Using the gut in acute care patients

Therapeutic options for postoperative ileus in colorectal surgery

M. Luyer (NL)
Therapeutic options for postoperative ileus in colorectal surgery

Misha Luyer
Surgeon
Disclosure for M.D.P. Luyer

In compliance with COI policy, ESPEN requires the following disclosures to the session audience:

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shareholder</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Grant / Research Support</td>
<td>ZonMw, GSK, Medtronic, Fondsnutsohra, KWF</td>
</tr>
<tr>
<td>Consultant</td>
<td>Medtronic</td>
</tr>
<tr>
<td>Employee</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Paid Instructor</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Speaker bureau</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Other</td>
<td>No relevant conflicts of interest to declare</td>
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</tbody>
</table>

Presentation includes no discussion of off-label use of a drug or medical device
Surgery = inflammation = complications

- Postoperative ileus
Mechanism of postoperative ileus
Mechanism of postoperative ileus

Neurogastroenterol Motil (2015) 27, 743–749

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Postoperative options

- Postoperative chewing gum POSToperatively
  - Many studies with different results
- Coffee postoperatively (Br J Surg 2012 Nov; 99 (11); 1530-8)
  - Small effect, anastomotic leakage confounding factor between groups
- Reduction of opioids (ERAS programs) and Alvimopan
  - Alvimopan has an effect, not widely available
Vagus Nerve stimulation (BEFORE)

- Mechanically

- Via enteral nutrition
Vagal Nerve Stimulation - nutrition


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Experimental work

Improvement of intestinal motility

ASA GUIDELINES
Direct start of early nutrition in advanced rectal surgery

Prospective, RCT

- Open advanced rectal surgery, n=123
- Intervention: direct enteral nutrition vs total parenteral nutrition

Outcomes
- Postoperative ileus
- Anastomotic leakage
- Surgical complications
- LOS

Direct start of early nutrition in advanced rectal surgery

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Early enteral nutrition group (n=61)</th>
<th>Early parenteral nutrition group (n=62)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex_no.(M/F)</td>
<td>41/20</td>
<td>43/19</td>
<td>P=0.80</td>
</tr>
<tr>
<td>Age_yr</td>
<td>64.0±1.4</td>
<td>65.0±1.2</td>
<td>P=0.58</td>
</tr>
<tr>
<td>BMI_kg/m²</td>
<td>25.7±0.5</td>
<td>26.6±0.6</td>
<td>P=0.25</td>
</tr>
<tr>
<td>Weight loss preoperative_ % of 6 months</td>
<td>3.3±0.7</td>
<td>2.0±0.9</td>
<td>P=0.18</td>
</tr>
<tr>
<td>Surgery for Primary or recurrent rectal carcinoma no.</td>
<td>45/16</td>
<td>51/11</td>
<td>P=0.26</td>
</tr>
<tr>
<td>Low anterior resection_no.</td>
<td>25</td>
<td>27</td>
<td>P=0.93</td>
</tr>
<tr>
<td>Abdominoperineal excision_no.</td>
<td>29</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Hartmann_no.</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Debulking_no.</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Loop colostoma_no.</td>
<td>21</td>
<td>16</td>
<td>P=0.38</td>
</tr>
<tr>
<td>Permanent colostoma_no.</td>
<td>35</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Ileostoma_no.</td>
<td>2</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>No stoma_no.</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Duration of surgery_min</td>
<td>255±15</td>
<td>236±11</td>
<td>P=0.31</td>
</tr>
<tr>
<td>Estimated blood loss_ml (median (IQR))</td>
<td>1498 (3560)</td>
<td>1200(1900)</td>
<td>P=0.15</td>
</tr>
</tbody>
</table>
Direct start of early nutrition in advanced rectal surgery

<table>
<thead>
<tr>
<th></th>
<th>Parenteral nutrition n=62</th>
<th>Enteral nutrition n=61</th>
</tr>
</thead>
<tbody>
<tr>
<td>POI (%)</td>
<td>35%</td>
<td>16%</td>
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</tbody>
</table>
Direct start of early nutrition in advanced rectal surgery

<table>
<thead>
<tr>
<th>Complication</th>
<th>EN N=61</th>
<th>PN N=62</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound infection</td>
<td>11</td>
<td>13</td>
<td>P=0.43</td>
</tr>
<tr>
<td>Intra-abdominal or pelvic abscess</td>
<td>11</td>
<td>13</td>
<td>P=0.13</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>1</td>
<td>9</td>
<td>P=0.009</td>
</tr>
<tr>
<td>Intra-abdominal or pelvic abscess or anastomotic leak</td>
<td>11</td>
<td>14</td>
<td>P=0.24</td>
</tr>
<tr>
<td>UTI</td>
<td>4</td>
<td>9</td>
<td>P=0.13</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4</td>
<td>8</td>
<td>P=0.19</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>4</td>
<td>7</td>
<td>P=0.27</td>
</tr>
<tr>
<td>Positive central line culture</td>
<td>4</td>
<td>6</td>
<td>P=0.38</td>
</tr>
<tr>
<td>Line sepsis</td>
<td>3</td>
<td>4</td>
<td>P=0.51</td>
</tr>
<tr>
<td>Other infectious complications:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intestinal fistel (1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine leak (2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nephritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thromboflebitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intestinal fistel (3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine leak (3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholecystitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oesophagitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thromboflebitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidydimitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total infectious complications</td>
<td>44</td>
<td>74</td>
<td>P=0.28</td>
</tr>
</tbody>
</table>
High-fat nutrition

Stomach

Vagal Afferents

Vagal Efferents

Brain

α7-nACh receptor

Macrophage

Bacterial products
Stimulation of the Autonomic Nervous system in colorectal Surgery (SANICS)

Prospective, single blind RCT

• Elective open colorectal surgery, n=120
• Intervention: gum chewing (sham-feeding)
• Placebo: dermal patch

Outcomes
• Postoperative ileus
• Inflammation
• Surgical complications
• LOS

SANICS

flowchart

139 assessed for eligibility
(older than 18 years of age undergoing elective colorectal surgery)

19 excluded
15 declined to participate
2 unwilling or unable to chew gum
2 unwilling to receive the dermal patch

120 randomly allocated

58 assigned to chewing gum
62 assigned to dermal patch

6 excluded
2 excluded during surgery
1 unable to chew gum
3 withdrew

52 completed the study
60 completed the study

SANICS
Postoperative ileus and inflammation

## SANICS complications

<table>
<thead>
<tr>
<th>Clavien-Dindo classification</th>
<th>Chewing gum ((n = 52))</th>
<th>Dermal patch ((n = 60))</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No complication</td>
<td>26</td>
<td>29</td>
<td>0.9</td>
</tr>
<tr>
<td>Grade I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deviation from normal postoperative course</td>
<td>16</td>
<td>15</td>
<td>0.5</td>
</tr>
<tr>
<td>Grade II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Requiring pharmalogical treatment</td>
<td>5</td>
<td>5</td>
<td>0.8</td>
</tr>
<tr>
<td>Grade III_a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention not under general anaesthesia</td>
<td>1</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Grade III_b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention under general anaesthesia</td>
<td>2</td>
<td>9</td>
<td>0.05</td>
</tr>
<tr>
<td>Grade IV</td>
<td></td>
<td></td>
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<tr>
<td>Life threatening</td>
<td>0</td>
<td>0</td>
<td>0.9</td>
</tr>
<tr>
<td>Grade V</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Van den Heijkant et al, Br J Surg. 2015*
Postoperative ileus and Anastomotic leakage

Table 2 Postoperative ileus in relation to anastomotic leakage and reoperations.

<table>
<thead>
<tr>
<th></th>
<th>No POI (n = 69)</th>
<th>POI (n = 43)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anatomostic leakage</td>
<td>1</td>
<td>9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Reoperations</td>
<td>1</td>
<td>12</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Fisher’s exact test.

Sex          1.6  0.42–6.08  0.49
Age          1.02  0.96–1.09  0.52
BMI          0.88  0.73–1.06  0.18
ASA classification 0.88  0.24–3.25  0.85
ASA I        1.34  0.26–6.92  0.72
ASA II       0.76  0.18–3.15  0.70
ASA III      1.15  0.13–10.12  0.90
History of abdominal surgery 0.27  0.03–2.20  0.22
Diabetes mellitus 0.44  0.05–3.72  0.45
NSAID use     0    0            1.00
Alcohol use   0.26  0.05–1.31  0.10
Neoadjuvant treatment 0.75  0.34–1.68  0.49
Surgical procedure 0.77  0.54–1.09  0.14
Colon or rectum surgery 0.16  0.02–1.3  0.09
Duration of surgery 1    0.99–1.01  0.81
Blood loss during surgery 0.79  0.22–2.8  0.71
Creation of a stoma 0.11  0.01–0.91  0.04
Days of epidural anaesthesia 0.48  0.23–1  0.05
Sed, intervention 0.16  0.11–1.89  0.28
POI          12.57  2.73–120.65  0.0005

ASA, American Society of Anesthesiologists; BMI, body mass index; NSAID, non-steroidal anti-inflammatory drug; POI, postoperative ileus.

Colorectal Dis. 2017 Jul;19(7):667-674
Conclusions

- Enteral nutrition reduces POI
- Chewing gum (Sham-feeding) reduces POI
- Relation between POI and Anastomotic Leakage

- Clinical Study with perioperative nutrition
Stimulation of the Autonomic Nervous system in colorectal Surgery (SANICS II)

The effects of stimulation of the autonomic nervous system via perioperative nutrition on postoperative ileus and anastomotic leakage following colorectal surgery (SANICS II trial): a study protocol for a double-blind randomized controlled trial

Emmeline G Peters1,2, Boudevijn JJ Smeets1, Marloes Dekkers1, Marc D Buise3, Wouter J de Jonge2, Gerrit D Slooter4, Tammo S de Vries Reilingh5, Johannes A Wegdam6, Grard AP Nieuwenhuijzen1, Harm JT Rutten1, Ignace HJT de Hingh1, Mickael Hillgmann1, Wim A Buurman7 and Misha DP Luyer7

Stimulation of the Autonomic Nervous system in colorectal Surgery (SANICS II)

Prospective RCT
- Double-blind, multicenter
- Elective open/lap colorectal surgery

Design
- Intervention: enteral nutrition just before, during, and directly after surgery
- Control: no enteral nutrition
- N = 280

• Outcomes
  - Postoperative ileus, Anastomotic leakage
  - Local and systemic inflammatory response
  - Surgical complications
  - Quality of Life

SANICS II

Protocol

**Intervention** – nutrition to patient

**Control** – nutrition to black box

Start nutrition → 3 hrs → **Surgery** → x hrs → Stop nutrition

**Enteral nutrition** → 9 + x hrs


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Vagus Nerve stimulation (BEFORE)

- Mechanically

- Via enteral nutrition
Mechanical vagus nerve stimulation

Neurogastroenterology & Motility. 2017;29:e13075

Catharina Cancer Institute
Mechanical vagus nerve stimulation

Neurogastroenterology & Motility. 2017;29:e13075

Catharina Cancer Institute
Take home messages

• Postoperative ileus incidence is high

• Treatment is symptomatic

• Relation with Anastomotic leakage

• Coffee and chewing gum postoperatively may be beneficial and easily implemented

• Vagus nerve stimulation seems promising, definitive results need to be awaited
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