PERCUTANEOUS TIBIAL NERVE STIMULATION TO MODULATE THE MICTURITION REFLEX: AN EXPERIMENTAL STUDY IN FEMALE CATS

Hypothesis / aims of study
The tibial nerve is a mixed (sensory and motor) nerve that originates from the spinal level L₄ to S₃. Percutaneous stimulation of this nerve (PTNS) has been successfully applied in the treatment of overactive bladder syndrome. The physiological mechanism is still unknown, but it is presumed that signals from and towards the bladder are modulated by afferent stimulation through the sacral plexus. The present study was designed to investigate whether PTNS can modulate the micturition reflex in female cats and which areas of the central nervous system are involved in this process.

Study design, materials and methods
7 female cats (mean 3.7 kg, range 2.5-4) were anesthetized with xylazine (0.5 mg/kg/hour i.v.) and ketamine (5 mg/kg/hour i.v.). After adequate anaesthesia and analgesic depth were reached (i.e. the eyelash reflex was almost absent and no paw retraction on moderate pinching), cystometry was performed to determine the baseline micturition reflex volume (MRV) in each animal. Body warm saline (39 °C) was used at a filling rate of 1 ml/minute until a clear bladder contraction occurred. MRV was determined by measuring the collected voided volume and the catheterised residual volume. This was repeated 2 times. After a 60-minute pause, 2 acupuncture needles were placed in the vicinity of the tibial nerve in 1 leg. Both needles were connected to a battery driven stimulator. Flexion of the toes on activation of the stimulator confirmed correct needle placement. MRV was determined again with continuous tibial nerve stimulation (1-4 mA, 200 microsec., 10 Hz) at the level of the motor response, which did not result in paw retraction or an increase of blood pressure and hart rate. Stimulation and bladder filling were stopped immediately when the micturition reflex occurred and cystometry was continued until baseline values were reached. This was repeated at least once. Between cystometries was a resting period of 5 minutes. The protocol was performed twice in the same animal. Between two sessions was a period of one week. In 2 cats, that responded positively on PTNS (i.e. an increased MRV during PTNS), MRV was also determined during percutaneous median nerve stimulation (PMNS). Statistical analyses were performed with the Wilcoxon signed Ranks Test.

Results
In 2 cats the micturition reflex was absent. In the other 5 at baseline mean MRTV was 54 cc (SD 26). During PTNS mean MRV significantly increased to 71 cc (SD 30, p= 0.001). After PTNS at repeated cystometries mean MRV returned to a baseline value of 54 cc (SD 27, p = 0.002). Stimulation of the median nerve had no effect on MRV. The results in the individual cats are presented in table 1.

<table>
<thead>
<tr>
<th>Cat</th>
<th>Baseline</th>
<th>During PTNS*</th>
<th>After PTNS*</th>
<th>During PMNS**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22 (1.2)</td>
<td>31 (1.4)</td>
<td>20 (3.5)</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>47 (2.8)</td>
<td>55 (3.6)</td>
<td>46 (1.4)</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>44 (12.3)</td>
<td>61 (7.1)</td>
<td>47 (12.0)</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>102 (4.7)</td>
<td>116 (1.3)</td>
<td>101 (0.7)</td>
<td>97 (4.2)</td>
</tr>
<tr>
<td>5</td>
<td>56 (7.1)</td>
<td>63 (11.1)</td>
<td>54 (8.4)</td>
<td>55 (9.6)</td>
</tr>
</tbody>
</table>

*Percutaneous Tibial Nerve Stimulation, **Percutaneous Median Nerve Stimulation

Interpretation of results
Percutaneous tibial nerve stimulation in a cat model appears to be effective in inhibiting the micturition reflex, since MRV significantly increased during stimulation. This effect is reversible since MRV returned to baseline values afterwards. A carry-over effect could be
demonstrated in 1 cat: it took 103 minutes before baseline values were reached. As was suspected, the sacral plexus seems to be involved in modulating the micturition reflex by acute tibial nerve stimulation (L4-S3), since stimulation of the median nerve (C7-C8) did not change the MRV. Furthermore, increased sympathetic activity has been linked to suppression of bladder reflexes [1]. However, this theory was not supported by our study, since during both PTNS and PMNS blood pressure and heart rate were not altered. Moreover, pain was ruled out since no paw retraction occurred during either PTNS or PMNS. Both anesthesia and analgesic depth were superficial since the eyelash reflex had not completely disappeared and stimulation at a higher intensity did result in paw retraction, indicating pain. Finally, from this study it is not possible to determine whether suprasacral (i.e. pontine and/or cortical) areas are involved in the neuromodulation process as was suggested in the literature [2].

Concluding message
In this anesthetized cat model it could be proven that acute stimulation of the tibial nerve reversibly modulates the volume at which the micturition reflex occurs. These experiments show that sacral reflex pathways seem to be involved in this mechanism and not pain, sympathetic or cervico-thoracic reflex pathway activation.

References

FUNDING: CystoMedix Inc., Anoka, MN, USA