EFFECT OF NORMAL AND PRE-ECLAMPTIC PREGNANCIES ON PLASMA CHOLINESTERASE IN NIGERIAN WOMEN

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ABSTRACT

Background: Pre-eclampsia can be devastating and life-threatening for both mother and baby, particularly in developing countries. It is a major cause of maternal and foetal mortality and morbidity. Early diagnosis and management are very important to the reduction of mortality and morbidity. A sensitive diagnostic and prognostic marker will therefore be of great value. There is paucity of data on the effect of pre-eclamptic pregnancy on plasma cholinesterase activity especially in Nigerians.

Objective: Our aim was to determine the changes in plasma cholinesterase concentration in normal and pre-eclamptic pregnancies in Nigerians.

Setting: Antenatal Clinic and Prenatal Diagnostic and Therapy Centre in a Tertiary University Teaching Hospital in Lagos.

Patients and Methods: Plasma cholinesterase concentration was determined using a colorimetric method in 30 healthy non-pregnant, 30 healthy pregnant, 30 and 27 pregnant women with mild and severe pre-eclampsia, respectively, between 28 and 41 weeks of gestation. Cholinesterase activity was re-assessed 6 weeks *postpartum*.

Results: The mean plasma cholinesterase levels in healthy non-pregnant women, women with normal pregnancy, pregnant women with mild pre-eclampsia and those with severe pre-eclampsia were 3594±1042, 2135±422, 1781±330 and 1630±326 (m/L), respectively. Six weeks *postpartum*, the mean cholinesterase levels in the normal pregnant, mild eclamptic and severe eclamptic groups were 3212±346, 3157±750 and 2864±700 (/L), respectively.

Conclusions: Our study suggests that normal pregnancy, mild and severe pre-eclampsia cause a significant ($p < 0.01$) reduction in plasma cholinesterase activity compared to non-pregnant state, with the greatest decrease in severe pre-eclamptic pregnancy. This decline does not return to normal non-pregnant state in subjects with severe pre-clampsia within six weeks postpartum. The place of plasma cholinesterase concentration as a diagnostic and prognostic marker in pre-eclamptic and eclamptic pregnancies should be further explored.

Keywords: *Cholinesterase, Eclampsia, Pre-eclampsia, Pregnancy, Succinylcholine.*

INTRODUCTION

Eclampsia is a life-threatening complication of pregnancy. It is the occurrence of one or more convulsions superimposed on pre-eclampsia. Preeclampsia is pregnancy-induced hypertension in association with proteinuria (> 0.3 g in 24 hours) ± oedema, and virtually any organ system may be affected (1). Although outcome is often good, pre-eclampsia can be devastating and life-threatening for both mother and baby, particularly in developing countries (2,3). It may also lead to an increased risk of cardiovascular disease in later life. Although the cause is not fully understood, factors thought to have a role include genes, the placenta, the immune response, and maternal vascular disease (4,5).

A multisystem disorder usually associated with raised blood pressure and proteinuria, preeclampsia is relatively common, causing about 2-10% of maternal and foetal mortality and morbidity (7,8). There has never been any evidence suggesting an orderly progression of disease beginning with mild pre-eclampsia progressing to severe preeclampsia and then on to eclampsia. The disease process can begin mild and stay mild, or can be initially diagnosed as eclampsia without prior warning. Pre-eclampsia usually occurs in a woman's first pregnancy but may occur for the first time in a subsequent pregnancy. Less than one in 100 women with pre-eclampsia will develop eclampsia or (convulsions or seizures) or coma. Up to 20% of all pregnancies are complicated by high blood pressure. Complications resulting from high blood pressure, pre-eclampsia, and eclampsia may account for up to 20% of all deaths that occur in pregnant women (9).

Pre-eclamptic and eclamptic pregnancies are associated with significant hepatic dysfunction (10). Plasma cholinesterase is a mucoprotein produced in the liver which is responsible for most of the recovery from muscle paralysis produced by succinylcholine.

Previous studies have provided conflicting data regarding plasma cholinesterase activity in pre-eclamptic pregnancies (11). Tourtellotte and Odell have reported (12) that there is a decrease in plasma cholinesterase activity in pre-eclamptic pregnancy when compared to normal pregnancy. However, Pritchard (13) reported that there is no significant difference in plasma cholinesterase activity between normal and pre-eclamptic pregnant patients.

Magnesium sulphate is frequently used to prevent and treat convulsions in pre-eclamptic pregnant patients. In pre-eclamptic patients, magnesium is known to cause prolongation of succinylcholine duration of action. The prolongation of action of succinylcholine in the presence of magnesium in pre-eclamptic patients could be explained if there is a significant reduction in plasma cholinesterase activity. There is paucity of data on the effect of pre-eclamptic pregnancy on plasma cholinesterase activity. To the very best of our knowledge, there is no study that has reported the effect of pre-eclampsia on cholinesterase activity in Nigerians. Therefore, we studied plasma cholinesterase activity in healthy non-pregnant, normal and pre-eclamptic pregnancies in 117 Nigerians.

PATIENTS AND METHODS

The subjects (n=117) were adult (18-39 years) Nigerian females attending the Prenatal Diagnosis and Therapy Centre of the College of Medicine of the University of Lagos and the Antenatal Clinic of the Lagos University Teaching Hospital. A thorough history was taken and physical examination done. Thirty healthy non-pregnant women, 30 women with normal pregnancy, 30 pregnant women with mild preeclampsia and 27 women with severe pre-eclampsia were recruited for this study after informed consent. All patients had vaginal delivery.

For the purpose of this study, a patient was classified as a case of severe pre-eclampsia if any two of the following signs were present: (1) systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg; (2) proteinuria (>3+ on dipstick [500 mg/dL]); (3) facial oedema. On the other hand, a patient who had pregnancy-induced systole hypertension of 140 to <160 mmHg (or diastole hypertension of 90 to <110 mmHg) with proteinuria of 2+ (100 mg/dL) was classified as having mild pre-eclampsia. Blood pressure measurement was done using Mercury sphygmomanometer with appropriate size cuff in sitting position with the arm at level of the heart and phase V Korotkoff sound (sound disappearance) was used to measure diastolic blood pressure. Proteinuria was assessed with Combur® Test dipstick (Roche Diagnostics GmbH). Six mls of heparinized blood was collected from each patient and the plasma was separated for cholinesterase assay. All the blood samples were drawn at the time of admission before patients received any fluids or medications. Cholinesterase assays were done between 28 and 41 weeks of gestation for the pregnant groups and repeated 6 weeks post-partum. A colorimetric method was used in the determination of plasma cholinesterase activity. The kit (Cat. No. 190) manufactured by Randox Laboratories Ltd., United Kingdom was used. Briefly, butyryl cholinesterase hydrolyses butyrylthiocholine to give thiocholine and butyrate. The reaction between thiocholine and dithiobisnitrobenzoic acid yielded 2-nitro-5- mercaptobenzoate, a yellow compound that was measured at 405 nm in a Beckman Model 24 recording spectrophotometer at 24°C. Duplicate cholinesterase activities were measured for each patient plasma and mean of the two results was reported.This study was in accordance with the ethical standards of the Helsinki Declaration of 1975 and 1983, and those of the College of Medicine of the University of Lagos and Lagos University Teaching Hospital, Lagos, Nigeria.

Statistics

Results were expressed as means ± standard deviation (SD) and analyzed for statistical significance using one-way analysis of variance (ANOVA) and the Scheffe's post-hoc test. The significance level considered was p<0.05, except where otherwise stated.

RESULTS

The mean plasma cholinesterase levels in healthy non-pregnant women, women with normal pregnancy, pregnant women with mild preeclampsia and those with severe pre-eclampsia were 3594±1042, 2135±422, 1781±330 and 1630±326 (m/L), respectively. Six weeks after vaginal delivery, the mean plasma cholinesterase levels in the normal pregnant, mildly eclamptic and severely eclamptic groups were 3212±346, 3157±750 and 2864±700 (m/L), respectively (table 1).

Table 1: Effects of normal pregnancy and pre-eclampsia on plasma cholinesterase concentration

Group	Plasma cholinesterase (m/L)	Post-partum
Healthy non-pregnant (Control) (n=30)	3594 ± 1042	N/A
Healthy pregnant (n=30)	2135 ± 422^*	3212 ± 346[c]
Mild pre-eclampsia (n=30)	1781 ± 330^**[a]	3157 ± 750[c]
Severe pre-eclampsia (n=27)	1630 ± 326^**[a]	2864 ± 700[c]

Values are mean ± SD
N/A: Not applicable
^: Values of cholinesterase pre-partum (28-40 weeks of gestation)
*: Significantly different from the control group at <0.05
**: Significantly different from the control group at <0.01
a: Significantly different from the corresponding pre-partum group at <0.01
b: Significantly different from the corresponding pre-partum group at <0.05
c: Significantly different from the control group at <0.05
d: Significantly different from the normal pregnant group at <0.05

DISCUSSION

Cholinesterase is an enzyme that catalyzes the hydrolysis of the neurotransmitter acetylcholine into choline and acetic acid, a reaction necessary to allow a cholinergic neuron to return to its resting state after activation. In this present study, the pregnant state caused a significant reduction (p<0.05) in plasma cholinesterase concentration when compared to the healthy non-pregnant female. Preeclampsia further caused a significant reduction (p<0.05) in plasma cholinesterase than the normal pregnant state. Our findings are at variance with a previous study that reported that there is no significant difference in plasma cholinesterase activity between normal and pre-eclamptic pregnant patients (12). The reason for this difference is not clear but may be due to differences in methods of assay, severity of eclampsia or may be genetic in nature. Our findings are, however, in consonance with those of Kambam *et al*., (11) who got a significant reduction in plasma cholinesterase activity in pre-eclamptic pregnant women when compared to healthy non-pregnant (p<0.001) and healthy pregnant women (p<0.001). In addition, in present study, it was noted that the worse the eclampsia, the lower the plasma cholinesterase level.

In pregnancy (in patients with HELLP syndrome [haemolysis, elevated liver enzymes, low platelets], eclampsia, *etc*, plasma cholinesterase activity is markedly decreased, resulting in a prolonged succinylcholine effect (14,15). In such patients there is a wide variability in the neuromuscular blocking effect, onset and duration of paralysis caused by succinylcholine (16,17). The mechanisms by which normal and eclamptic pregnancies cause a reduction in plasma cholinesterase activity are not fully known. Various explanations including haemodilution, hepatic dysfunction, and hypoalbuminaemia have been offered as possible mechanisms for the decrease in plasma cholinesterase activity in pregnancy (10). It has been reported that it is possible to predict the duration of apnoea and time to twitch recovery following the administration of succinylcholine, utilizing correlation with plasma cholinesterase concentration (18). Prolongation of apnoea from

succinylcholine has been observed in the presence of low plasma cholinesterase activity in normal pregnancy (19).

Present study also demonstrated that, while the plasma cholinesterase level of the normal and mildly eplamptic pregnancies approached that of the healthy non-pregnant state after parturition, that of the severely eclamptic subject did not return to the non-pregnant state within six weeks. The reason for these observations is not too clear. It may, however, not be unconnected with liver derangement, though it has been reported that patients with acute fatty liver of pregnancy, HELLP syndrome, pre-eclampsia had rapid improvement in liver functions postpartum (20).

We recommend that severely pre-eclamptic patients should be monitored for longer than six weeks postpartum. We also advocate that consideration should be given to the use of a peripheral nerve stimulator when succinylcholine is administered to pre-eclamptic and eclamptic pregnant women. Future research should be targeted at exploring the place of cholinesterase activity as both a diagnostic tool and a prognostic marker in pre-eclamptic and eclamptic pregnancies.

CONCLUSIONS

Our study suggests that normal pregnancy and preeclampsia cause a significant ($p<0.01$) reduction in plasma cholinesterase activity when compared to the healthy non-pregnant state. Our data also show that there is a significant ($p< 0.01$) greater decrease in plasma cholinesterase concentration in women with severe pre-eclampsia compared with those with mild eclampsia. This decline does not return to normal state in subjects with severe preeclampsia within six weeks postpartum. Finally, cholinesterase level may become a diagnostic and prognostic marker in pre-eclamptic and eclamptic pregnancies.

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