The influence of \( E_2 \) and \( P_4 \) on \textit{in vitro} NO\textsubscript{x} production in the porcine myometrium during first half of pregnancy

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Abstract

The aim of the present study was to determine 1) concentrations of NO\textsubscript{x} in the myometrium of pregnant gilts, and 2) the influence of estradiol-17\( \beta \) (\( E_2 \)) and/or progesterone (\( P_4 \)) on NO\textsubscript{x} production by the porcine myometrium on days 5, 10, 15, 20, 25, 30, 35, 40 and 60 of pregnancy (\( n = 5 \) per day). Total NO\textsubscript{x} concentrations were determined using a microplate assay method based on the Griess reaction. During the first 60 days of gestation, a triphasic pattern in the concentration of NO\textsubscript{x} in the porcine myometrium was observed with a peak on days 10-15, 30 and 60 of gestation. We also demonstrated the stimulatory effect of \( E_2 \) and/or \( P_4 \) on \textit{in vitro} NO production by the porcine myometrium. The stimulatory effect of steroid hormones on NO\textsubscript{x} release depended on the treatment dose of steroids and day of pregnancy. These data suggest that locally produced NO may inhibit spontaneous uterine contraction and therefore is involved in the maintenance of myometrial quiescence during pregnancy.

Key words: nitric oxide, NO\textsubscript{x}, myometrium, steroid hormones, pregnancy, pig

Introduction

Myometrial quiescence is necessary for successful termination of term gestation. The contraction of the uterine myometrium often results in preterm labour, one of the leading causes of infant mortality and morbidity. Several regulatory factors influence uterine activity, including steroid hormones and substances that suppress or stimulate myometrial contractility. In the rat, myometrial quiescence during pregnancy correspond with elevated progesterone levels, and increased contractile activity is associated with a decrease in progesterone and increase in estradiol (Bedford et al. 1972).

During pregnancy, the myometrium is under the influence of circulating neurohumoral factors, locally released neurohumoral factors and local physical factors like myometrial stretching due to increasing uterine volume as well as placental and myometrial hormones and autacoids like histamine, prostaglandins or nitric oxide. Nitric oxide (NO) is a potent vasodilator produced from L-arginine via three distinct isoforms of NO synthase (NOS) (Knowles and Moncada 1994). NO is an endogenous vasodilator that activates cytosolic guanlyte cyclase in vascular smooth muscle leading to active vasodilation. Experimental and clinical studies (Yallampalli and Garfield 1993, Yang et al. 1996) strongly suggest that increased NO synthesis...