

# AMISULPRIDE FOR THE TREATMENT OF IDIOPATHIC GASTROPARESIS: RESULTS OF A DOUBLE-BLINDED PLACEBO-CONTROLLED STUDY

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**INTRODUCTION:** Drug treatment options for patients with delayed gastric emptying (GE) are scarce, with metoclopramide being the only FDA-approved drug. A recent meta-analysis reported that antipsychotics, such as sulpiride could have clinical efficacy in functional dyspepsia.<sup>1</sup> In gastroparesis however, these drugs were only tested in diabetic patients, but not in patients with idiopathic gastroparesis.<sup>2</sup> Therefore, we aimed to assess the efficacy of amisulpride on symptoms and gastric emptying.

**METHODS:** A randomized double-blinded placebo-controlled trial was performed in UZ Leuven from 2013 to 2024. Non-diabetic patients with gastroparesis symptoms and delayed GE ( $\geq 75$  min) were included. After a 2-week run-in period, patients were randomized either to amisulpride 25mg TID, or placebo TID for 6 weeks, followed by a 6-week open-label extension with amisulpride (25mg TID for 3 weeks then 50mg TID for 3 weeks). The primary endpoint was the change in the Gastroparesis Cardinal Symptom Index (GCSI) at week 6. Individual symptoms and psychosomatic scores, including anxiety, depression, and somatization scores, were also collected. GE breath tests (meal 250 kcal) were performed at randomization and week 6.

**RESULTS:** Out of the 49 patients screened, 42 were randomized in the trial. Three patients stopped the treatment prematurely or were lost to follow-up. Thus, data were available in 39 patients (32 female patients (82%), mean age  $38 \pm 14$  years); 21 in the amisulpride group, and 18 in the placebo group. Baseline characteristics were similar in the two groups, with a mean GCSI score of  $2.64 \pm 0.89$ .

After 6 weeks, the GCSI score significantly decreased in the amisulpride group ( $2.72 \pm 0.94$  to  $2.17 \pm 1.17$ ;  $p=0.02$ ), but not in the placebo group ( $2.54 \pm 0.85$  to  $2.11 \pm 1.24$ ;  $p=0.11$ ). However, the total GCSI score at 6 weeks and the  $\Delta$ GCSI compared to baseline were not different between the 2 groups (Table 1). None of the GCSI subscales differed between amisulpride and placebo groups, and the same was true for epigastric pain and the psychological questionnaires (Table 1). Patients in the amisulpride group reported more weeks with overall improvement, based on weekly reports (16.6% vs 1.4%;  $p=0.007$ ). Finally, the change in GE time was similar in both groups (Table 1). Two patients stopped amisulpride for somnolence.

After 12 weeks, the  $\Delta$ GCSI score as compared to baseline was higher in the group initially allocated to amisulpride vs. the group initially treated with placebo ( $1.14 \pm 1.00$

vs  $0.52 \pm 1.03$ ;  $p < 0.05$ ). The decrease was significant on the fullness subscale but not on the nausea/vomiting or bloating subscales.

**CONCLUSION:** At 6 weeks, treatment with amisulpride was not superior to placebo in patients with idiopathic gastroparesis. However, a longer treatment period could be warranted to reach a higher treatment efficacy.

Table 1. Comparison of scores at 6 weeks between amisulpride and placebo groups

	Amisulpride (n=21)	Placebo (n=18)	p-value
Total GCSI score	$2.16 \pm 1.17$	$2.11 \pm 1.24$	0.93
$\Delta$ Total GCSI	$0.56 \pm 0.91$	$0.43 \pm 1.10$	0.69
GCSI Nausea subscale	$1.25 \pm 1.06$	$1.04 \pm 1.12$	0.45
$\Delta$ Nausea GCSI subscale	$0.51 \pm 0.89$	$0.51 \pm 1.09$	0.81
Fullness GCSI subscale	$2.36 \pm 1.40$	$2.69 \pm 1.53$	0.49
$\Delta$ Fullness GCSI subscale	$0.57 \pm 1.35$	$0.21 \pm 1.01$	0.35
Bloating GCSI subscale	$2.88 \pm 1.54$	$2.59 \pm 1.52$	0.63
$\Delta$ Bloating GCSI subscale	$0.60 \pm 1.11$	$0.59 \pm 1.72$	0.95
Epigastric pain (0-100)	$41.3 \pm 33$	$45.9 \pm 35.6$	0.17
SF-NDI	$101 \pm 55$	$101 \pm 56$	0.79
VSI	$65.2 \pm 18.6$	$53.8 \pm 18.7$	0.02
HAD	$10.4 \pm 8.0$	$11.4 \pm 5.7$	0.33
PHQ-15	$11.8 \pm 6.3$	$9.6 \pm 5.9$	0.40
Gastric emptying (min)	$78.2 \pm 39$	$93.2 \pm 41.4$	0.29
$\Delta$ Gastric emptying	$40.5 \pm 84.1$	$42.2 \pm 83.9$	0.96

$\Delta$  were calculated from W0 to W6.

GCSI: Gastroparesis Cardinal Symptom Index

SF-NDI: Short Form – Nepean Dyspepsia Index; VSI: Visceral Sensitivity Index;

HAD: Hospital Anxiety and Depression Scale; PHQ-15: Patient Health Questionnaire

1. Ford AC, Luthra P, Tack J, et al. Efficacy of psychotropic drugs in functional dyspepsia: systematic review and meta-analysis. *Gut* 2017; 66: 411–420.
2. Mansi C, Savarino V, Vigneri S, et al. Gastrokinetic effects of levosulpiride in dyspeptic patients with diabetic gastroparesis. *Am J Gastroenterol* 1995; 90: 1989–1993.