II, four from Group IV, and none from Group III (P>0.05 between groups by Barnet Woolf test; P=0.04 between Groups 1 and II or IV by Fischer exact test).

DISSCUION

Platelets play an important role in hemostasis during and after surgery.[18] Among multiple factors, interactions of drugs used in anesthesia with platelet function have been implicated to aggravate the risk of perioperative bleeding.[19]

Several studies of the effects of inhalational anesthetic agents on platelet function have been reported since Ueda (2) demonstrated in 1971 that clinical concentrations of halothane inhibited ADP-induced platelet aggregation.[20] Sevoflurane in particular has recently been the subject of several investigations; however, the results remain contradictory. The aim of this study is to assess the effects of sevoflurane and isoflurane on the coagulation system through measuring different coagulation profile including platelet count, prothrombin time and activity which is considered as a screening test for the extrinsic pathway of the coagulation cascade.[21]

Activated partial thromboplastin time was measured as a screening test for the intrinsic pathway of the coagulation system.[22] Bleeding time was also measured as a screening test for inherited and acquired disorders of platelet function. Platelet aggregation tests were performed which are more specific and sensitive tests for the assessment of platelet function.[23] pH values were assessed to exclude the effects of both acidoses which inhibits platelet aggregation, or alkalosis which enhances aggregation.[24] Body temperature was assessed to exclude the effect of hypothermia on the coagulation system as body temperature < 35 oC decreases platelet aggregation.[25] Primary hemostasis consists of platelet adhesion to subendothelial collagen, then activation, aggregation and finally the formation of a platelet plug. Erythrocytes are involved in this process because they flow in the center of the vessel and push platelets towards the site of action on the vessel wall enhancing shear forces which in turn activate platelets.[26] So, red blood cells count and hemoglobin levels were assessed to exclude anemic patients from the present study. In this study, body temperature values, red blood cells count, hemoglobin level, blood pH values were insignificantly changed during the predetermined times of measurements in both isoflurane (I) and sevoflurane (S) groups.

In women with pregnancy-induced thrombocytopenia, mean values of PFA were increased compared with normal pregnant patients suggesting that despite a pregnancy-induced increased platelet reactivity, platelet function is lowered. However, despite platelet values lower than 100 G litre–1 in approximately half of the patients, only four had PFA values

slightly increased above normal, with PFA-ADP and PFA-EPI both increased in three of them. This demonstrates that overall platelet function remains within physiological values in most of the patients with pregnancy-induced thrombocytopenia despite a platelet count below 100 G litre–1. In normal pregnant women, platelet reactivity is known to be increased, if platelet agonists such as ADP are still present, counterbalancing the decreased platelet number.3 Despite such reassuring results, it must be noted that in only one patient from Group II was the platelet count lower than 70 G litre–1 (namely 60 G litre–1) and thus these results cannot be extrapolated to normal pregnant patients with even lower platelet counts.

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