

Alosetron of 7.¹ Due to safety concerns (constipation [25%] and ischaemic colitis [0.1%]) Alosetron is not licensed in the UK. Ondansetron (OND) is a 5HT₃ RA, widely and safely used for nausea, with constipation as a side effect.

Methods We recruited 125 patients meeting the Rome III criteria from primary and secondary care to a two centre randomised, double-blind, placebo-controlled, crossover trial. Screening comprised of blood tests, rectal biopsy and a 1-week baseline Bristol stool form diary before randomisation to placebo (PLA) or OND for 5 weeks. Efficacy was optimised by dose titration during weeks 1–3 starting at 4 mg daily, increasing (max 8 mg three times a day) or decreasing as required. A 2-week washout preceded 5 weeks of the opposite therapy to that received in treatment 1. Symptom diaries including stool form, frequency, pain, bloating and urgency were completed daily. Transit using the Metcalf method was measured after each treatment period.² The primary endpoint was the difference in average stool form between baseline and the last 2 weeks of each treatment. Stool consistency “responders” were defined as experiencing >50% reduction in the days/week with stool form 6 or 7. Analysis is presented by intention to treat.

Results 80 women and 28 men completed the study (mean age 40.8, range 18–72, and 41.5, range 25–60). The mode dose of OND was <4 mg a day. Stool form improved significantly in the OND arm, mean change 1.4 (95% CI 1.2 to 1.6), vs 0.5 (95% CI 0.3 to 0.7) compared to PLA, $p < 0.0001$. Stool frequency improved on OND, mean 0.86 (95% CI 0.8 to 1.4), vs 0.44 (95% CI 0.4 to 0.89) on PLA, $p < 0.01$, as did urgency score 0.6 (95% CI 0.8 to 0.4) vs 0.3 (95% CI 0.5 to 0.2) $p < 0.001$. There were no significant improvements in pain or bloating. 74% of patients preferred OND while 26% preferred PLA or had no preference, $\chi^2 p < 0.0001$. 70% were “stool consistency responders” while taking OND compared with 33% taking PLA giving a NNT of 2.7. Whole gut transit slowed significantly while taking OND, 25 (13.5–47.5) h compared to 16 (7–29) h with PLA $p < 0.001$. 9% receiving OND complained of constipation compared to 2% on PLA, all but one responded to dose reduction alone. 2% withdrew because of constipation. There was no case of ischaemic colitis.

Conclusion Using dose titration Ondansetron acts to slow whole gut transit and is highly effective in IBS-D with a low incidence of constipation.

Competing interests None declared.

REFERENCES

1. Cremonini F. *Neurogastroenterol Motil* 2003.
2. Metcalf A. *Gastroenterology* 1987.

OC-092 CONTRALESIONAL APPLICATION OF THE NOVEL BRAIN STIMULATION INTERVENTION TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) RESTORES BRAIN AND SWALLOWING FUNCTION IN THE HUMAN PHARYNGEAL MOTOR CORTEX

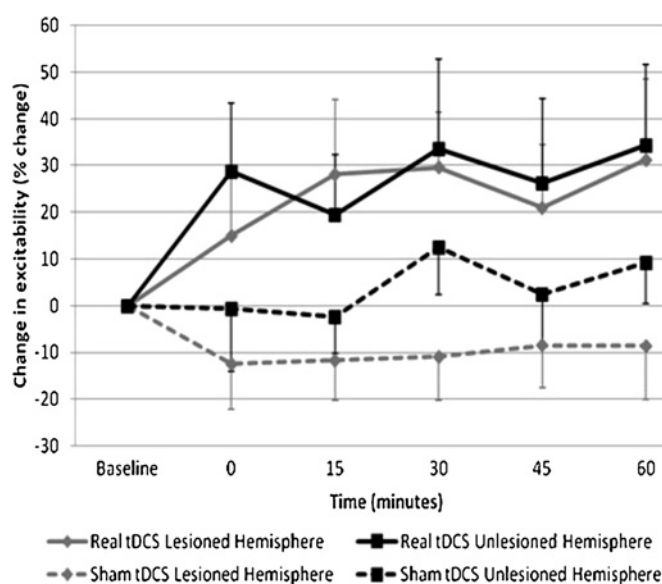
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Introduction Recovery of swallowing function in unilateral dysphagic stroke patients is associated with increased pharyngeal motor cortex excitability of the unlesioned hemisphere. “Virtual-lesioning” the human pharyngeal motor cortex transiently disrupts swallowing neurophysiological and behavioural function for up to 45 min. During this window of opportunity we trialled the effects of contralesional tDCS, a novel non-invasive brain stimulation technology, on “virtual-lesion” induced brain and behavioural changes to swallowing function.

Methods In 15 healthy volunteers (eight males, 21–61 years old) hemispheric lateralisation and cortical excitability of pharyngeal and hand motor cortex were mapped using Transcranial Magnetic Stimulation via an intraluminal catheter with electromyography and pressure sensors. Volunteers then received a “virtual-lesion” to the strongest pharyngeal projection and were randomised to either 10 min of 1.5mA Anodal tDCS (Active) or Sham to the unlesioned hemisphere on separate days. In *Experiment 1*, effects of tDCS on cortical excitability were compared to baseline over 60 min. In *Experiment 2*, swallowing behavioural measurements using a swallowing reaction time task were used to calculate a time window for challenge swallows. Swallowing behaviour was assessed for 60 min after tDCS and compared to baseline. Data were compared using repeated measures ANOVA.

Results *Experiment 1*; compared to sham, active tDCS abolished the inhibitory effects of the “virtual-lesion” bilaterally ($p = 0.017$) with a maximum increase in excitability from baseline of 34% in the unlesioned hemisphere (Abstract OC-092 figure 1). No significant changes were observed in the hand. *Experiment 2*; compared to sham, active tDCS significantly improved challenge swallow performance ($p = 0.025$) with a maximal improvement of 174%.



Abstract OC-092 Figure 1 Experiment 1—Changes in pharyngeal excitability.

Conclusion Contralesional tDCS reverses the neurophysiological and behavioural consequences of a “virtual-lesion” in healthy individuals and has therapeutic potential for dysphagia rehabilitation.

Competing interests None declared.

OC-093 AEROPHAGIA DURING MEALS AND POSTPRANDIAL GAS-CONTAINING REFLUX IN PATIENTS WITH GORD NOT RESPONDING TO PPI

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Introduction A significant number of GORD patients (30%) continue to perceive symptoms despite PPI therapy. Impedance-pH studies have shown that proximal extent of reflux and presence of gas in the refluxate are the only parameters associated with symptoms

perception in refractory GORD. Increased air swallowing (aerophagia) is often suspected based on clinical evaluation. More recently, increased air swallowing between meals was demonstrated, using oesophageal impedance, in a group of patients with increased abdominal gas (x-ray). Aerophagia during meals, however, may be more relevant for GORD patients with postprandial symptoms. We hypothesised that mealtime air swallowing may impact on postprandial reflux patterns and symptoms in patients with refractory GORD. We **aimed** to assess aerophagia during meals and postprandial gas reflux in GORD patients, responding or refractory to PPI.

Methods Mealtime air swallows were quantified using ambulatory impedance-pH monitoring. Normal values were established from 39 healthy controls (mean age 39, range 22–62; Shay *et al* 2004). We studied 44 consecutive patients (mean age 48, range 19–78) with typical reflux symptoms and pathological oesophageal 24 h acid exposure. 18 were fully responsive and 26 were partially or unresponsive to PPI. Mealtime air swallows were defined as swallows with fast impedance increase ($>3000\Omega$ from baseline) in the distal recording segment. Mealtime air swallow frequency (air swallows/10 min meal) was calculated.

Results There was no difference in mealtime air swallow frequency (mean \pm SEM 8.6 ± 1.0 vs 8.0 ± 0.7 per 10 min) or total mealtime air swallows (67.1 ± 8.3 vs 54.0 ± 5.3) between GORD patients and controls. In the GORD group, PPI-refractory patients had a higher frequency (10.5 ± 1.4 vs 5.9 ± 0.8 , $p < 0.05$) and number (83.1 ± 12.7 vs 47.8 ± 7.3 , $p < 0.05$) of mealtime air swallows compared to PPI-responders. PPI-refractory patients had a higher number (25.5 ± 4.0 vs 16.8 ± 3.3 , $p < 0.05$) and proportion ($70.3 \pm 3.0\%$ vs $54.0 \pm 6.0\%$, $p < 0.05$) of post-prandial gas-containing reflux episodes than PPI-responders. There was no difference between GORD patients in fasting air swallowing or 24 h acid exposure.

Conclusion GORD patients had similar mealtime air swallowing to controls, but both groups had large inter-individual variability. Within GORD patients, PPI non-responders had more mealtime air swallowing than responders. Consequently non-responders had more reflux episodes containing gas, an important factor in reflux perception in GORD patients, who have hypersensitivity to oesophageal distension. Mealtime air swallowing may be amenable to behavioural therapy as an “add on” treatment in patients with incomplete response to PPI and objective aerophagia during meals.

Competing interests None declared.

OC-094

ASSESSMENT OF OBSTRUCTIVE DEFECATION BY HIGH RESOLUTION MANOMETRY COMPARED TO MAGNETIC RESONANCE DEFECOGRAPHY

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Introduction Patients with obstructive defecation may have abnormalities of anorectal function or structure. Standard investigation by manometry shows only fair agreement with patient symptoms and defecography. Anorectal high resolution manometry (HRM) may improve diagnostic accuracy by differentiating pressure effects caused by contraction vs straining and by avoiding movement artifacts.

Aims This study compared HRM findings with magnetic resonance (MR) defecography in the clinical assessment of patients with obstructive defecation defined by Rome III criteria as straining at stool with the sensation of incomplete evacuation, blockage sensation or digital facilitation.

Methods HRM was performed by a solid state catheter with 10 circumferential sensors at 6 mm separation across the anal canal and

two placed 5 cm proximal in the rectum (Manoscan AR 360, Given). Resting tone, squeeze pressure and dynamic pressure activity during bearing down were analysed. Findings were referred to MR defecography (1.5T, Philips) performed with 250 ml enema labelled with paramagnetic contrast as reference standard for pelvic floor anatomy and function.

Results 188 consecutive patients (155 female; age 19–93) referred with symptoms of obstructive defecation had full investigation. MRI diagnosis revealed anorectal dyssynergia with paradoxical contraction in 59 and structural pathology in 124 patients (rectocele ($n=68$) and rectocele with intussusception ($n=33$), pelvic floor descent with enterocele ($n=28$) or prolapse ($n=7$), pelvic floor descent ($n=87$) most patients had multiple pathologies. Five patients were excluded because of inconclusive MRI findings. Compared to patients with dyssynergia, those with structural pathology had lower resting (65 vs 86 mm Hg; $p < 0.003$); and squeeze pressure (150 vs 181 mm Hg; $p < 0.011$). On simulated defecation a negative rectoanal pressure gradient was more evident in dyssynergia than structural pathology ($p < 0.0001$). In patients with dyssynergia on MRI, HRM showed paradoxical contraction or failure to increase abdominal pressure without anal relaxation (sensitivity 100% (59/59); specificity 94% (117/124)). One patient with normal findings on MRI but paradoxical contraction on HRM had an anal fissure. A pattern of high intra-rectal pressure with a steep, positive pressure gradient indicating outlet obstruction in the anal canal was observed on HRM in $n=26$ patients with rectocele with intussusception on MRI.

Conclusion Diagnostic agreement between anorectal HRM and MR defecography is high and pressure measurements accurately identify recto-anal dyssynergia. A steep intraanal pressure gradient is indicative of outlet obstruction by structural pathology as a cause of obstructive defecation.

Competing interests None declared.

Gastroduodenal free papers

OC-095

ASSESSMENT OF CANDIDATE GENES TO ASSIST PROGNOSIS IN GASTRIC CANCER

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Introduction Gastric cancer remains the fourth most prevalent cancer and the second leading cause of cancer-related death in the world. Prognostic models for survival are inadequate. In this retrospective study of archival material we used a panel of 32 RNA probes to characterise gene expression in gastric cancer patients with aggressive disease and those who survived long term.

Methods The University Hospital pathology database was searched for all gastric adenocarcinomas diagnosed between April 2005 and September 2006. The patients' age, sex, tumour stage and survival was recorded. Sixty cancers ($n=60$) were identified; paraffin sections retrieved and processed using HTG Molecular's qNPA technology to hybridise RNA probes specific to each gene sequence. Tissues sections were placed directly into the 96 plate wells before hybridisation and automated reading. Each plate contained generic anchor sequences hybridised to linker probes, creating gene-specific hybridisation spots to measure each qNPA probe. Each tissue section was analysed 2 or 3 times, gene expression quantitated and an average numerical value derived. Data sets were analysed for normal distribution using the Kolmogorov–Smirnov statistic method. T-test was used with Welch correction on those samples which passed while Mann–Whitney test was used on those that did not. The expression of the 32 genes was compared between patients with metastatic disease ($n=30$) and 5-year survivors ($n=10$).