

Postoperative Ileus reduction by Nicotine gum CHewing after Operation

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The aim of this project is to study the effect of nicotine gum chewing in the prevention or reduction of POI and reduction of opioid use on patients who underwent elective colorectal surgery, and evaluate its safety and possible adverse effects.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Interventional

Summary

ID

NL-OMON40219

Source

ToetsingOnline

Brief title

PINOCHIO-trial

Condition

- Gastrointestinal motility and defaecation conditions
- Gastrointestinal therapeutic procedures

Synonym

lack of peristalsis postoperative, postoperative ileus

Research involving

Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Stichting Coolsingel Rotterdam

Intervention

Keyword: nicotine gum, postoperative ileus, randomised controlled trial, vagal nerve

Outcome measures

Primary outcome

Main study parameter/ endpoint

- Duration from surgery until first passage of feces and full tolerance of solid food

Secondary outcome

Secondary study parameters/ endpoints

- First bowel sound, and passage of flatus after surgery
- CRP, IL-1, IL-6, TNF- α , white bloodcell (WBC) level
- Postoperative opioid consumption
- Patient hospitalization length
- Cardiovascular complications

Study description

Background summary

Postoperative ileus (POI) is a common complication after abdominal surgery. It is a transit cessation of bowel mobility after surgery and presents as an inability to tolerate enteral nutrition, associated with nausea, abdominal distension, and lack of flatus and defecation. Although bowel function literally recovers within 3 to 5 days after operation, in more than 50% cases however, it is not fully recovered 4 days post operation.

Delayed recovery of bowel function leads to other serious morbidity such as pulmonary complications, hospital-acquired infections, longer hospitalization, and of course this results in a large increase of medical cost as well.

Surgical procedures trigger two different phases of POI: an early neurogenic phase and a late inflammatory response. The latter one is considered to be a

more clinically relevant cause of gastrointestinal dysmotility [6]. Multimodal fast-track perioperative care programs, including adequate pain relief, minimal invasive surgery, early enteral nutrition, are now being clinically used on patients in order to shorten the duration of POI, but limited effects restricted its further implementation. At the same time, with regard to the second phase of POI pathophysiology, the inhibition of the inflammatory (2nd) phase, remains unsolved.

Recently, stimulation of vagus nerve has been targeted for the prevention of POI. A number of studies concentrate on the physical, pharmacological, electrical stimulations of the vagus nerve in order to prevent or attenuate POI. In experimental models, cholinergic anti-inflammatory pathway mediated by the vagus nerve could significantly increase bowel motility as well as control inflammatory cell recruitment and thus prevent the pathological changes of POI.

Sham feeding, which mimics the cephalic phase of digestion, stimulates the electrical, motor, and secretory activities of the gastrointestinal tract through neurohormonal and vagal pathways. Since Asao et al. first demonstrated that gum chewing, as a form of sham feeding, stimulated bowel motility and aided the early recovery from POI in the clinic, several randomized clinical trials have reported similar results on patients who underwent various types of surgery.

Nicotine, a selective cholinergic agonist, is considered as an essential regulator of the *cholinergic anti-inflammatory pathway*. In animal models, nicotine has been shown to improve survival rates of sepsis by stimulating alpha7 nicotinic acetylcholine receptor (nAChR)]. Experimental studies have also shown the effect of specific alpha7 receptor agonist (AR-R17779) ameliorating POI in rats [7], while other nAChR also play important roles mediating the cholinergic anti-inflammatory pathway. In addition, clinical evidence showed pre-operative nicotine administration significantly reduced postoperative opioid consumption, while reducing opioids was also an important strategy of shortening POI. Interestingly, the alpha7 nicotinic receptor also plays a role in nicotine-caused analgesia, so its activation induced by nicotine may benefit the control of postoperative pain as well as shortening POI.

Based on the above reasons, and because nicotine gum chewing combines the cephalic vagal reflex induced by gum chewing, its cholinergic anti-inflammatory effect and analgesic modulation induced by nicotine administration, it might be beneficial for the prevention of POI. Nicotine gum (2 mg) chewing may reduce POI and result in better patient outcomes such as reducing postoperative opioid consumption, accelerating the recovery of bowel motility, shortening the length of hospitalization and thus improving the postoperative recovery and quality of life as well as saving medical costs.

Study objective

The aim of this project is to study the effect of nicotine gum chewing in the prevention or reduction of POI and reduction of opioid use on patients who underwent elective colorectal surgery, and evaluate its safety and possible adverse effects.

Study design

randomized controlled trial (pilot)

Intervention

In total the patient will chew 1 piece of gum before operation and 3 times per day after surgery until the first passage of defecation.

Study burden and risks

There is no serious extra risk for a patient that is participating in this trial. The possible side effects of Nicorette are mostly seen in higher dosage. Vena puncture risks are minimal.
Possible benefit: earlier recovery of bowel motility after surgery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

- Elective colorectal surgery because of carcinoma
- >18 years of age
- Signed informed consent

Exclusion criteria

- Severe chronic cardiovascular disease or current acute cardiovascular disease
i.e. recent myocard infarct, Prinzmetal variant angina, instable angina pectoris, palpitations, recent cerebrovascular accident, intermittent claudication
- Severe liver- or kidney disease
i.e. cirrhosis, hepatitis, less than 40% of kidney function left.
- Oral or pharyngeal infection, esophagitis
- Hypersensitivity to any component of the nicotine gum
- Pregnant/ breast feeding
- Elevated risk of choking for any reason
- Unable to chew gum for any reason
- Previous colorectal surgery

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Prevention

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	29-01-2015
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nicorette
Generic name:	nicotine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO	
Date:	07-10-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO	
Date:	07-02-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO	
Date:	29-12-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO	
Date:	05-01-2015
Application type:	Amendment

Review commission:

METC Erasmus MC, Universitair Medisch Centrum Rotterdam
(Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-003679-36-NL
CCMO	NL46159.078.13