Impact of Gastrografin in clinical practice in the management of adhesive small bowel obstruction

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Background: Gastrografin (GG) has been shown to accelerate the resolution of adhesive small bowel obstruction (ASBO) and decrease length of stay (LOS) in hospital. Consequently, we instituted a protocol recommending the routine use of GG in patients with ASBO. This study reviews patient outcomes after protocol implementation.

Methods: We conducted a retrospective review of all patients with ASBO from January 1997 to December 2007. Data were categorized by admission date and use of GG. The outcomes reviewed were protocol uptake, median LOS in hospital and operative rate. Results were analyzed using the Mann–Whitney *U* test and the 2-tailed Fisher exact test.

Results: There were 710 patients with ASBO overall. Sixteen of 376 (4.3%) patients received GG before institution of the protocol (period 1), whereas 195 of 334 (58.4%) received GG thereafter (period 2). In period 2, use of GG was limited to between 58% and 69% of all potentially eligible patients per year. Fifty-seven of 710 (8%) patients required surgery. In period 1, there were no significant differences in median LOS in hospital ($p = 0.29$) and operative rate ($p = 0.65$) between patients who received GG and those who were managed without GG. In period 2, patients receiving GG had a greater median LOS in hospital (3 [range 2–5] v. 2 [range 1–5] d, $p = 0.048$) but significantly lower operative rates (5.1% v. 12.9%, $p = 0.018$). Overall, the median LOS decreased over time (period 1: 4 [2–7] d v. period 2: 2 [1–5] d, $p = 0.010$). The operative rate did not vary substantially between periods (7.7% v. 8.4%, $p = 0.42$).

Conclusion: The introduction of a protocol has increased the proportion of eligible patients receiving GG. However, protocol nonadherence and factors other than GG usage have influenced LOS in hospital and operative rates. Demonstrated benefits from previously published clinical trials have thus not been replicated within our setting.

Contexte : Il a été démontré que la gastrografine (GG) accélère la résorption de l'occlusion de l'intestin grêle causée par des adhérences (OIGA) et réduit la durée du séjour à l'hôpital. Nous avons donc établi un protocole recommandant l'usage de routine de la GG chez les patients qui ont une OIGA. Cette étude passe en revue les résultats pour les patients après l'application du protocole.

Méthodes : Nous avons effectué une analyse rétrospective des dossiers de tous les patients qui avaient une OIGA de janvier 1997 à décembre 2007. Les données ont été classées en fonction de la date d'admission et de l'usage de la GG. L'adoption du protocole, la durée médiane du séjour à l'hôpital et le taux d'interventions ont constitué les résultats, que nous avons analysés au moyen du test *U* de Mann–Whitney et de la méthode exacte bilatérale de Fisher.

Résultats : Au total, 710 patients avaient eu une OIGA. Seize patients sur 376 (4,3 %) avaient reçu de la GG avant l'instauration du protocole (période 1) tandis que 195 sur 334 (58,4 %) avaient reçu de la GG par la suite (période 2). Au cours de la période 2, l'usage de la GG a été limité à un total se situant entre 58 % et 69 % des patients qui pouvaient être admissibles par année. Cinquante-sept patients sur 710 (8 %) ont dû subir une intervention chirurgicale. Au cours de la période 1, il n'y avait pas de différences significatives aux niveaux de la durée médiane du séjour à l'hôpital ($p = 0,29$) et du taux d'interventions ($p = 0,65$) entre les patients qui ont reçu la GG et ceux qui ont été traités sans GG. Au cours de la période 2, la durée médiane du séjour à l'hôpital a été plus longue (3 [intervalle de 2 à 5] c. 2 [intervalle de 1 à 5] j, $p = 0,048$) chez les patients qui ont reçu la GG, mais leurs taux d'interventions ont été beaucoup moins élevés (5,1 % c. 12,9 %, $p = 0,018$). Dans l'ensemble, la durée médiane du séjour à l'hôpital a diminué avec le temps (période 1: 4 [2–7] j c. période 2: 2 [1–5] j, $p = 0,010$). Le taux d'interventions n'a pas varié considérablement entre les périodes (7,7 % c. 8,4 %, $p = 0,42$).

Conclusion : La mise en œuvre d'un protocole a augmenté le pourcentage des patients admissibles qui reçoivent de la GG. L'inobservation du protocole et des facteurs autres que l'usage de la GG ont toutefois eu un effet sur la durée du séjour à l'hôpital et les taux d'interventions. Les bienfaits démontrés à la suite d'essais cliniques publiés antérieurement ne se sont pas reproduits dans notre contexte.

Gastrografin (GG) has revolutionized the nonoperative management of adhesive small bowel obstruction (ASBO).^{1,2} It is a radio-opaque, water-soluble hypertonic liquid contrast agent given orally or via nasogastric (NG) tube to patients with ASBO and is increasingly being used as a triaging and therapeutic tool.^{3,4} Gastrografin initially was used in a diagnostic capacity, and its passage was monitored using radiographs to determine whether it reached the cecum.⁵ Depending on its transit, patients could be triaged to either a nonoperative or operative course.

A randomized controlled trial conducted in our institution has shown that GG also confers therapeutic benefits by accelerating the resolution of ASBO and decreasing length of stay (LOS) in hospital.⁴ Other studies have confirmed this finding, though there is debate in the literature about whether GG use decreases the need for surgery.^{6,7} The body of evidence suggesting improved outcomes from GG is compelling and, in September 2003, a protocol was introduced in our institution recommending the routine use of GG for initial management of ASBO.

Whereas multiple studies have demonstrated the value of GG, there is minimal literature evaluating the use of GG in clinical practice. Its impact outside a trial setting in a sample of sufficient size has not been adequately assessed. This study investigates the impact of instituting a protocol advocating routine GG use in patients with ASBO. In particular, we examined whether GG use increased in practice, how its use impacted LOS in hospital and its impact on operative rates. We sought to investigate whether institution of a protocol successfully replicated proposed trial benefits within a clinical setting.

METHODS

Using the International classification of diseases (ICD)-10 code "small bowel obstruction," we searched an electronic database (Concerto 6.3) at Middlemore Hospital, Auckland, New Zealand, for patients discharged between January 1997 and December 2007 with a diagnosis of small bowel obstruction. Manual screening of records was then carried out to identify the patients with ASBO. Only outpatients presenting to the hospital with abdominal pain and a subsequent diagnosis of ASBO were included.

Diagnostic criteria for ASBO were previous abdominal surgery, confirmatory clinical features (e.g., abdominal pain, distension, vomiting, obstipation, high-pitched bowel sounds, empty rectum on digital rectal exam) and supporting radiological evidence (e.g., computed tomography scan,

abdominal radiograph). Patients with other causes of bowel obstruction were excluded.

We recorded demographic data, type of treatment received (traditional conservative, GG or operative) and LOS in hospital. We categorized patients into 2 groups depending on whether they were admitted before or after September 2003 and whether they received GG. September 2003 was used as a cut-off date between the 2 groups as the hospital protocol was introduced at this stage.

Gastrografin protocol

The Middlemore Hospital protocol states that once the diagnosis of ASBO has been established, a dose of 100 mL of GG should be given as soon as practicable either orally or via NG tube. If the patient fails to pass flatus or a bowel movement after 4 hours, an abdominal radiograph should be obtained within the next 24 hours. If contrast has reached the cecum, oral intake is permitted. However, if contrast has not reached the large bowel, a clinical judgment should be made to determine whether conservative or operative management is required.

Statistical analysis

All data were recorded using SPSS 13.0 Software (SPSS Inc.). We determined statistical significance using the Mann-Whitney *U* test for continuous data and the 2-tailed Fisher exact test for categorical data.

RESULTS

From January 1997 to December 2007, there were 710 patients with ASBO: 415 (58.5%) women and 295 (41.5%) men with a mean age of 59.8 years. During this period, 211 (30%) patients received GG. Of the 653 patients who were managed nonoperatively, 200 (31%) received GG. Overall, nonpassage of GG was observed in 22 patients, and 9 of them required surgery. A total of 57 (8%) patients required surgery during the study period.

Period 1 (January 1997 to August 2003)

In all, ASBO was diagnosed in 376 (53%) patients. Sixteen of 376 (4.3%) patients received GG. There were no significant differences in median LOS in hospital ($p = 0.29$) and operative rate ($p = 0.65$) between patients who received GG and those who did not (Table 1). The median LOS in hospital was not significantly different when comparing only

the patients who were managed nonoperatively ($p = 0.19$; Table 2).

Period 2 (September 2003 to December 2007)

In all, ASBO was diagnosed in 334 (47%) patients. Of these, 195 (58.3%) patients received GG. After the introduction of the GG protocol in period 2, use of GG was limited to between 58% and 69% of all potentially eligible patients per year (Table 3). Patients receiving GG had a greater median LOS in hospital in period 2 (3 [range 2–5] v. 2 [range 1–5] d, $p = 0.048$) than in period 1, even when comparing only the patients who were managed nonoperatively (Table 2; 3 [range 2–4] v. 2 [range 1–3] d, $p = 0.006$). Forty-nine of 139 patients who did not receive GG had a LOS in hospital of 1 day compared with 45 of 195 patients who received GG ($p = 0.020$). Patients who

received GG had significantly lower operative rates (5.1% v. 12.9%, $p = 0.018$) than those who did not receive GG.

Periods 1 and 2 combined

Table 4 shows that the median LOS in hospital decreased over time (4 [range 2–7] v. 2 [range 1–5] d, $p = 0.010$). This decrease was also observed when comparing only patients who were managed nonoperatively (Table 2; 3 [range 2–6] v. 2 [range 1–4] d, $p = 0.012$). Patients who received GG had a slightly shorter median LOS in hospital (3 [range 2–5] v. 3 [range 2–6] d, $p = 0.028$) than those who did not receive GG. This difference did not remain significant when comparing only those patients who were managed nonoperatively (3 [range 2–4] v. 3 [range 2–5] d, $p = 0.09$). We observed a trend toward lower operative rates among patients who received GG (5.2% v. 9.2%, $p = 0.10$). The overall operative rates remained unchanged between the 2 time periods (7.7% v. 8.4%, $p = 0.42$).

DISCUSSION

Water-soluble contrast agents such as GG have added to the armory in the nonoperative management of ASBO. Initially thought to be of diagnostic use alone, GG is now known to have a much more important role as a triaging and therapeutic tool.^{2,5} The benefits of GG use have been demonstrated in multiple studies, and its use has been gradually incorporated into clinical practice.^{1,2,4,6–8}

Since the introduction of our protocol in September 2003, use of GG dramatically increased to 58%–69% and has remained at that level since then. The median LOS in hospital has decreased over time, and overall operative rates remain unchanged. However, we observed a greater median

Table 1. Median length of stay in hospital and operative rate in all patients with ASBO

Period; variable	Gastrografin	No Gastrografin	Total no. of patients	<i>p</i> value*
Period 1†				
No. patients	16	360	376	
LOS, median (IQR) d	4 (3–7)	4 (2–7)	4 (2–7)	0.29
Operative rate, %	6.3	7.8	7.7	0.65
Period 2‡				
No. patients	195	139	334	
LOS, median (IQR) d	3 (2–5)	2 (1–5)	2 (1–5)	0.048
Operative rate, %	5.1	12.9	8.4	0.018
Total				
No. patients	211	499	710	
LOS, median (IQR) d	3 (2–5)	3 (2–6)		0.028
Operative rate, %	5.2	9.2		0.10

ASBO = adhesive small bowel obstruction; IQR = interquartile range; LOS = length of stay in hospital.
 *Mann-Whitney *U* test.
 †January 2007 to August 2003 (before Gastrografin protocol established).
 ‡September 2003 to December 2007 (after Gastrografin protocol established).

Table 2. Median length of stay in hospital in patients with ASBO managed nonoperatively

Period; variable	Gastrografin	No Gastrografin	Total no. of patients	<i>p</i> value*
Period 1†				
No. patients	15	332		
LOS, median (IQR) d	4 (3–7)	3 (2–6)	3 (2–6)	0.19
Period 2‡				
No. patients	185	121		
LOS, median (IQR) d	3 (2–4)	2 (1–3)	2 (1–4)	0.006
Total				
No. patients	200	453	653	
LOS, median (IQR) d	3 (2–4)	3 (2–5)	3 (2–5)	0.09

ASBO = adhesive small bowel obstruction; IQR = interquartile range; LOS = length of stay in hospital.
 *Mann-Whitney *U* test.
 †January 2007 to August 2003 (before Gastrografin protocol established).
 ‡September 2003 to December 2007 (after Gastrografin protocol established).

Table 3. Proportion of patients receiving Gastrografin

Period, mo/yr	No. of patients who received Gastrografin (%)
9/03–8/04	24 of 70 (34)
9/04–8/05	50 of 72 (69)
9/05–8/06	54 of 92 (58)
9/06–8/07	61 of 88 (69)
9/07–10/07	6 of 10 (60)

Table 4. Median length of stay in hospital and operative rate across both time periods

Variable	Period 1*	Period 2†	<i>p</i> value
LOS, median (IQR) d	4 (2–7)	2 (1–5)	0.010‡
Operative rate, %	7.7	8.4	0.42§

IQR = interquartile range; LOS = length of stay in hospital.
 *January 2007 to August 2003 (before Gastrografin protocol established).
 †September 2003 to December 2007 (after Gastrografin protocol established).
 ‡Mann-Whitney *U* test.
 §2-tailed Fisher exact test.

LOS in hospital and decreased operative rates among patients who received GG when only period 2 was considered. The median LOS in hospital remained greater among patients who received GG, even when comparing only those who were managed nonoperatively. Our results suggest that periods 1 and 2 may be differentiated by additional factors besides the introduction of the GG protocol, influencing results when the data are considered collectively.

Our data showed an increase in GG usage from 4.3% in period 1 to 58.3% in period 2, which can be attributed to our protocol. The low usage of GG in period 1 was likely owing to unfamiliarity with GG and relative lack of availability. Whereas the increased use of GG in period 2 is encouraging, up to 42% of potentially eligible patients did not receive GG. Furthermore, minimal improvement has been observed after the initial increase. Our results identify protocol nonadherence as an important factor preventing optimal management of patients with ASBO. There are multiple potential causes for this. The 710 patients with ASBO were identified based on the discharge diagnosis of ASBO. Initial clinical uncertainty about the cause of small bowel obstruction may have prevented timely administration of GG. The initial "therapeutic window" would thus remain underutilized. Late administration of GG may also have affected LOS in hospital and operative rate data. Patients with mild cases of ASBO may not have received GG, as they would have demonstrated notable clinical improvement on repeated clinical review, another factor that may influence data on LOS in hospital. Furthermore, owing to high staff turnover, the initial treating doctor may have been unfamiliar with hospital protocol. Some patients may have been unsuitable for contrast administration, and risk of aspiration may have been a deterrent in the management of elderly patients. Although the increased use of GG after the establishment of our protocol is encouraging, a greater proportion of potentially eligible patients should be receiving GG to ensure that the benefits observed in previous trials are achieved.

The median LOS in hospital significantly decreased after the implementation of our GG protocol (i.e., when comparing periods 1 and 2); however, we observed no clinically significant difference in LOS in hospital when comparing patients who received GG with those who did not. In period 2, the median LOS in hospital was greater in patients who received GG than those who did not, which is contradictory to the previously demonstrated triaging and therapeutic benefits of GG.^{1,2,4,8} Data from period 1 preclude statistically significant analysis owing to the small number of patients who received GG ($n = 16$). When the data for period 1 and period 2 are combined, the median LOS in hospital for patients who received GG was marginally lower than for those who did not receive GG. However, the data are skewed by the large number of patients in period 1 who did not receive GG. When comparing only patients who were managed nonoperatively, those

who received GG also had a greater median LOS in hospital in period 2 than in period 1, though no significant difference was observed when the combined data (periods 1 and 2) were analyzed ($p = 0.09$). Findings in this analysis may also be affected by skewing of data from period 1. The data thus suggest that while median LOS in hospital has decreased over time, this decrease may not be attributable to the introduction of GG. The decrease may be a combination of improved ward management and perioperative care and improved access to radiology services.

The benefits of GG in reducing LOS in hospital, as demonstrated in previous trials, have not been replicated in our study.⁷⁻⁹ This may be owing to GG being administered after an initial trial of conventional nonoperative management rather than immediately on admission. This is a limitation of our study, as accurate data regarding the timing of administration of GG were not available. The addition of another diagnostic/therapeutic tool may have influenced clinical decisions, as the treatment team may have had a higher threshold to persist with nonoperative management with patients who received GG. This is reflected in the decreased operative rates in period 2 and the greater median LOS in hospital when comparing only patients who were managed nonoperatively. Furthermore, the LOS in hospital for patients with mild ASBO managed without GG was recorded as 1 day, thereby skewing the results against the use of GG.

Previous studies have shown conflicting results regarding the decreased need for surgery following GG use. Some studies that show a decreased need for surgery have used GG after a 48-hour period of unsuccessful conservative management, and these studies have been conducted in an environment of low operative threshold.^{6,10} Hence, when patients receive GG, they may be benefitting from the additional time spent pursuing nonoperative treatment rather than from the GG itself. A randomized controlled trial by Choi and colleagues⁶ also showed a dramatically decreased need for surgery, but the random assignment of patients in this study was different from that in comparable studies. Some studies that have compared the efficacy of GG versus conservative therapy on admission have not shown a decreased need for surgery.⁹ In our study, the use of GG was associated with decreased operative rates in period 2, with no significant differences overall. However, the use of GG did not decrease the total proportion of patients undergoing surgery across the 2 periods. Thus, it appears that a different subgroup of patients are having surgery. Whereas a higher threshold for surgery appears to persist in patients who receive GG, the additional time to surgery may allow ASBO to resolve nonoperatively in a greater proportion of patients. In our institution, patients in whom a trial of GG fails are not automatically assigned to an operative course. Nonoperative management is often continued, depending on clinical assessment. Multiple studies have shown that up to 30% of patients who have

hold-up of contrast in the small bowel after 24 hours can still be managed nonoperatively.^{3,11,12} Patients who do not receive GG have surgery after a failed initial trial of “drip and suck” (i.e., the use of intravenous fluids and nasogastric tube drainage) therapy. This trial period is at the discretion of the treatment team, and differences in operative threshold are likely among clinicians.

CONCLUSION

The establishment of a protocol has increased the use of GG in patients with ASBO in our institution. However, previously demonstrated benefits from trials have not been replicated in our clinical setting.^{1,2,4,8} Factors other than GG use and protocol nonadherence owing to initial diagnostic uncertainty may have influenced patient management. Barriers to GG protocol adherence need to be addressed to replicate the previously demonstrated benefits of GG.

Competing interests: None declared.

Contributors: Drs. Thakore and Hill designed the study. Drs. Thakore, Abbas, Mahmood and Kahokehr acquired the data, which Drs. Srinivasa, Abbas, Mahmood and Kahokehr analyzed. Dr. Srinivasa wrote the article, which all other authors critically reviewed. All authors approved publication of the article.

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