Urol Res (1993) 21:333–337

Urological Research

Stimulated pressure response of the ileocolonic junctional zone and its use as a continence mechanism in a canine model

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Received: 8 February 1993 / Accepted: 28 May 1993

Summary. Mechanisms for maintaining passive continence in the efferent limb of urinary diversions include compression of tissue, peristalsis, equilibration of pressure and use of valves. Motor activity and pressure in the ileum, ileocecal valve (ICV) and the colon were evaluated in dogs. Spontaneous activity and pressure were compared with stimulated pressure response and activity. Stimulation was performed at the pelvic nerve and the small nerves in the mesenterium, as well as direct neurostimulation of the bowel. Resting pressure at the ICV was 12.7 ± 0.4 cmH_2O rising to 26.4 ± 2.2 cmH_2O during spontaneous depolarization. Stimulation of the pelvic nerve resulted in increased colonic motor activity with unchanged pressure. Electric stimulation of small mesenterical nerves to the ICV increased pressure in the ICV to 35.0 ± 4.1 cmH_2O, while direct myoelectric stimulation of the ICV zone increased the intraluminal pressure to 75.0 ± 3.2 cmH_2O. Termination of the electric stimulation was followed by a slow decrease of pressure to the resting level over a period of 30–45 s. Maintaining continence at the ICV with long-term constant or intermittent stimulation seems feasible.

Key words: Ileocecal valve – Electric stimulation – Urinary diversion – Continence

Continent urinary diversion can utilize the ileocecal junctional zone for constructing a nipple, which uses reinforced tissue in the ileocecal area to form a passively continent efferent limb. In the Mainz pouch technique the terminal ileum is invaginated into the mixed ileocolonic pouch, whereas the Indiana pouch is built of plicated terminal ileum as the efferent limb and a slightly reinforced ileocecal valve (ICV).

Continence is achieved in the Mainz pouch by compressing the lumem through intussusception, thereby creating a seal of tissue coaptation. Peristalsis of the terminal ileum, the sphincteric mechanism of the ICV itself, a plication of the terminal ileum for sphincteric compression and, if necessary, slight intussusception of the ICV help to prevent leakage in the Indiana pouch. Moreover valves (Mitrofanoff) or equilibration of the pressure (Kock, Hendren-King) can be used to achieve passive continence.

This study in dogs was performed to ascertain the electric activity and pressure response of the normal unstimulated bowel (ileum, colon, ileocecal junctional zone), to determine pressures in the ICV and define the sphincteric area. The pressure response of the ICV to electric stimulation of the ICV and adjacent segments of bowel was measured.

While currently used urinary diversions apply the principles of valves, equilibration of pressure, peristalsis and compression for maintaining a "passive continence", neurostimulation of bowel segments could possibly lead to an "actively continent sphincter".

Materials and methods

In eight adult mongrel dogs weighing between 10 and 17.5 kg, anaesthesia was induced with pentobarbital (30 mg/kg intravenously) following premedication with acepromazin maleate (0.15 mg/kg intramuscularly). The dogs were kept ventilated with air through an endotracheal tube. The ileum and colon were exposed through a midline laparotomy. All experiments were performed after the animal had fasted for at least 12 h.

The colon was opened about 20 cm aboral of the ileocecal valve (ICV), the ileum about 15 cm from the ICV. The bowel was cleaned by rinsing with saline until clear irrigation fluid was obtained.

A 4F four-channel pressure membrane catheter (Heyer-Schulte, Goleta, Calif.) was positioned from the ileum through the ICV into the colon. One pressure sensor was placed in the colon, one balloon close to the ICV on the colonic side and the third balloon on the ileal side of the ICV. In a second experiment, the pressure balloons were placed from the colon through the valve to record pressure and activity in the ileum as well as in the ileocecal junctional zone.

Pressures were measured with Gould Statham P50 pressure transducers and recorded on a four-channel polygraph (Grass Model 7), which was calibrated prior to and after every study.

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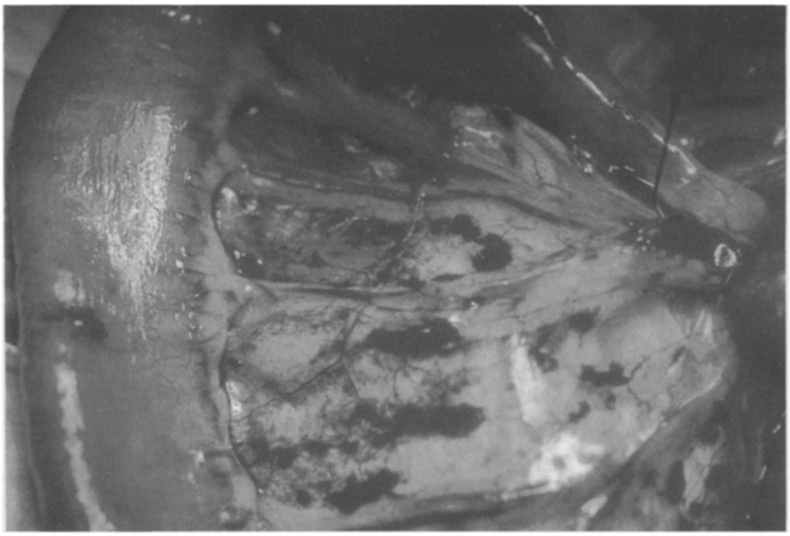

Fig. 1. Mesenterium with neurovascular structures

Electric stimulation was performed with a bipolar nerve stimulator (Model Urys 800, Urosystems, Sunnyvale, Calif.). Pulse duration was 200 ms, pulse repetition rate 10 Hz and amplitude 1 – 10 V. The neutral electrode was placed either on the abdominal wall or next to the active electrode on the bowel wall or the mesenterium.

Stimulation was performed for up to 3 h on three different spots:

1. Direct stimulation of the bowel wall on the ileum, colon or the ileocolonic junction

2. Stimulation of small nerves spreading to the bowel (colon, ileum or the ICV). The nerves were isolated together with accompanying vessels in the mesenterium (Fig. 1, 2)

3. Stimulation of the pelvic nerve, which had been isolated bilaterally on the pelvic floor lateral to the prostate

Constant or intermittent stimulation was performed at the various locations.

For determination of the leak pressure through the ICV, the colon was filled with saline and pressures recorded in the colon. The colon was filled until leakage through the ICV was measured and seen. Then stimulation of mesenterical nerves and direct stimulation of the ICV was performed and leak pressure and filling volume of the "colonic reservoir" recorded.

Fig. 2. Mesonerve to the ileocecal valve on the nerve hook

Results

Neural stimulation of the pelvic nerve

Stimulation of the pelvic nerve with 2 V did not result in changes in peristalsis or in recorded pressure. Colonic motility was increased during stimulation with 7 V and 10 V, but no pressure increase in the colon or ICV was noted. Pelvic nerve stimulation did not produce pressure or activity changes in the ICV or the distal ileum.

Stimulation of nerves in the mesenterium

Stimulation of efferent nerves to the bowel within the mesenterium resulted in different effects. Stimulation of a nerve spreading to the ICV area and to the distal ileum (with 5 V, 7 V, 10 V) increased the motility of the ileum and the pressure in the distal ileum and the ICV. Colonic motility and resting pressures were not affected (Fig. 3).

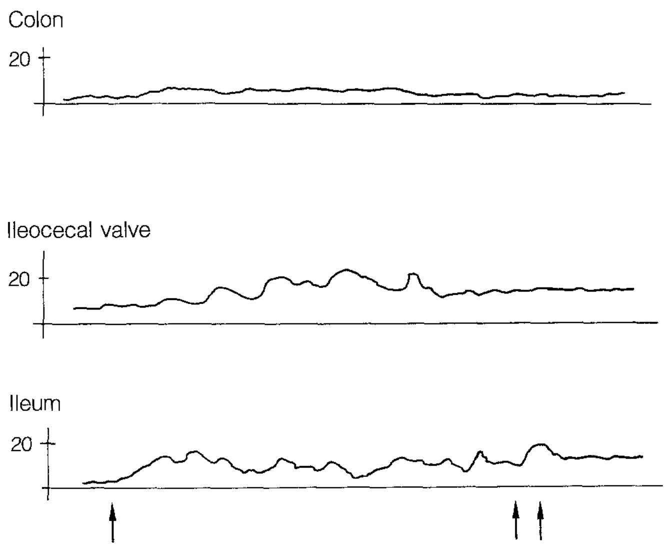

Fig. 3. Pressure in the colon and ileocecal valve (ICV) during stimulation of a mesenteric nerve to the ICV with 200 ms, 7 V, 10 Hz for 1 min (between *single* and *double arrows*)

Stimulation of a nerve in the direction of the colon elevated colonic motor activity and raised the pressure in the colon and the ICV. No effect was noted below an amplitude of 5 V. Effects increased with higher current.

Stimulation of a nerve leading to the ileum or jejunum had several effects:

1. The bowel contracted slightly over a length of about 2–3 cm

2. With constant stimulation the pressure increase was reduced to about 50–60% above the resting level, while areas of the bowel within 10–15 cm of the stimulated spot started contracting

3. After 3–4 min of increased activity the originally contracted area began to show a pressure increase. The stimulated bowel area thereafter remained contracted for as long as stimulation was maintained

4. A slow decline in pressure to the resting tone ensued 30 s to 1 min after the end of the stimulation. Stimulation of a nerve leading to the large bowel did not cause marked contraction of the bowel, but did result in an increase in bowel motility

Direct neuromuscular stimulation of the bowel and the ICV

Stimulation of the ileum with a small needle directly hooked into the muscularis showed similar but more pronounced results than stimulation of a nerve in the mesenterium. First, a pressure increase in the stimulated area was followed by increased activity of the bowel around the contracted area within a distance of 5–6 cm. After 2 min the bowel around the stimulated area went siltent with no more peristalsis or further contraction of the stimulated region. Contraction of the ileum in an area about 1–1.5 cm long surrounded by unstimulated ileum around was sustained for a maximum of 3 h stimulation (Fig. 4). Stimulation was terminated after 3 h, but could have been maintained for longer.

Stimulation of the ICV resulted in a pressure increase in the ileocolonic junction area with a "sphincteric zone" 2–3 cm long extending from the ICV into the distal ileum. A stimulation threshold was determined with 2 V amplitude. Pressure increase at the ICV was directly correlated with the amplitude (Fig. 5). A slow decrease in pressure started 5–7 s after the end of stimulation and the ICV returned to normal resting pressure after 30–45 s (Figs. 6, 7).

Less current was necessary to achieve the same intraluminal pressure rise at the ICV with two or four electrodes as compared with stimulation using only one electrode. Positioning of the ground electrode closer to the stimulating electrode (3–4 mm away) also resulted in higher intraluminal pressures at the ICV.

Leak pressure and volume through the ICV

While filling the colon with saline (10 ml/min), leakage occurred through the ICV without a change in colonic pressure. The unstimulated ICV could usually hold 60–70 ml. Stimulation of the ICV area (7 V or 10 V) along a nerve in the mesenterium allowed filling of the

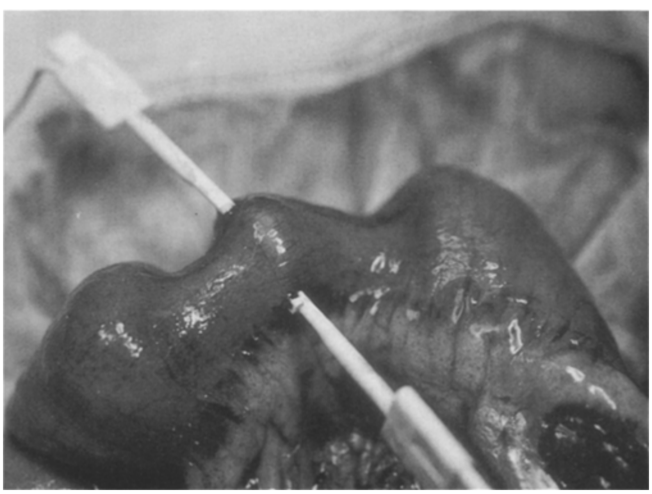

Fig. 4. Contracted ileum during direct myoelectric stimulation with 200 ms, 5 V, 10 Hz for 2 h

Fig. 5. Myoelectric stimulation of the ICV with filling of the colon (200 ms, 5 V, 10 Hz)

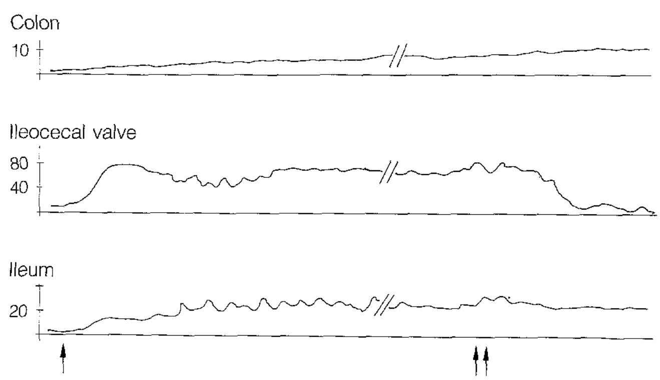

Fig. 6. Pressure in the colon, ICV and ileum during direct stimulation of the ICV with 5 V, 10 Hz for 60 min (between *single* and *double arrows*)

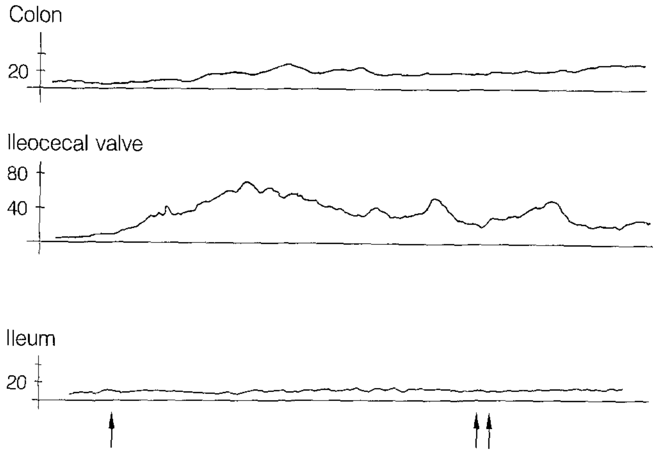

Fig. 7. Pressure in the colon, ICV and ileum during direct stimulation of the ICV with 7 V, 10 Hz for 5 min (between *single* and *double arrows*)

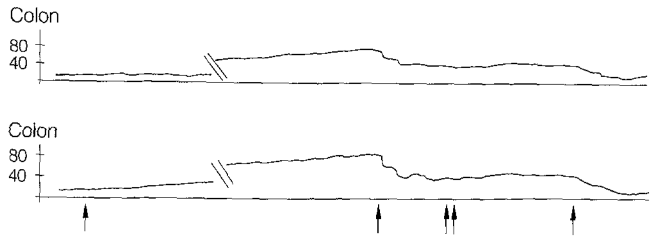

Fig. 8. Pressure in the colon during stimulation of the ICV for 20 min. There is slight leakage through the ICV after filling with 520 ml. At 40 s after the end of the stimulation there is massive leakage through the valve. *First to second single arrows*, Duration of stimulation; *double arrow*, start of leakage through the ICV; *third single arrow*, massive leakage through the ICV

Table 1. Colonic reservoir leak pressure versus volume

	Volume (ml)	Pressure at the ICV (cmH_2O)
Spontaneous	60 ± 5.6	12.7 ± 0.4
Mesonerve	220 ± 10.4	35.0 ± 4.1
Direct stimulation	410 ± 8.4	75.0 ± 3.2

ICV, Ileocecal valve

pouch with 220 ± 10.4 ml before leakage occurred. The pressure in the colon rose to 35 ± 4.1 cmH_2O before reaching the leak pressure in the ICV.

Direct stimulation the muscularis mucosae at the ICV with four electrodes (2 V) or a single electrode (5 V) permitted filling of the pouch up to 420 ± 8.4 ml before the leak point of 75 ± 3.2 cmH_2O pressure in the junctional zone was exceeded (Table 1).

Stimulation of the ICV area could be sustained for up to 3 h: 2 V with four electrodes and 5 or 7 V with a single electrode. No leakage of the fully filled pouch was noted as long as the colonic pressure was kept below 75 cmH_2O. With the colon only partially filled (300 ml, compared with a leak volume of around 420 ml leakage through the ICV only started 15–20 s after termination of the myoelectric stimulation (Fig. 8). This phenomenon can be explained by the slow decrease in intraluminal pressure in the "sphincteric zone" after neurostimulation. Repeated stimulation during this pressure decline resulted in an increase in pressure again, thus sustaining continence at the efferent limb. Histologic evaluation of the ileocecal junctional area showed increased density of smooth muscle fibers up to 1 cm beyond the ICV. A concentric arrangement of the fibers in the valve area and towards the ileal side was demonstrated.

The entrance into the cecum (appendix) also showed increased thickness of smooth muscles. Anatomically the opening was much wider and did not represent a sphincteric zone as shown at the ICV.

Discussion

Spontaneous phasic motor activity of the terminal ileum, the colon and the ICV and a decrease in irregular activity and motility close to the ICV were noted [4].

Resting pressures at the ileocolonic junctional zone were well above the resting pressures of the colon and the ileum. A peristaltic wave traversed the ICV with consecutive pressure rise, whereas in about 70% of all colonic pressure increases, a rise in ICV pressure preceded the colonic pressure wave.

Stimulation of the pelvic nerve with "retrograde" spread from the point of stimulation caused increased peristalsis only in the colon, while stimulation of nerves in the mesenterium increased motility and intraluminal pressure in the ileum and the ICV. Direct myoelectric stimulation of the ICV area allowed intraluminal pressure increases, so that filling of the colonic reservoir to a pressure of 75 cmH_2O, corresponding to a volume of 420 ml, was feasible.

No "rundown" or fatigue occurred in the bowel despite prolonged stimulation with frequencies up to 10 Hz. In guinea pigs fast excitatory potentials (EPH) have been observed in different myenteric neurons of the colon. Repetitive stimulation evoked slow depolarization potentials with no "rundown", i.e. no reduction in the amplitude throughout a train of repetitive pulses. This phenomenon was characteristic of colon neurons, whereas in the small bowel myenteric neuron EPHs become progressively reduced with successive stimuli [8, 12, 15, 17].

The myoelectric pattern of motor and electric activity in pouches has been demonstrated to be similar to that in normal terminal ileum. Pacesetter potentials occur in the ileum at about 9 cycles per minute. Distension of the pouch does not seem to alter the frequency or incoordination of this motor activity [1, 3].

Characteristic of small bowel are slow waves of spontaneous depolarization, which can originate anywhere along the intestine and then propagate down the bowel [14, 16]. In fed animals, slow waves are followed by action potentials with contraction of the bowel wall at random. These irregular contractions culminate in a period of large-amplitude contractions when every slow wave is followed by an action potential. This period of bowel activity lasts about 10–15 min every 30–60 min [9].

The stimulating current only affects a small area of the gut when the bowel wall is stimulated with suprathreshold current density. Using only a small needle electrode hooked into the muscularis, the area of depolarization and consecutive contractions could be limited. No side effects in the bowel wall such as necrosis or burning due to high current densities were seen in our studies [5].

Pulses longer than 1 ms seem to depolarize smooth muscle cells and lead to contraction. Pulses with a duration of less than 1 ms, however, affect only the intrinsic nervous system in the bowel wall [7]. Mixed responses can be expected with the latter type of stimulation as inhibitory as well as excitatory signals can be transmitted. Therefore the reaction can vary between relaxation and contraction [10].

The pulse duration and current density chosen in our experiments seem to affect the smooth muscle cells directly and lead to contraction waves in the bowel wall. Ouyang [11] has shown that basal slow wave activity in the ileum is superimposed by spike activity that initiates smooth muscle contractions in the bowel. Contraction and tonus of the ICV, however, can be maintained by the presence of a tonic pressure within the sphincteric area alone, and no additional spike activity is necessary to maintain the continence function of this functional sphincteric zone [2, 6, 13].

In our canine experiments, stimulation of small nerves together with their accompanying vessels in the mesenterium led to coordinated contraction of the ileum or ileocecal area depending on the innervation area of the particular efferent nerve. This technique of stimulation proved to be delicate, as the neurovascular bundle in the mesenterium was thin and friable, so that only short-term stimulation with a nerve hook seems to be applicable. No cuff electrode could be implanted for long-term use around these neurovascular structures.

The resting pressure in the ICV has been demonstrated to be 12.7 ± 0.4 cmH_2O in our study. This tonus is not sufficient to maintain a closed efferent limb when an ileal or ileocolonic pouch is pre-positioned. Therefore myoelectric stimulation with maintenance of increased pressure is necessary. No fatigue was observed with stimulation for up to 3 h. A slight pressure increase following stimulation as an "off response" could be demonstrated as well as a slow constant decline of the intraluminal pressure to the resting pressure over 30–45 s. This characteristic would make intermittent stimulation of the ICV possible, thus potentially avoiding long-term fatigue.

A set of small flat electrodes could be placed around the ICV area with the ground electrode close to the positive electrode. Thus a voltage of 2 V, just above the threshold, could be used for prolonged stimulation. With the termination of the stimulation pulse the ileocolonic junctional area would relax, thus allowing the urine-filled pouch to empty passively through the relaxed valve. Afterwards neurostimulation could keep the efferent limb continent again.

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