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Platelet intracellular free calcium concentrations in normotensive and hypertensive pregnancy.

Abstract

This thesis is concerned with changes that occur in human platelet intracellular free calcium concentration $[Ca^{2}+]_{i}$ in normal pregnancy, pregnancy induced hypertension and pre-eclampsia.

Platelets are anucleate, circulatory cells whose reactivity has been shown to alter in both uncomplicated normotensive pregnancy and pregnancies where there is associated hypertension.

Platelets have also been extensively used as an easily sampled model of vascular smooth muscle cells, as both cell types have a calcium-dependent contraction coupling mechanism and homologous surface receptors which allow hormones to exert their effects on both tissues via intracellular signal transduction.

Intracellular free calcium plays a major role as a second messenger involved in the process of cell activation. For many years this has been known to be the key trigger for such processes such as contraction and exocytosis.

This thesis and study has utilized the contemporary fluorescent indicator, fura-2, which may be loaded into small, intact, living cells to measure platelet intracellular free calcium concentration. An increase in the basal platelet intracellular free calcium concentration has been demonstrated, both in a pilot cross-sectional study and a prospective, longitudinal study of normotensive uncomplicated nulliparous pregnancy by the third trimester returning to preconceptual levels within 6 weeks of the puerperium. These data seem to

reflect increased platelet reactivity when measured ex-vivo, rather than any primary changes in vascular smooth muscle tension (Kilby MD et al. 1990. A cross-sectional study of basal platelet intracellular free calcium concentration in normotensive and hypertension primigravid pregnancy. Clinical Science. 78: 75-80; Kilby MD et al. 1993. Changes in platelet intracellular free calcium in normal pregnancy. British Journal of Obstetrics & Gynaecology. 100: 375-379).

A cross-sectional study investigating nulliparous women revealed a significant increase in basal intracellular free calcium concentration in those women whose pregnancies were complicated by both essential hypertension (Kilby MD et al. 1993. Platelet cytosolic calcium in human pregnancy complicated by essential hypertension. American Journal of Obstetrics and Gynecology. 169: 141-143) and in pregnancy induced hypertension and pre-eclampsia (Kilby MD et al. 1992. Calcium and platelets in normotensive and hypertensive human pregnancy. Journal of Hypertension. 10: 997-1003).

Although in-vitro studies of platelet reactivity in pre-eclampsia indicates platelet 'exhaustion', this study confirms that these platelets are indeed hyperactive, as reflected by an elevated intracellular free calcium concentration and indeed the platelets are stimulated by circulating angiotensin II concentrations (Baker PN, Kilby MD, Broughton-Pipkin F. 1992. The effects of angiotensin II on platelet intracellular free calcium concentration in human pregnancy. Journal of Hypertension. 10: 55-60; Baker PN, Kilby MD, Broughton-Pipkin F. 1993. Angiotensin II induced increase in platelet intracellular free calcium concentration in hypertensive and normotensive pregnancy. American Journal of Obstetrics and Gynecology. 169: 749-750). In addition, a positive association was noted between platelet intracellular free calcium concentration and arterial blood pressure in normal and hypertensive subjects.

Studies on umbilical cord blood from neonates born to women both with normotensive and hypertensive pregnancies indicated that platelet intracellular

free calcium concentration from the feto-placental circulation reflected hyporeactivity in platelets previously noted by in-vitro studies (Kilby MD, et al. 1994. Neonatal and maternal platelet cytosolic calcium in normotensive and hypertensive pregnancy. Archives of Disease of Childhood (Fetal and Neonatal Edition). 71: F6-F10).