PERTINENT FORMAT FOR ABSTRACT SUBMISSION TO NVF-SIF JOINT MEETING 2003

Abstracts should be in English. Please use Word 6.0 or higher version. Page settings: A4 landscape, margins left 1 inch; right 1.79 inch. Lettertype Times, size 10. Use max 24 lines, not exceeding 2500 characters and use correct English (spelling checker). Title should be in capitals, followed by <return>. Authors on the next line(s), followed by <return>. Affiliations on next line(s), followed by 2x <return>. You may use the subheadings Introduction; Methods; Results; Conclusions. If so, please use bold printing and start sections on new line. References should be given in the text as [Author et al., Fund Clin Pharmacol 12:23-24, 2002].

BASELINE FUNCTION OF PLACENTAL VASCULAR K_{ATP}-CHANNELS IN HEALTHY AND IN DIABETIC WOMEN.

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Introduction: During pregnancy an optimal vascular function in the placenta is essential for normal fetal development and growth. Endothelial dysfunction in the fetal placental vascular bed in diabetes type 1 (DM) may contribute to the elevated perinatal morbidity and mortality in DM. The placental vascular bed is unique because it lacks autonomic innervation. Regulation of the placental circulation completely depends on locally produced vasoactive mediators.
DM has been associated with endothelial dysfunction, in particular concerning the release of endothelium derived relaxing factors. One such factor is endothelium-derived hyperpolarising factor (EDHF) of which the identity remains unknown. EDHF relaxes smooth muscle cells at least partly by opening of ATP-dependent K^+-channels (K_{ATP}-channels). We investigated whether the potassium efflux through K_{ATP}-channels contributes to the baseline vascular tone in the fetal placental vascular bed in diabetic patients as compared with healthy controls.
Methods: We collected 11 placentas: 4 placentas of diabetic patients and 7 of healthy controls. Within 20 minutes from delivery a suitable cotyledon was selected for ex-vivo dual perfusion. Fetal and maternal inflow were kept constant, perfusion fluid was oxygenated with 95 % O_2 / 5% CO_2, temperature was 37 ° C and pH 7,4. A continuous measurement of fetal arterial blood pressure was performed. Because the perfusion flow was set at a constant level, the pressure in the circulation was considered to be a measure of the vascular resistance. By adding increasing concentrations of the K_{ATP}-channel blocker glibenclamide the K_{ATP}-channel dependent component of the baseline vascular tone in the fetal placental circulation was quantified. Concentration-response curves to glibenclamide were fit by the sigmoid E_{max} model (GraphPad Prism), and the calculated E_{max} and EC_{50} were compared by two-tailed unpaired Student t-tests (SPSS).
Results: Baseline fetal arterial pressure was comparable in DM and controls (mean ± SEM: 22.8 ± 2.8 versus 19.8 ± 0.4 mmHg). In controls, glibenclamide increased fetal arterial pressure concentration-dependently up to 56.3 ± 5.7 mmHg. In diabetes, a maximum pressure of 37.6 ± 4.2 mmHg was reached. The net glibenclamide-induced increase in pressure was attenuated in diabetes as compared with controls (14.7 ± 5.6 versus 36.5 ± 5.8 mmHg, P=0.03). The log EC_{50} did not differ between groups.
Conclusion: Glibenclamide induces vasoconstriction, pointing towards a functional role of K_{ATP}-channels in the regulation of baseline vascular tone in the placenta. In diabetes, this vasodilator mechanism appears to be impaired.