Refining CT colonography methods

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Colon distension, perceived burden and side effects of CT colonography for screening using hyoscine butylbromide or glucagon hydrochloride as bowel relaxant

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Abstract

Objective: Compare colonic distension and perceived burden of CT colonography between participants receiving hyoscine butylbromide and glucagon hydrochloride as bowel relaxant.

Materials and methods: Data were collected within a screening trial. Participants received 20 mg hyoscine butylbromide intravenously or 1 mg of glucagon hydrochloride intravenously (if hyoscine butylbromide contra-indicated). Colon distension per segment was assessed using a 4-point scale (prone and supine). Data on perceived burden of CT colonography were collected using a questionnaire two weeks after the examination. Outcome measures between groups were compared using propensity score matching. We used a stratified Wilcoxon–Mann–Whitney test statistic for quantitative and Cochran–Mantel–Haenszel statistics for categorical variables.

Results: 541 participants were included: 336 (62%) received hyoscine butylbromide and 205 received glucagon hydrochloride. All hyoscine butylbromide recipients had an adequately distended colon, compared to 96% in the glucagon hydrochloride group (RR 7.31, 95% CI: 1.61–33.28). More glucagon hydrochloride recipients scored the insufflation as rather or extremely burdensome (25% vs. 16%; overall mean score 2.7 vs. 2.4; P < 0.001) and more found the entire CT colonography rather or extremely burdensome (14% vs. 7%; 2.2 vs. 1.9; P = 0.001). Most frequently reported side effects were a dry mouth in the hyoscine butylbromide group (15%) and nausea in the glucagon hydrochloride group (13%).

Conclusion: Compared to glucagon hydrochloride, premedication with hyoscine butylbromide results in significantly more adequately distended colons and a less burdensome procedure. When hyoscine butylbromide can be used, it is the preferred bowel relaxant.
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Introduction

Computed tomography (CT) colonography is a well established method for large bowel imaging in symptomatic patients and for screening [1, 2]. To enable good visualisation of the bowel mucosa, adequate distension is essential. Outside the USA, both hyoscine butylbromide and glucagon hydrochloride are widely used as bowel relaxants. Hyoscine butylbromide is not licensed for this application in the USA.

Several studies have evaluated the effect of hyoscine butylbromide and/or glucagon hydrochloride on colonic distension during CT colonography or barium enema [3–11]. Some of these studies showed that the use of intravenously administered hyoscine butylbromide results in better overall colonic distension compared to no medication [4–6, 10]. For glucagon hydrochloride this has not been demonstrated, not in comparison to no medication [5, 8, 9] or to placebo [7]. One study that compared the effect of hyoscine butylbromide and glucagon hydrochloride on the distension during barium enema reported that hyoscine butylbromide resulted in significant less abdominal cramps of the rectosigmoid compared to glucagon hydrochloride [11]. In contrast, two head-to-head comparisons of hyoscine butylbromide and glucagon hydrochloride in CT colonography failed to detect a significant difference in colonic distension [5, 7]. The use of glucagon hydrochloride for improved colonic distension is therefore still controversial.

If there is no measurable difference in distension between hyoscine butylbromide and glucagon hydrochloride, the decision to use hyoscine butylbromide or glucagon hydrochloride will depend on other factors, such as costs, differences in related burden and side effects. Hyoscine butylbromide is substantially less expensive than glucagon hydrochloride. We here report on a study that compared colonic distension, experienced burden, and side effects between participants receiving hyoscine butylbromide or glucagon hydrochloride as bowel relaxant for CT colonography.

Materials and methods

Study population

Data were collected in the COCOS trial in Amsterdam during an invitational colorectal cancer (CRC) screening trial in the Netherlands, between December 2009 and December 2010. Details about the invitation and participant recruitment have been described previously [12]. Ethical approval was obtained from the Dutch Health Council [2009/03WBO, The Hague, the Netherlands]. Results on CT colonography yield have been published elsewhere [13].
CT colonography
The bowel preparation consisted of a low-residue diet for one day, combined with
two times 50 mL of iodinated contrast agent (Telebrix, Guerbet, Aulnay-sous-Bois,
France) for tagging on the day prior to the study and 50 mL 1.5 hour before the
examination.
Colonic distension was obtained with an automatic carbon dioxide (CO2) insufflator
(PROTOCO2L, Bracco, EZEM, Lake Success, USA) after intravenous administration
of 20 mg hyoscine butylbromide (Buscopan, Boehringer-Ingelheim, Ingelheim,
Germany) or 1 mg glucagon hydrochloride (GlucaGen, Novo Nordisk A’S, Bagsvaerd,
Denmark) if hyoscine butylbromide was contraindicated (glaucoma, prostatism,
tachycardia or cardiac arrhythmias). Glucagon hydrochloride was contraindicated
in case of diabetes mellitus (type I or type II) of in case of a pheochromocytoma. In
case both hyoscine butylbromide and glucagon hydrochloride were contraindicated,
no bowel relaxants were administered. The aim was to insufflate at least 2.5 L and
a maximum of 3 litre (1.3 left decubitus, 0.9 supine and 0.8 right decubitus) within
a maximum insufflation time of 5 minutes, before the first images were obtained.
Previous studies indicated that the maximum pharmacological effect of 10–20 mg
hyoscine butylbromide is reached after 2–8 minutes [14] and that the aperistaltic
effect of 40 mg glucagon hydrochloride i.v. starts after approximately 22 seconds
until approximately 23 minutes [15]. During the remaining part of the procedure,
during which the images were obtained, the insufflation machine was still insufflating
CO2 in order to keep the bowel sufficiently distended.
All scans were performed in supine and prone position with a 64-slice CT scanner
(Brilliance, Philips Healthcare, Best, the Netherlands), using a low-dose protocol:
detector rows 64×0.625 mm, slice thickness 0.9 mm, reconstruction interval 0.7 mm,
tube voltage 120 kV and tube current 25 reference mA.

Image evaluation
All CT colonographies were read on a Philips workstation with enhanced 3D
visualisation software (View Forum). Bowel distension was assessed on 2D images in
the supine and prone position separately, for each of the six colon segments (caecum,
ascending colon – ileocaecal valve to right colic flexure, transverse colon – right colic
flexure to left colic flexure, descending colon – left colic flexure to the flexure of the
sigmoid, sigmoid – S-shaped flexure until second rectal valve and rectum).
One experienced CT colonography observer (not blinded), who successfully finished
a structured training programme including 175 training cases and 25 test cases
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Category 1 (0-25% distended)  Category 2 (25%-50% distended)

Category 3 (50%-75% distended)  Category 4 (75%-100% distended)

Figure 1a-1d Examples of distension scale used

(with colonoscopy verification) [16], evaluated the distension (minimal diameter of lumen) per colon segment on a 4-point scale (based on the worst distended part): 1 very poor distension (< 25% distended), 2 poor distension (25–50% distended), 3 sufficient distension (50–75% distended) and 4 optimal distension (> 75% distended). Examples are provided in Figure 1 (no reference available). Additionally, a combined score for distension was noted per segment, which was equal to the highest score in the supine or prone position for each segment. An overall judgment was also given on whether the distension in all segments (in at least one of both positions) was sufficient for allowing evaluation for intracolonic lesions of 6 mm and larger.
**Evaluation of discomfort during the procedure**

During the procedure, one of two research trainees (MCdH, TNB) was responsible for the insufflation of CO2. Before the study started they had been trained by a third research trainee with a CTC performance experience of 300 scans. During the procedure, a research nurse or the other research trainee was responsible for measuring weight and blood pressure and making notes of reported side effects. They were both aware of the medication that was administered prior to insufflation. Blood pressure was measured in all participants before the examination (baseline), after the insufflation of carbon dioxide was completed, and in case the participant experienced light-headedness or other side effects (like nausea) at the end of the procedure. Hypotension was defined as a systolic blood pressure (SBP) of < 90 mmHg or a decrease of > 20% from baseline SBP [17]. During the insufflation of CO2, participants were asked to score perceived pain in each of the three positions described above on an anchored 11-point pain score, in which 0 reflected no pain and 10 the worst imaginable pain. In addition, participants were instructed to report any additional complaints – next to possible bowel cramps – that occurred during the examination. When a participant reported symptoms (nausea, vomiting, dry mouth, sweating, light-headedness or collapse), we checked whether the participant was familiar with these complaints, to be sure that they were induced by the examination and not by a pre-existing condition.

**Evaluation of perceived pain and perceived burden**

All participants received a validated questionnaire on perceived burden by mail two weeks after the screening procedure. At that point, participants had already been informed about the final result of the screening procedure. This questionnaire was based on questionnaires that had been used in previous colorectal cancer screening pilots [12]. It contained questions on the perceived burden and perceived pain of the insufflation of CO2 and the overall procedure. All items were scored on a 5-point Likert scale (1 = not at all; 2 = slightly; 3 = somewhat; 4 = rather; 5 = extremely). The questionnaire also contained questions on the most burdensome part of the CT colonography (preparation, examination, abdominal symptoms afterwards or waiting for the results) and the willingness to undergo CT colonography in the future. Participants were instructed to complete the questionnaire as soon as possible and to return it by mail in a pre-paid envelope. Returned questionnaires were automatically scanned and imported into a database.
Statistical analysis
The primary outcome measures were adequate colonic distension and perceived burden of the entire CT colonography procedure. Within each group we calculated the proportion of participants with adequate colonic distension, as well as the proportion of participants that experienced the examination as not at all, slightly, somewhat, rather or extremely burdensome. Secondary outcome measures were the distension score per segment, combined and per position (supine and prone), the perceived burden related to the insufflation of CO2 and to changing from position during the procedure, and differences in frequency and nature of side effects.

We used propensity score stratification to adjust for a possible selection bias in making comparisons. The propensity score was based on the estimated probability of having hyoscine butylbromide rather than glucagon hydrochloride given a number of observed variables. Propensity scores were calculated using multivariable binary logistic regression analyses, based on sex, age, socioeconomic status and body mass index. Subsequently, participants were assigned to one of five strata based on the quintiles of the propensity score distribution in the study group. This resulted in five groups of participants that are approximately balanced on the variables used to calculate the propensity score. This procedure is considered to be effective in removing 95% of the selection bias associated with covariates [18].

Within each stratum we then calculated a relative risk, and across strata we calculated a weighted relative risk, similar to fixed effects meta-analysis. To evaluate statistical significance, we used a stratified Wilcoxon–Mann–Whitney test statistic for quantitative variables and a Cochran–Mantel–Haenszel statistics for categorical variables, with macros in SAS version 9.2 (macros available at http://support.sas.com). To adjust for multiple testing, we used a Bonferroni correction method for stacked comparisons; only two-sided P values of less than 0.0017 were considered to be significant in the analysis of secondary outcome variables.

Results
Between December 1, 2009 and 31 December, 2010, 541 of 564 screening participants were eligible for inclusion in this study, because they received either hyoscine butylbromide or glucagon hydrochloride as bowel relaxant. As shown in Figure 2, 17 participants had to be excluded because they received no medication (contraindicated) and six participants because of missing data on weight and/or height, needed for calculation of the body mass index, a variable used in the calculation of
the propensity scores. Of the remaining 541 participants, 336 (62%) received hyoscine butylbromide (47% male; mean age 59±6.3 years, age range 51–74 years) and 205 (38%) received glucagon hydrochloride (54% male; mean age 62±6.4 years, age range 50–75 years) prior to insufflation. Hyoscine butylbromide was contraindicated because of tachycardia, glaucoma, prostatism, cardiac arrhythmias, or because of a combination of these reasons in 1, 11, 60, 112, and 21 of participants, respectively. Propensity scores ranged from 0.31 to 0.85. Baseline characteristics per stratum are displayed in Table 1. The participants were divided in five different strata with the following cut-offs for propensity scores: 0.51, 0.60, 0.68 and 0.73.

The perceived burden questionnaire was returned by 279 hyoscine butylbromide recipients (83%) and by 205 glucagon hydrochloride recipients (80%). Participants that received hyoscine butylbromide returned their questionnaire after a median of 26 days (IQR 17–27); participants that received glucagon hydrochloride returned it after a median of 25 days (IQR 17–27).

**Distension**

Overall colonic distension was deemed adequate for diagnosis of intracolonic lesions of 6 mm and larger in all 336 participants that received hyoscine butylbromide and in 197 of the 205 (96%) participants in the glucagon hydrochloride group. After adjusting for differences in sex, age, socioeconomic status and body mass index
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Table 1 Baseline characteristics per stratum

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Hyoscine butylbromide</th>
<th>Glucagon hydrochloride</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (median, IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stratum 1</td>
<td>69 (68–72)</td>
<td>70 (67–72)</td>
</tr>
<tr>
<td>Stratum 2</td>
<td>64 (62–66)</td>
<td>64 (62–66)</td>
</tr>
<tr>
<td>Stratum 3</td>
<td>59 (56–61)</td>
<td>59 (57–62)</td>
</tr>
<tr>
<td>Stratum 4</td>
<td>55 (53–58)</td>
<td>56 (55–58)</td>
</tr>
<tr>
<td>Stratum 5</td>
<td>53 (52–55)</td>
<td>54 (52–57)</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stratum 1</td>
<td>57</td>
<td>76</td>
</tr>
<tr>
<td>Stratum 2</td>
<td>49</td>
<td>55</td>
</tr>
<tr>
<td>Stratum 3</td>
<td>64</td>
<td>60</td>
</tr>
<tr>
<td>Stratum 4</td>
<td>49</td>
<td>28</td>
</tr>
<tr>
<td>Stratum 5</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>Body mass index (median, IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stratum 1</td>
<td>26 (23–28)</td>
<td>25 (23–27)</td>
</tr>
<tr>
<td>Stratum 2</td>
<td>26 (24–28)</td>
<td>27 (23–29)</td>
</tr>
<tr>
<td>Stratum 3</td>
<td>26 (24–28)</td>
<td>26 (23–28)</td>
</tr>
<tr>
<td>Stratum 4</td>
<td>26 (24–29)</td>
<td>26 (23–29)</td>
</tr>
<tr>
<td>Stratum 5</td>
<td>29 (27–32)</td>
<td>30 (28–33)</td>
</tr>
<tr>
<td>Socioeconomic status (mean, SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stratum 1</td>
<td>3.1 (1.3)</td>
<td>3.5 (1.3)</td>
</tr>
<tr>
<td>Stratum 2</td>
<td>3.5 (1.3)</td>
<td>3.1 (1.4)</td>
</tr>
<tr>
<td>Stratum 3</td>
<td>3.1 (1.4)</td>
<td>3.1 (1.4)</td>
</tr>
<tr>
<td>Stratum 4</td>
<td>3.2 (1.5)</td>
<td>3.2 (1.5)</td>
</tr>
<tr>
<td>Stratum 5</td>
<td>2.7 (1.4)</td>
<td>2.8 (1.3)</td>
</tr>
</tbody>
</table>

Stratum 1 to 5 represents the following categories of propensity scores: (1) ≤ 0.51, (2) 0.52 ≤ 0.59, (3) 0.60 ≤ 0.67, (4) 0.68 <= 0.72, (5) > 0.72.
a Socioeconomic status defined as 1 (very low) to 5 (very high).

between both groups through propensity score stratification, the weighted RR was 7.31 (95% CI: 1.61–33.28), indicating a significant difference. None of the participants with inadequately distended colons were diagnosed with diverticular disease, which is a known predisposing condition for poor distension of the sigmoid [19]. The mean distension per segment in the supine and prone position is displayed in Table 2. In the supine position there was significantly better distension of the sigmoid in the hyoscine butylbromide group. In the prone position, hyoscine butylbromide gave a significantly better distension of the descending colon and sigmoid. When both positions were combined, the only significant difference in distension was found in the sigmoid, in which hyoscine butylbromide gave a significantly better distension compared with glucagon hydrochloride.
Table 2 Mean distension per colon segment in participants receiving hyoscine butylbromide or glucagon hydrochloride

<table>
<thead>
<tr>
<th></th>
<th>Hyoscine butylbromide</th>
<th>Glucagon hydrochloride</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supine (n = 336 vs. n = 205)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caecum</td>
<td>3.98</td>
<td>3.98</td>
<td>0.87</td>
</tr>
<tr>
<td>Ascending colon</td>
<td>3.99</td>
<td>3.98</td>
<td>0.45</td>
</tr>
<tr>
<td>Transverse colon</td>
<td>3.98</td>
<td>3.94</td>
<td>0.09</td>
</tr>
<tr>
<td>Descending colon</td>
<td>3.90</td>
<td>3.82</td>
<td>0.17</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>3.33</td>
<td>2.93</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rectum</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td></td>
<td>Prone (n = 336 vs. n = 204)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caecum</td>
<td>3.90</td>
<td>3.93</td>
<td>0.47</td>
</tr>
<tr>
<td>Ascending colon</td>
<td>3.96</td>
<td>3.95</td>
<td>0.45</td>
</tr>
<tr>
<td>Transverse colon</td>
<td>3.26</td>
<td>3.32</td>
<td>0.70</td>
</tr>
<tr>
<td>Descending colon</td>
<td>3.91</td>
<td>3.78</td>
<td>0.001</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>2.73</td>
<td>2.32</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rectum</td>
<td>3.99</td>
<td>4.00</td>
<td>0.66</td>
</tr>
<tr>
<td></td>
<td>Combined (n = 336 vs. n = 204)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caecum</td>
<td>3.99</td>
<td>3.99</td>
<td>0.36</td>
</tr>
<tr>
<td>Ascending colon</td>
<td>4.00</td>
<td>4.00</td>
<td>0.56</td>
</tr>
<tr>
<td>Transverse colon</td>
<td>3.99</td>
<td>3.97</td>
<td>0.11</td>
</tr>
<tr>
<td>Descending colon</td>
<td>3.97</td>
<td>3.93</td>
<td>0.24</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>3.44</td>
<td>3.06</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rectum</td>
<td>3.99</td>
<td>4.00</td>
<td>0.66</td>
</tr>
</tbody>
</table>

P values < 0.0017 were considered to be significant.
n.a. = not applicable, due to inflated rectal balloon in the supine position.
Hyoscine butylbromide resulted in significantly more scans that were adequately distended (RR 7.31, 95% CI: 1.61–33.28).

Perceived burden

Figure 3 summarises our findings, including the P values calculated with the stratified Wilcoxon–Mann–Whitney test statistic. Insufflation of CO2 was experienced as rather or extremely painful by 18% of hyoscine butylbromide participants and by 33% of glucagon hydrochloride participants, and was experienced more often as rather or extremely burdensome by participants who received glucagon hydrochloride (25% vs. 16%). Changing from position during the procedure was indicated as not or only slightly burdensome by 82% of participants receiving hyoscine butylbromide vs. 75% receiving glucagon hydrochloride.

Twenty-one percent of participants who received glucagon hydrochloride scored the entire procedure (including insufflation and scanning) as rather or extremely painful compared to 10% of hyoscine butylbromide participants. Glucagon hydrochloride participants experienced the entire procedure more often as rather or extremely
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burdensome (14% vs. 7%; P overall difference = 0.0012). In both groups most participants indicated that the examination itself was the most burdensome aspect (38% of hyoscine butylbromide participants vs. 42% of glucagon hydrochloride participants), followed by the bowel preparation (29% and 31%, respectively).

The entire screening procedure turned out worse than expected in 17% of hyoscine butylbromide participants and in 34% of glucagon hydrochloride participants, was experienced as expected by 21% and 17% of participants, and turned out better than expected in 62% and 49% of participants, respectively (P overall difference = 0.001).

There was no significant difference in number of participants that would probably or definitely participate in a next screening round (94% of hyoscine butylbromide and 88% of glucagon hydrochloride participants, P overall difference = 0.22).

![Figure 3](image)
Pain scores and side effects reported during performance of procedure

The mean of the pain scores reported during insufflation of CO2 by participants that received hyoscine butylbromide and glucagon hydrochloride were 0.6 vs. 0.7 in the right decubitus position (P = 0.96), 2.8 vs. 3.1 in the supine position (P = 0.30) and 4.9 vs. 5.3 in the left decubitus position (P = 0.02). During the examination 78 (23%) of hyoscine butylbromide participants and 53 (26%) of glucagon hydrochloride participants indicated that they had additional complaints that they had not been familiar with prior to the examination (RR 0.96, 95% CI: 0.86–1.07). Details on nature and number of side effects are provided in Table 3. Most reported side effects in participants receiving hyoscine butylbromide were a dry mouth (15%) and hypotension (6%), while participants that received glucagon hydrochloride reported most frequently nausea (13%) and sweating (11%).

Table 3 Symptoms – other than abdominal cramps - that occurred during the screening procedure

<table>
<thead>
<tr>
<th></th>
<th>Hyoscine butylbromide n = 336</th>
<th>Glucagon hydrochloride n = 205</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>7 (2%)</td>
<td>27 (13%)</td>
</tr>
<tr>
<td>Vomit</td>
<td>1 (&lt; 1%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>51 (15%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>20 (6%)</td>
<td>10 (5%)</td>
</tr>
<tr>
<td>Sweating</td>
<td>5 (2%)</td>
<td>22 (11%)</td>
</tr>
<tr>
<td>Light headedness</td>
<td>3 (1%)</td>
<td>7 (3%)</td>
</tr>
<tr>
<td>Collaps</td>
<td>2 (1%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

No significant difference in occurrence of side effects; RR 0.96, 95% CI: 0.86–1.07

Discussion

We compared the proportion of adequately distended colons and the difference in experienced burden between participants receiving hyoscine butylbromide or glucagon hydrochloride as bowel relaxant during CT colonography. We found that the distension of the sigmoid was significantly better in participants who received hyoscine butylbromide and that fewer of these participants experienced their procedure as burdensome. There was no significant difference in experienced pain or in the occurrence of side effects, but the nature of the most frequently reported side effects was different between both arms.

Of all studies that compared distension with hyoscine butylbromide vs. glucagon hydrochloride, our prospective study included the largest number of participants.
We aimed to insufflate at least 2.5–3 litres within a maximum insufflation time of 5 minutes to be sure that the images were obtained between 2 and 8 minutes after administration of the bowel relaxant medication. Data on side effects were collected prospectively, directly during the procedure. Data on perceived burden and pain were collected with a questionnaire that was based on and validated in previous studies [12].

This study has also some potential limitations that should be acknowledged. As this study was performed within a population-based screening trial, in which we wanted to mimic daily practice as much as possible, we did not randomly allocate participants prior to the examination to hyoscine butylbromide or glucagon hydrochloride. Since this could have led to groups that were not comparable at baseline – in contrast with randomisation – we created five groups of patients that were similar in terms of their probability of receiving hyoscine butylbromide rather than glucagon hydrochloride, based on factors possibly affecting distension, perceived burden and pain. This way we approximated five different trials, in which participants had a similar probability of receiving hyoscine butylbromide rather than glucagon hydrochloride. We then analysed our data in a stratified way, as if we had performed five separate trials and performed a meta-analysis on them, to correct for possible differences. The use of propensity score stratification is considered to be effective in removing 95% of the selection bias associated with covariates. Due to the fact that older men more often suffer from prostatism, the percentages of males in the glucagon hydrochloride and hyoscine butylbromide groups were somewhat different within two of the five strata. The glucagon hydrochloride group in stratum 1 (low chance of receiving hyoscine butylbromide) contained relatively more men than the hyoscine butylbromide group, while in stratum 4 (higher chance of receiving hyoscine butylbromide) the percentage of men was relatively low in the glucagon hydrochloride group.

Both the physician that was responsible for insufflation of CO2 and the research nurse/physician responsible for noting reported side effects, were aware of the administered medication. This was also the case for the physician that scored the distension. However, study participants were not aware of the possible differences between hyoscine butylbromide and glucagon hydrochloride and possible side effects of both bowel relaxants.

We used operator judgment in evaluating distension, since we believe that in determining whether the colon is adequately distended, the most important question is whether the radiologist feels that he might miss lesions of 6 mm and larger because of insufficient insufflation. A single observer scored distension, allowing for
consistency in ratings. We did not score all scans for the existence of diverticular disease, which is a known risk factor for poor distension of the sigmoid [19]. We were therefore not able to include this factor in the calculation of the propensity score. However, none of the eight participants with insufficient distension of the sigmoid in both positions were diagnosed with diverticular disease. Therefore, we feel that our results are representative.

Until now only two studies have compared colonic distension during CT colonography between hyoscine butylbromide and glucagon hydrochloride [5, 7]. The first study [7] that was presented at the RSNA congress in 2003 compared the bowel distension between 50 participants receiving placebo, 50 participants receiving glucagon hydrochloride and 50 participants receiving hyoscine butylbromide. The second study [5] compared mean bowel length, mean colon volume and radial distensibility (all automatically obtained) between placebo, glucagon hydrochloride and hyoscine butylbromide, and included 80 average risk participants per group. Both studies showed no significant difference in distension or radial distensibility between hyoscine butylbromide and glucagon hydrochloride. In contrast to these studies, we found that hyoscine butylbromide resulted in a significantly better distension of the sigmoid in both the supine and prone position, and in a higher number of adequately distended scans, compared to glucagon hydrochloride. This difference might in part be explained by the larger number of participants in our study: 336 receiving hyoscine butylbromide and 205 receiving glucagon hydrochloride. To our knowledge, only one study – reported in an abstract only [7] – investigated whether there was a difference in experienced abdominal discomfort and pain and in willingness to return on another occasion between participants receiving placebo, glucagon hydrochloride and hyoscine butylbromide. That study found that patients who received placebo reported significantly higher discomfort and pain, compared to patients who received a bowel relaxant, and that they were less willing to undergo CT colonography again. Whether there were any differences between the glucagon hydrochloride and hyoscine butylbromide group was not reported. As we evaluated differences in perceived burden and pain between participants who received hyoscine butylbromide or glucagon hydrochloride, our results cannot be compared to that study. We showed that participants who received hyoscine butylbromide experienced their examination as less burdensome compared to the participants that received glucagon hydrochloride, but that the perceived pain was not different between both groups. The significant difference in experienced burden might be related to the difference in the nature of the side effects between
participants that received hyoscine butylbromide or glucagon hydrochloride. The most often reported side effect in the hyoscine butylbromide group was a dry mouth, followed by hypotension, while the most often reported side effect in the glucagon hydrochloride group was nausea followed by sweating. It is imaginable that the experience of a dry mouth is less burdensome than the experience of nausea during the procedure, and that the different nature of the side effects in both arms is one of the most important explanations for the differences in experienced burden that were found in our study, rather than the number of side effects that occurred. In contrast with previous studies [5, 7], our study showed that hyoscine butylbromide resulted in a better distension of the sigmoid and in a significantly higher number of adequate distended colons, compared to glucagon hydrochloride. Previous studies already showed that glucagon hydrochloride does not result in significant better distension compared to no medication [5, 7–9]. If glucagon hydrochloride indeed has no positive effect on colonic distension (which we cannot conclude from our findings because of the absence of a placebo group), it should only be used when it has a beneficial effect on the experienced burden, compared to placebo. Whether the side effects of glucagon hydrochloride outweigh the possible benefits on experienced discomfort, as shown for CT colonography [7], is still unknown.

**Conclusions**

Our study results suggest that when hyoscine butylbromide can be used, it should be preferred as bowel relaxant during CT colonography over glucagon hydrochloride. Hyoscine butylbromide results in a significantly better colonic distension and a less burdensome examination, with lower costs as an additional advantage. Whether glucagon hydrochloride should still be used as an alternative for hyoscine butylbromide needs to be evaluated in a placebo-controlled study in which the primary focus should be on the evaluation of number of adequately distended colons, possible differences in experienced burden, and side effects.

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