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Title (type in CAPITAL LETTERS, leave one blank line before the text) PELVIC STIMULATIONS AT FIXED BLADDER VOLUMES: IMPACT ON URINE PRODUCTION, SYSTEMIC ARTERIAL PRESSURE AND RENAL BLOOD FLOW

Aims of Study Bladder filling activates a reflectory change in blood pressure, renal blood flow and urine production. This has been substantiated since one hundred years in animal models. It is not a hydrodynamic response since diversion of urine by cutting the ureters does not change the response. These previous studies all have been passive bladder filling investigations. In this study we investigated the effect of nerve stimulated bladder contractions in pigs and their effect on Urine Production (UP), Renal Blood Flow (RBF) and systemic Arterial Pressure (AP). Methods and materials In Five Danish landrace female pigs (Yorkshire/Lancaster) weight 35 kg on average, anaesthesia was induced and maintained with Ketamine and Midazolam. A double lumen catheter (8-F.) was placed in the bladder through an abdominal midline incision for bladder fillings, bladder emptying and bladder pressure recordings. A catheter was placed in the right femoral artery for Arterial pressure (AP) monitoring. The renal vessels and ureters were identified through bilateral flank incisions. An ultrasonic flow probe 3mm (InVivo, Denmark) was placed on the renal arteries to measure the Renal Blood Flow (RBF). Both midurethers were cannulated with 8-F. baby feeding tubes, placed in the kidney pelvis and connected to an especially designed pressure transducer system for urine production measurements. The flow probes and the catheters (connected to pressure transducers) were attached to an amplifier (SCXI, National Instruments), recorded and analysed (BioBench, National Instruments) using a PC. A dissection down to the lateral margin of the coccygeal bone was performed in order to identify the pelvic nerves according to Wen et al. A cuff-electrode was placed on the right pelvic nerve.

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Electrical current was applied to the nerve using a custom-made stimulator set on the parameters: 20 secs stimulations in trains of 4 (P1,P3,P4) and 10 (P2), squared-shaped wave, 100-µs duration, 30 pulses/s, 2x threshold. Study design: After the surgical preparation the animal was left resting for a recovery period of 90 minutes. AP, RBF and Urine Production were monitored continuously. Four patterns of stimulations were performed (P1, P2, P3, P4). After each stimulation pattern the animal was given a period of twenty minutes to recover from bladder fatique. The stimulation's intervals in P1 P2 P4 were 5 min and in P2 2 min.Before P3 the right pelvic nerve was cut cranially to the cuff and before P4 the left pelvic nerve was cut. Five minutes before each of this four stimulation patterns the bladder was emptied and slowly filled with 100 cc of saline solution at room temperature. Both kidneys renal blood flow, bladder pressure, AP and urine production were measured continuously before, during and after pelvic nerve stimulations. Results The urine production rate in both kidneys changed neither during pelvic stimulation patterns nor during the resting period. The means of urine production during resting periods vs. stimulation periods were 0,339 ml/min vs 0,338 ml/min (p= 0,23) in the right kidney and 0,346 vs. 0,322 (p= 0,48) in the left kidney. Both the AP and RBF decreased after the stimulation (5,54-mm/Hg drop of arterial pressure and between 5 and 15-ml/min drop of RBF) before returning to the baseline value in less than a minute. Conclusions An electric stimulation on the pelvic nerve with duration of 20 seconds causes a drop in the systemic arterial pressure and the renal blood flow, but does not elicit any effect on the urine production, which remains constant during both the stimulations and resting periods. The hemodynamic response thus seems faster reacting than the urine production response.

Fig 1 Decreasing of arterial pressure and renal blood flow in the right and left renal artery, subsequently to four bladder stimulations



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