REPRODUCTIVE BIOLOGY

ORIGINAL RESEARCH

Influence of estradiol-17β and progesterone on nitric oxide (NO) production in the porcine endometrium during first half of pregnancy

Aneta Andronowska[1], Marcin Chruściel
Institute of Animal Reproduction and Food Research of Polish Academy of Sciences, Department of Reproductive Histophysiology, Olsztyn, Poland

Received: 5 January 2008; accepted: 6 March 2008

SUMMARY

The purpose of the study was to examine: 1/ endometrial concentrations of nitrate/nitrite (NO*x*) in pregnant pigs, and 2/ the influence of estradiol-17β (E_2) and/or progesterone (P_4) on NO*x* production by porcine endometrium during the first half of pregnancy. Total NO*x* concentrations were determined using a microplate assay method based on the Griess reaction. Evident fluctuations of endometrial NO*x* content were found during the examined time of pregnancy (days 5, 10, 15, 20, 25, 30, 35, 40 and 60 of pregnancy). The NO*x* concentration was highest on days 10 and 15, and then lowered until day 60 of pregnancy. In addition, we demonstrated the stimulatory effect of E_2 and/or P_4 on NO *in vitro* production by porcine endometrial slices. The medium content of NO*x* depended on the steroid type, treatment dose and day of pregnancy. It is possible that the observed differences in the strength of the stimulatory action of E_2 and/or P_4 on

[1]Corresponding author: Institute of Animal Reproduction and Food Research of Polish Academy of Sciences, Tuwima 10, 10-747 Olsztyn, Poland; email: aneta@pan.olsztyn.pl

endometrial NO*x* production are associated with activation of different isoforms of NOS. *Reproductive Biology 2008* ***8*** *1:43-55.*
Key words: nitric oxide, NO*x*, endometrium, pregnancy, pig

INTRODUCTION

Nitric oxide (NO) is a major mediator of numerous biological processes, including vascular functions [15], neurotransmission [5], hormone secretion [24] and inflammation [21]. Nitric oxide is synthesized from L-arginine by nitric oxide synthases (NOSs), the family of enzymes in which three isoforms have been identified: neuronal NOS (nNOS), inducible NOS (iNOS) and endothelial NOS (eNOS; [18]).

It has been demonstrated that NO generated in the cyclic and gravid uterus [1, 2, 30] plays an important role in maintaining uterine quiescence during pregnancy [9, 12]. Moreover, NO affects the endometrium which the vascular function changes during the estrous cycle and pregnancy [4, 22, 30]. In many species NO generation is up-regulated during pregnancy and down-regulated during delivery [6, 12, 23, 26, 31, 32]. In rats, production of NO, measured as nitrites and nitrates concentrations (NO*x*, stable products of NO oxidation), increases during mid-gestation and markedly decreases during spontaneous delivery and postpartum period [32]. Others have also reported a decrease in NOS activity in rat [23] and rabbit [26] uterine tissue at term. An increase in NOS content in the uterus may be important in the maintenance of pregnancy, and a decrease in NOS at term may play a role in initiation of labour.

It has been suggested that ovarian steroid hormones, progesterone (P_4) and estradiol-17β (E_2), are important modulators of NOS activity [3, 11]. Administration of E_2 to ovariectomized pigs increased NADPH-diaphorase (marker for NOS) activity in the endothelium of the blood and lymph vessels of the uterine broad ligament [34, 35]. In the rat uterus, E_2 inhibited iNOS expression but stimulated eNOS [33] and *in vitro* NO production [7]. The effect of P_4 on NOS expression is tissue-dependent. In the rat uterus and placenta, P_4 up-regulates iNOS expression and NO production [7].