ORIGINAL ARTICLE

Use of Gascon and Pronase either as a pre-endoscopic drink or as targeted endoscopic flushes to improve visibility during gastroscopy: A prospective, randomized, controlled, blinded trial

P. BHANDARI¹, S. GREEN¹, H. HAMANAKA², T. NAKAJIMA², T. MATSUDA², Y. SAITO², I. ODA² & T. GOTODA²

¹Portsmouth Hospitals Trust, Portsmouth, UK, and ²The National Cancer Centre Hospital, Tokyo, Japan

Abstract

Objective. To assess whether endoscopic flushes of the bubble-bursting agent Gascon and the mucolytic agent Pronase are as effective in terms of improving endoscopic mucosal visibility as a pre-endoscopic drink of the same agents. Material and methods. A total of 112 patients attending a Japanese tertiary referral centre for upper gastrointestinal endoscopy were randomized to receive either the standard Japanese procedure of a pre-endoscopic drink of water containing Gascon and Pronase with endoscopic flushes of 20-ml aliquots of water, or no pre-endoscopic therapy but endoscopic flushes of 20-ml aliquots of water containing Gascon, with or without Pronase as necessary. Results. Visibility scores were significantly better in the pre-endoscopic drink group than in either of the endoscopic flush groups. The group receiving a pre-endoscopic drink required fewer flushes during the procedure and there was no difference in the endoscopic time between the three groups. Conclusions. Our results suggest that endoscopic spraying of these bubble-bursting and mucolytic agents is not able to offer equivalent improvements in endoscopic mucosal visibility when compared with the standard Japanese therapy of a pre-endoscopic drink of these agents. The addition of Pronase to the spray solution had no measurable benefit over Gascon alone. We therefore cannot recommend endoscopic spraying of mucous clearing agents over their use as a pre-endoscopic drink.

Key Words: Endoscopy, gascon, mucolytic, pronase, simethicone, visibility

Introduction

Since the advent of gastrointestinal endoscopy, practitioners have been frustrated by foam and mucus obscuring the field of view. Mucosal toileting techniques with bubble-bursting agents such as Gascon (simethicone) have been used since the 1950s [1–3] and more recent studies have shown that the addition of a mucolytic such as Pronase further improves mucosal visualization [4,5]. These mucosal toileting techniques have become standard practice in Japan [6,7], where cancers tend to be detected earlier than in the West. Patients there are routinely asked to drink 100 ml of water containing 2 ml of Gascon and 20,000 units of Pronase 10 min prior to the endoscopy. These medications are freely available in Europe but it is not usual practice for them to be used. One explanation for this is concern amongst Western endoscopists of an increased risk of aspiration during the procedure if a drink is taken beforehand.

Minimally invasive techniques such as photodynamic therapy and endoscopic mucosal resection (EMR) are now able to offer excellent results for cancers detected at early stages. EMR often offers complete cure but can only be considered for tumours that are well characterized at endoscopy. Detection and characterization of early changes can be achieved through a variety of diagnostic techniques, including chromoendoscopy, high-magnification endoscopy, confocal endoscopy and narrow-band imaging, but all depend upon optimized mucosal views. In addition, chromoendoscopy requires a clear field in order

Correspondence: Susannah Green, Gastroenterology Department, Queen Alexandra Hospital, Portsmouth, PO6 3LY, UK. E-mail: susi@doctors.org.uk

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that the dye binds to the intended cells rather than the
overlying mucous [8,9]. Effective and acceptable
mucosal toileting techniques are therefore increas-
ingly vital as advanced endoscopic techniques become
used more frequently.

In an attempt to provide the proven benefits of
Gascon and Pronase [9–12] without the theoretical
increased risk of pulmonary aspiration associated with
a pre-endoscopic drink, this study was designed to
compare the effectiveness and practicality of spraying
Gascon, with or without Pronase, directly onto the
mucosa as intermittent flushes through the biopsy
channel of the endoscope during the procedure, com-
pared with identical treatment given as a drink prior to
endoscopy (conventional Japanese mucosal toileting).

Material and methods

Patients

The Japanese national screening programme for gas-
tric cancer involves the majority of people over the age
of 40 years undergoing an annual barium swallow.
The tertiary referral centre in which this trial was set
accepts patients for gastroscopy either directly
(patients with abnormal results on these tests or
with appropriate symptoms), or as referrals from other
hospitals where early cancers have been detected that
are thought to be suitable for EMR. This study was
restricted to the screening population because there
are differences in the endoscopy technique for those
requiring a therapeutic procedure (e.g. the use of
zoom scopes and special dyes requiring additional
time). A total of 148 of these patients were recruited
into this study over a 2-week period. Patients were
excluded from the study if they had previously under-
gone oesophagectomy or gastrectomy, if the endo-
scopy revealed a lesion requiring a therapeutic
procedure such as EMR or if there was active gastro-
intestinal bleeding or strictures in the upper gastro-
intestinal tract. The results from 112 patients were
therefore available for analysis (Figure 1).

Pre-medication and endoscopic procedure

The study gained ethical approval and informed con-
sent was obtained from all participants. Sealed envel-
opes were used to randomly allocate patients to one of
three groups, as follows. Group S: standard Japanese
procedure comprising a pre-endoscopic drink of
100 ml of water, 2 ml of Gascon and 20,000 units
of Pronase. During the endoscopy, flushes of 20-ml

![Figure 1. Flowchart showing the disposition of the study patients.](image-url)
aliquots of water were used as required. Group G: no pre-endoscopic preparation. During the endoscopy, flushes of 20-ml aliquots of pre-mixed solution containing 100 ml of water and 2 ml of Gascon were used as required. Group GP: no pre-endoscopic preparation was given. During the endoscopy, flushes of 20-ml aliquots of pre-mixed solution containing 100 ml of water, 2 ml of Gascon and 20,000 units of Pronase were used as required.

All patients underwent routine gastroscopy, including chromoendoscopy, by one of 14 experienced unblinded endoscopists. The endoscopist was free to use as many flushes as deemed necessary to produce a satisfactory view. Once all flushes had been given, one extra photograph was taken from each of four pre-defined areas: the oesophagogastric junction, the antrum, the lower body and the upper body of the stomach. A record was kept of the total time taken to perform the procedure (from intubation to extubation) and the number of flushes required.

A single, blinded investigator who was experienced in endoscopy but had played no part in the endoscopic procedure then reviewed all of the pictures and assigned each of them a score between one and three for mucosal visibility: 1 = no adherent mucus and clear view of the mucosa; 2 = a thin coating of mucus but not obscuring vision; and 3 = adherent mucus obscuring vision.

The individual scores for each of the four photographs taken were then totalled for each patient to give an overall visibility score ranging from four to 12.

A second blinded investigator separately reviewed and scored the pictures from 20 patients and the results were compared with the original assigned scores.

### Statistical analysis

The sample-size calculations showed that 35 participants were required in each treatment group (105 patients overall) to detect a 20% improvement in visibility scores, from 7 to 5.6, assuming a standard deviation of 2 for each group and a power of 90%. Allowing for a 30% attrition rate, we aimed to recruit 150 participants.

Differences between the number of flushes and the time taken were analysed using ANOVA and Fisher’s least significant difference. As visibility scores were non-normally distributed, the Kruskal–Wallis and Dwass–Steel–Chritchlow–Fligner tests were used for these results. All analyses used SPSS software (SPSS Inc, Chicago, IL). A P-value of 0.05 was taken to be significant throughout.

### Results

A total of 112 patients were evaluable in the study, with a mean age of 61 years. The study population comprised 51 males (46%) and 61 females (54%). There were no significant differences between treatment groups (Table I) for a summary of outcome measures please see Figure 2.

#### Visibility

Visibility scores allocated by the two independent visibility score assessors correlated well (Cohen’s weighted kappa 0.604, standard error 0.187, 95% CI 0.237–0.971).

There were significant differences in the visibility scores assigned between groups (H = 17.8, P = 0.0001). The photographs taken from the pre-medicated Group S scored significantly better for visibility than either of the endoscopic therapy groups GP and G (P = 0.0002 and P = 0.0008, respectively). There was no significant difference in visibility scores between Groups GP and G (P = 0.999).

### Table I. Patient characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group S (n = 35)</th>
<th>Group G (n = 37)</th>
<th>Group GP (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender; n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (51)</td>
<td>14 (38)</td>
<td>19 (48)</td>
</tr>
<tr>
<td>Female</td>
<td>17 (49)</td>
<td>23 (62)</td>
<td>21 (52)</td>
</tr>
<tr>
<td>Age (years); mean (SD)</td>
<td>63 (1.9)</td>
<td>61 (1.6)</td>
<td>61 (2.1)</td>
</tr>
</tbody>
</table>

Figure 2. Outcomes.
Number of flushes needed

There were significant differences in the mean number of flushes used between groups \( (F = 12, P = 0.0001) \). Significantly fewer flushes were used during the procedure in those patients receiving conventional Japanese pre-medication (Group S) than either of the other groups (Group GP, \( P = 0.008 \); Group G, \( P < 0.001 \)). In the groups receiving endoscopic flush therapy only, significantly fewer flushes were used in the group with Pronase added to the Gascon mixture \( (P = 0.023) \).

Time taken for procedure

There was no significant difference in the time taken to complete the procedure between any of the three groups \( (F = 2.23, P = 0.112) \).

Safety

There were no complications in any of the groups. In particular, there were no clinically detectable cases of pulmonary aspiration.

Discussion

Optimal mucosal visualization is vital for thorough endoscopic inspection, particularly when using newer methods such as chromoendoscopy \([13–16]\). The use of bubble-bursting agents and mucolytics has been shown to improve mucosal visibility in previous trials \([17–20]\), but safety concerns have discouraged generalized use in the West.

We assessed a potentially more acceptable technique of spraying these agents endoscopically. Gascon (simethicone or dimethicone) is silicone-based and non-absorbable, with an excellent safety record. It causes gas bubbles to burst by reducing their surface tension and is marketed for the relief of abdominal bloating. Pronase is a mixture of proteases isolated from Streptomyces griseus. These agents were chosen for the study as they both have proven efficacy and have been adopted as standard treatment at the trial centre.

Our results showed that spraying the anti-foam and mucolytic agents endoscopically was not as effective in terms of improved mucosal visibility as pre-endoscopic treatment with the same combination, despite the endoscopist using a greater number of flushes to attempt to clear the mucus. We would ideally have compared the endoscopic flushes with Western standard practice, which in the UK would be to give no pre-endoscopic preparation and to use water endoscopic flushes, but were unable to do this in Japan as using mucous-clearing medication has become so accepted that it was considered unethical not to do so. Adding Pronase to the basic endoscopic flush mixture did not add any advantage in terms of mucosal visibility. The apparent superiority of a pre-endoscopic drink of mucous-clearing solution as compared to endoscopic flush therapy may reflect the more diffuse application of the solution or the 10-min delay between the drink and endoscopy.

No technique resulted in clinically detectable pulmonary aspiration but rates of aspiration during a standard gastroscopy are less than one in a thousand \([21]\) and a larger trial would therefore be needed to properly evaluate this risk.

We conclude that the standard Japanese practice of administering a pre-endoscopic drink containing a mucolytic and anti-bubble agent is superior in terms of endoscopic mucosal visibility to endoscopic application of either both agents or an anti-bubble agent alone. We cannot recommend applying these agents as an endoscopic spray.

Whether improved mucosal visibility results in a higher detection rate of early cancers or improved clinical outcomes remains unknown and well-designed large clinical trials will be needed in the future to evaluate this.

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References


