A randomized, double-blind, placebo-controlled, multicenter trial to evaluate the clinical efficacy of a single intrapyloric injection of botulinum toxin type A (Botox®) in patients with Idiopathic Gastroparesis. The BIG study.

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20470

Bron
NTR

Verkorte titel
BIG study

Aandoening

Idiopathic gastroparesis

Ondersteuning

Primaire sponsor: Leiden University Medical Center (LUMC), Department of Gastroenterology & Hepatology
Overige ondersteuning: Leiden University Medical Center (LUMC), Department of Gastroenterology & Hepatology

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Gastric emptying for solids.
1. Half-emptying time at visit 4 (follow-up; week 6) compared to Visit 1b (eligibility; week -1);
2. Emptying rate per hour at visit 4 (follow-up; week 6) compared to Visit 1b (eligibility; week -1);
3. One, two and four hour meal retention at visit 4 (follow-up; week 6) compared to Visit 1b (eligibility; week -1).
Gastroparesis Cardinal Symptom Index (GCSI) outcome;
4. Total GCSI score at visit 3, 4, 5 and 6 (follow-up; week 3, 6, 9 and 12) compared to visit 2 (randomization; week 0);
5. Mean GCSI score during follow-up (week 0-12) compared to mean GCSI score during eligibility and randomization (week -1-0).

Toelichting onderzoek

Achtergrond van het onderzoek

Introduction:

Gastroparesis is defined as delayed gastric emptying in the absence of mechanical gastric outlet obstruction. The true prevalence of gastroparesis is unknown. The etiology of gastroparesis is multifactorial; related to diabetes (1/3), postsurgical or due to systemic diseases, e.g. SLE, sclerodermia. The remaining cases (1/3) are idiopathic, i.e. of unknown cause.

Treatment of gastroparesis usually consists of dietary advice and administration of antiemetic and/or prokinetic agents. Dietary advice consists of frequent small-size meals. Antiemetics, like 5-HT3 receptor antagonists (e.g. granisetron, ondansetron, tropisetron), are used to relieve symptoms, whereas prokinetics are used to promote and increase gastric emptying rate. Metoclopramide, domperidon and erythromycin are frequently used, but their effects are variant and doubtful. Cisapride, a 5-HT4 receptor agonist, is no longer available due to serious adverse effects, i.e. prolongation of QT-interval and severe cardiac arrhythmias.
In therapy resistant cases enteral nutrition is provided to ensure adequate nutritional support. Enteral nutrition can be administered through a nasoduodenal tube, via a gastrostomy tube, i.e. a percutaneous endoscopic gastrostomy (PEG) or a jejunostomy tube. More recently intrapyloric botulinum toxin injection and gastric electrical stimulation have

been proposed as possible solutions.
In recent years several open-label pilot studies have shown the effect of intrapyloric botulinum toxin injection in severe gastroparesis. Ezzeddine et al. were the first to publish data on the effect of intrapyloric botulinum toxin injection in patients with severe diabetic gastroparesis and concluded that their results were encouraging. In a recent article Lacy et al. published their data and concluded intrapyloric botulinum toxin to be a possible addition in the treatment of mild-to-moderate diabetic gastroparesis. Miller et al. published their data on the effect of intrapyloric botulinum toxin injection in patients with severe idiopathic gastroparesis and concluded that intrapyloric injection of botulinum toxin accelerated gastric emptying and reduced symptoms of gastroparesis. Arts et al. showed improvement in gastric emptying for solids and symptom score after botulinum toxin injection, but did not show improvement in gastric emptying for liquids. All authors acknowledged the need for further evaluation of intrapyloric botulinum toxin injection in a double-blind, placebo-controlled design.

Drug under study:

botulinum toxin type A (Botox®).

Indication:

Idiopathic gastroparesis.

Study Design:

Randomized, double-blind, placebo-controlled, multicenter.

Primary objective:

To evaluate the efficacy of intrapyloric injection of botulinum toxin type A in idiopathic gastroparesis.

Patient population:

Patients with idiopathic gastroparesis.

Number of patients:

48 patients.

Number of centers:

Multicenter.

Dose levels:

Botulinum toxin type A (Botox®) 200 IU single injection or placebo single injection.

Route of administration:

Intrapyloric injection through gastroscopy.

Duration of study:

14 weeks (1 week wash-out; 1 week eligibility; treatment; 12 weeks follow-up).

Primary parameters:

- Half-emptying time (min), emptying rate per hour (%/h), one, two and four hour retention (%).

- Gastroparesis Cardinal Symptom Index (GCSI) outcome.

Secondary parameters:

Quality of life, psychometric evaluation.

Main criteria for inclusion:

- Presence of clinical symptoms associated with idiopathic gastroparesis; nausea, vomiting, early satiety, postprandial fullness and a baseline GCSI score ≥ 1;

- Delayed gastric emptying for solids as measured with scintigraphy;

- Absence of an obstructing structural lesion in the stomach or small intestine at prior diagnostic gastrointestinal endoscopy (performed within the previous 5 years) or judged absent by the responsible physician;

- Written informed consent prior to any study procedures being performed;

- Patients aged between 18 and 70 years inclusive.

Doel van het onderzoek

Several open-label pilot studies have shown a promising effect of intrapyloric botulinum toxin injection on symptoms in severe gastroparesis. However, data from randomized, double-blind, placebo-controlled studies are not yet available. We intend to evaluate the clinical efficacy of a single intrapyloric injection of botulinum toxin type A in patients with idiopathic gastroparesis.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

Intrapyloric injection of botulinum toxin type A 200 IU single injection or placebo single injection.

Scintigraphy for solid/liquid gastric emptying (before and after treatment).

Gastroparesis Cardinal Symptom Index questionnaire
QOL questionnaires.

Psychometric assessment and patient perception questionnaires.

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Patients are eligible to participate in this study if all of the following criteria are met:

1. Presence of clinical symptoms associated with idiopathic gastroparesis; nausea, vomiting, early satiety, postprandial fullness and a GCSI score ≥ 1 at Visit 1b (eligibility; week -1);

2. Delayed gastric emptying for solids at Visit 1b (eligibility; week -1) as measured with scintigraphy:

a. 2h retention ≥ 60%;

b. 4h retention ≥ 10%;

3. Absence of an obstructing structural lesion in the stomach or small intestine at prior diagnostic gastrointestinal endoscopy (performed within the previous 5 years) or judged absent by the responsible physician;

4. Patients, both male and female, must use adequate means of birth control during the study;

5. Patients must provide written informed consent prior to any study procedures being performed;

6. Patients aged between 18 and 70 years inclusive;

7. Patients (in the opinion of the investigator) must be able to understand the study and comply with the study requirements.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Patients are excluded from the study if any of the following criteria are met:

1. Patients with predominant abdominal pain/discomfort in the opinion of the investigator;

2. Presence of an obstructing structural lesion in the stomach or small intestine if observed during treatment gastrointestinal endoscopy (visit 2, randomization; week 0);

3. Patients taking drugs that interfere with the effect of botulinum toxin type A;

4. Patients previously treated with intrapyloric injection of botulinum toxin type A;

5. Females who are pregnant or lactating;

6. Patients with diabetes mellitus;

7. Patients with delayed gastric emptying due to systemic disorders, e.g. SLE, sclerodermia, hypothyroidism;

8. Patients with disorders of neuromuscular transmission, e.g. myasthenia gravis and Eaton-Lambert syndrome;

9. Patients with abdominal surgery in their medical history, except (laparoscopic) appendectomy, (laparoscopic) cholecystectomy and/or hysterectomy;

10. Patients with any condition which, in the opinion of the investigator, makes the patient unsuitable for entry into the study.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-06-2006
Aantal proefpersonen:	48

Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	09-05-2006
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL618
NTR-old	NTR677
Ander register	: P05.170
ISRCTN	ISRCTN32422510

Resultaten

Samenvatting resultaten
N/A