Original article

Novel chyme reinfusion device for gastrointestinal fistulas and stomas: feasibility study

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Background: High-output enterostomies and enteroatmospheric fistulas are common causes of intestinal failure, and may necessitate parenteral nutrition and prolonged hospital stay. Reinfusing lost chyme into the distal gut is known to be beneficial, but implementation has been limited because manual reinfusion is unpleasant and labour-intensive, and no devices are available. A new device is presented for reinfusing chyme easily and efficiently, with first-in-human data.

Methods: The device comprises a compact centrifugal pump that fits inside a standard stoma appliance. The pump is connected to an intestinal feeding tube inserted into the distal intestinal limb. The pump is activated across the appliance by magnetic coupling to a hand-held driver unit, effecting intermittent bolus reinfusion while avoiding effluent contact. Safety, technical and clinical factors were evaluated.

Results: Following microbiological safety testing, the device was evaluated in ten patients (median duration of installation 39·5 days; total 740 days). Indications included remediation of high-output losses (8 patients), dependency on parenteral nutrition (5), and gut rehabilitation before surgery (10). Reinfusion was well tolerated with use of regular boluses of approximately 200 ml, and no device-related serious adverse events occurred. Clinical benefits included resumption of oral diet, cessation of parenteral nutrition (4 of 5 patients), correction of electrolytes and liver enzymes, and hospital discharge (6 of 10). Of seven patients with intestinal continuity restored, one experienced postoperative ileus.

Conclusion: A novel chyme reinfusion device was developed and found to be safe, demonstrating potential benefits in remediating high-output losses, improving fluid and electrolyte balance, weaning off parenteral nutrition and improving surgical recovery. Pivotal trials and regulatory approvals are now in process.

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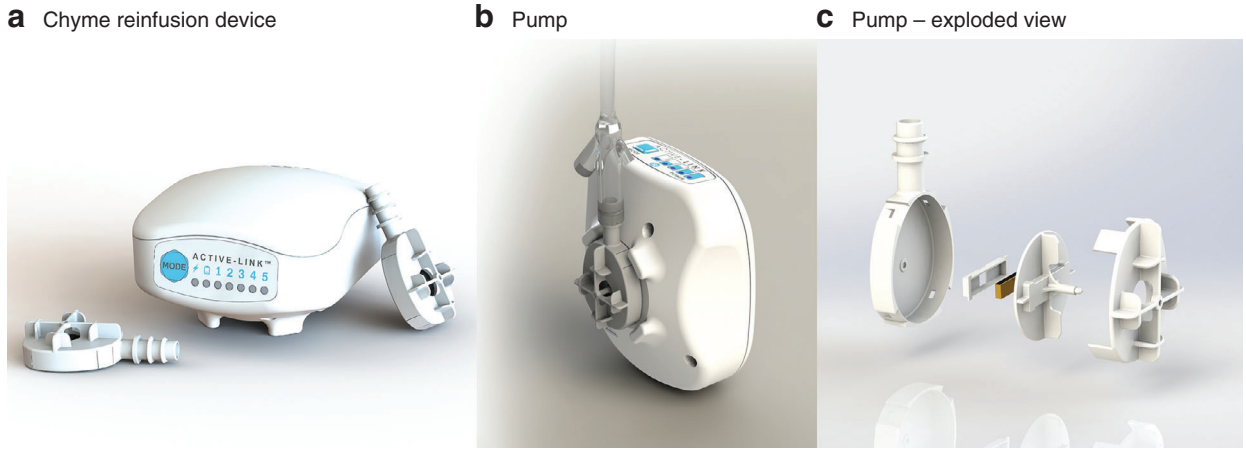
Introduction

High-output enterostomies and enteroatmospheric fistulas (EAFs) are challenging surgical problems responsible for substantial morbidity and mortality[1,2]. The disruption of bowel continuity and resulting loss of luminal content contributes to multiple complications, including excessive fluid and electrolyte losses, renal impairment, distal gut atrophy and nutritional insufficiency[2,3]. These patients may require extended periods of expensive inpatient care, often including parenteral nutrition (PN), which is attended by further risks including central line-associated bloodstream infection and liver dysfunction[4].

Reinfusion of chyme lost from a proximal fistula or stomal opening back into the downstream gut, when possible, has been proposed as an alternative management strategy for EAF and high-output enterostomies[5,6]. Chyme reinfusion (CR) has been shown in multiple studies to contribute to positive clinical outcomes, including restoration of fluid and electrolyte balance, reversal of intestinal failure, and weaning from PN, with few risks[6,7]. However, despite its benefits, CR has failed to gain popularity or widespread

Fig. 1 Chyme reinfusion device



a Chyme reinfusion device, encompassing a driver unit and centrifugal pump. **b** The pump connects to a feeding tube inserted into the distal limb, and magnetically couples to the base of the driver across the stoma appliance. The pump remains *in situ* inside the stoma bag, whereas the driver is applied to the outside of the bag to achieve intermittent bolus recycling, that is when the bag fills to around 200 ml, without direct contact with chyme. **c** Exploded view of the impeller pump design.

use[7], owing to a lack of dedicated equipment, few formalized evidence-based guidelines, labour-intensive processes, as well as the unpleasant nature of current workflows[7–9].

This project aimed to overcome these problems through the development of a novel purpose-built device for efficiently reinfusing chyme in an acceptable manner. Once developed, a first-in-human study was conducted to achieve device optimization, based on repeated clinical evaluation and patient feedback, and to generate feasibility-level outcome and safety data. A microbiological safety trial was also performed to evaluate whether CR posed a risk of bacterial overgrowth[10].

Methods

This study was approved by the New Zealand Health and Disability Ethics Committee, and all patients provided informed consent. Oversight was by an independent Data Safety Monitoring Committee (DSMC). The trial was registered (ACTRN12618001964202).

Design and development of novel chyme reinfusion device

The novel CR device was developed as a collaboration between surgical and engineering teams. Key design inputs were informed by literature review, and encompassed ease of use, efficiency, compatibility with activities of daily living, efficacy across an acceptable dietary range, and minimal manual contact with chyme[7]. Both bolus and continuous CR pumps were evaluated as potential solutions[5,11,12]. Bolus CR increases convenience but may induce symptomatic side-effects such as diarrhoea if a bolus is reinfused too rapidly or if an excessive volume is reinfused at one time, whereas continuous CR pumps necessitate either tethering patients to a stand and tubing, or a more complex wearable solution[5,7].

A wide range of pumps was evaluated before opting for a battery-powered, magnetically activated, centrifugal bolus CR pump. Multiple iterations were developed and tested at the benchtop before clinical testing. The device was further improved throughout the feasibility study to achieve the final design (*Figs 1* and *2*). A video of the device in use is available online (*Video S1*, supporting information). The device consists of a compact impeller with a neodymium magnetic bar that can be situated comfortably within a standard stoma appliance. The pump is connected to an intestinal 24–30-Fr gastric feeding tube (such as Entuit® (Cook Medical, Bloomington, Indiana, USA) or MIC Gastrostomy (Avanos Medical, Alpharetta, Georgia, USA)), inserted into the distal enterostomy or fistula limb. Activation of the pump is achieved at desired intervals by magnetic coupling to a battery-powered driver unit placed adjacent but external to the stoma appliance, to effect gradual bolus CR while avoiding effluent contact. Five driver speed selections were introduced to allow the user to control the rate of infusion manually, depending on comfort and viscosity. This solution enabled full user

control, without restricting patient independence or modifying the stoma appliance, while also fully isolating all electrical components from intestinal fluids.

Microbiological safety of chyme reinfusion

Bolus CR is performed only when the stoma appliance fills, which occurs at variable intervals of up to several hours. Based on the clinical experience of a senior author, it was known that up to 200 ml chyme could be infused gradually into the small intestine without excessive side-effects, for example over 60 s, titrated to patient comfort[11]. Under this regimen, there is a theoretical risk of adverse bacterial growth occurring in the static chyme between CR episodes, posing a risk of bacterial overgrowth or toxin exposure[10,13]. A systematic review[7] was undertaken, which revealed no reported microbiological complications in over 500 adult patients. Nevertheless, in order to evaluate the microbial safety of bolus CR in adults, a substudy investigating the microbial community and growth within stoma appliances was also conducted before initiating the feasibility trial.

The microbiological substudy protocol is detailed in *Appendix S1* (supporting information). In brief, a series of pilot effluent samplings were performed with aerobic and anaerobic incubation (LabTests, Auckland, New Zealand). Heavy colonization of chyme at baseline was identified, indicating the need for dilutions from 1 : 1000 to 1 : 100 000 with saline to enable reliable bacterial quantification. Stoma effluent was then sampled from five consecutive unselected patients presenting with a jejunostomy or ileostomy, at these dilutions at 30-min intervals, to obtain effluent that had been static in a stoma appliance for between 4 and 7 h. All samples were processed and cultured immediately. Phenotypic categorization of cultivable bacterial species present was performed based on colony morphology at each time step. Mean bacterial loads at each time point were used to generate bacterial growth curves.

Feasibility study

Recruitment

Participants were identified from inpatient lists and via referrals from the New Zealand Intestinal Failure Service. This population was different from that recruited into the microbiology safety study. Inclusion criteria were adult patients with high-output double enterostomy, EAF with an accessible distal limb, and temporary ileostomy. Initially, patients with high-output proximal enterostomies and fistulas were recruited, then two additional patients with a routine defunctioning ileostomy were added to extend feasibility testing to patients with thicker liquid chyme. Patients underwent a radiological leak test before starting CR if they had a distal anastomosis. Exclusion criteria were anastomotic leak or bowel obstruction, pregnancy, immunocompromise, or inability to understand risks and benefits.

The recruitment target was ten patients for this first-in-human device feasibility study, with the primary outcome of successful performance evidenced by efficient and effective CR across a range of viscosities. Safety was assessed by careful monitoring for adverse events. Secondary outcomes were patient-specific clinical outcomes, usability and gastrointestinal side-effects.

Set-up and data collection

The distal limb of the stoma or fistula was intubated with the feeding tube and participants were trained in device use. A specific frequency of use was not prescribed, but regular CR over a minimum of 3 weeks was encouraged. Data relating to pump use and technical problems were collected to inform progressive iterative design and workflow improvements. At the end of the 3 weeks, participants were given the option of continuing with CR until surgical stoma reversal or stopping CR.

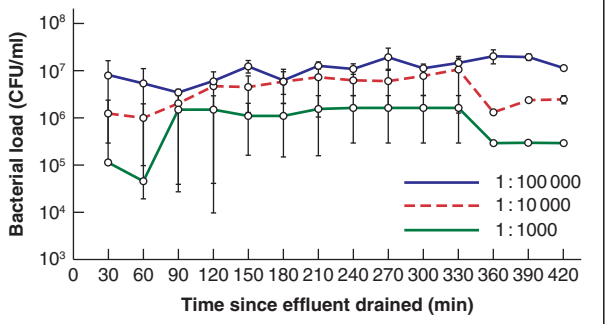
Patient data were reviewed for the 3 weeks preceding enrolment, then collected prospectively. These data comprised renal function (estimated glomerular filtration rate, eGRF[14]), liver enzymes, and nutritional parameters including weight, serum electrolytes, full blood count and fluid balance. Bowel charts and diet logs were instigated. Device usability and acceptability was evaluated using Likert scales, and patients completed diaries on symptoms and side-effects, with room for free comments. A study investigator also conducted regular, semistructured interviews addressing user experience, difficulties, bowel function and device-related side-effects or complications. Interviews were initially conducted daily, then decreased to weekly once participants became stable and confident with the intervention.

Fasting patients who resumed an oral diet after initiating successful CR were first started on a liquid diet with nutrient supplement drinks. Once these drinks were tolerated, the patients progressed to a low-fibre diet. Patients on PN were reviewed daily by a dietician, and PN volumes were altered according to sufficiency of increasing oral intake diet and with ongoing monitoring of bodyweight. PN was stopped if adequate caloric intake was achieved in the opinion of the independent nutrition service. Antidiarrhoeal medications (loperamide) and rehydration solutions were also weaned as CR progressed, and then titrated to need. Other medication doses were monitored carefully as

Fig. 2 Mode of device use

a The centrifugal pump component inserts into a feeding tube. **b** The pump and tube sit within the stoma output in the bag. When chyme reinfusion (CR) is required, the driver is brought up against the outside of the bag. **c** The pump latches magnetically across the bag into foot guides on the base of the driver. **d** The device is then activated by pressing the mode button. CR speed can be selected manually from 1 (slow/thin chyme) to 5 (fast/thick chyme). Activating the pump causes a motor to spin within the driver unit, and this rotation force is transferred to the centrifugal pump inside the bag by magnetic coupling, causing chyme to be drawn into the tube.

Fig. 3 Bacterial loads counted from stoma effluent



Values are mean(s.d.) bacterial loads counted from stoma effluent in five patients. Results are shown for three dilutions. CFU, colony-forming units.

CR was instituted, in view of the enhanced absorption that could occur.

If a patient underwent surgical stoma reversal while on therapy, time to gut function recovery was calculated using time to first bowel motion and tolerance of oral diet (GI2)[15], and a consensus definition of postoperative ileus was employed[16]. Time to discharge and postoperative complications were recorded.

Analysis

Data were analysed both quantitatively and qualitatively to encompass the key themes of device performance, usability, clinical outcomes, safety and side-effects. Clinical data were collected and synthesized across these themes for individual patients, and performance tracked over the course of the trial as improvements were introduced. Statistical analyses were performed on selected clinical outcomes (before *versus* after device use) using the paired Student's *t* test for data with a normal distribution and Wilcoxon matched-pairs signed-rank test for data with a non-normal distribution. The significance threshold was $P < 0{\cdot}050$.

Results

Preliminary microbiology safety study

All participants completed the full sampling protocol. Results were highly consistent between patients, with substantial presence of normal gut flora at baseline and no increase in bacterial loads across the sampling period, indicating that colonies remained within the lag phase for up to 7 h of testing (*Fig. 3*). The only potential pathogenic species identified were representative of normal gut flora (*Table S1*, supporting information). *Staphylococcus aureus* was not observed in any culture. These results were reported to the DSMC, which recommended that further sampling was not required, and that the feasibility study should proceed without microbiological concern.

Table 1 Clinical characteristics of the ten recruited patients

Patient no.	Sex	Age (years)	Aetiology	Anatomy	Bowel length	Primary indication for refeeding*	Intravenous fluid/PN requirement	Duration of pump installation (days)
1	M	47	Iatrogenic small bowel perforation with sepsis	Distal jejunostomy	1·5 m from DJ flexure to stoma; intact distal bowel except for sigmoid resection	High-output losses	Intravenous fluids	28
2	M	53	Bowel ischaemia after aortic dissection	Ileostomy with shortened gut	1·5 m from DJ flexure to stoma; 30 cm of ileum and 50 cm distal colon	High-output losses	Nil	234
3	M	71	Ulcerative colitis with pan-proctocolectomy and IPAA, followed by pouch leak	Ileostomy	Normal length of small bowel; colon and rectum resected	Trial of pouch function	Nil	104
4	F	68	Mesh erosion of small bowel with chronic sepsis	Mid small bowel stoma	1 m from DJ flexure to stoma; 1 m of ileum and intact distal colon	High-output losses	PN	50
5	M	68	Small bowel ischaemic perforation	Jejunostomy at 80 cm	80 cm from DJ flexure to stoma; intact distal bowel	High-output losses	PN	48
6	F	28	ERCP perforation, severe pancreatitis, sepsis and intestinal ischaemia	Ileostomy, with shortened gut	1·5 m from DJ flexure to stoma; 30 cm of small bowel and 60 cm of distal colon	High-output losses	PN	22
7	F	71	Radiation enteritis with small bowel strictures	Ileostomy with shortened gut	1·6 m from DJ flexure to stoma; 30 cm of ileum and distal colon	High-output losses	Nil	1
8	M	84	Anastomotic leak with enterocutaneous fistula	Enterocutaneous fistula (jejunum)	1·4 m from DJ flexure; intact distal bowel	High-output losses	PN	31
9	M	48	Low Hartmann's for rectal injury	Ileostomy	2·6 m of small bowel to stoma; intact distal colon except for sigmoid and rectal resection	Bowel rehabilitation	Nil	21
10	M	64	Adhesiolysis complicated by enterotomies, leak and abdominal wall dehiscence	Enteroatmospheric fistula	90 cm from DJ flexure to stoma; 1 m disconnected segment (*Fig. 4*) then 1 m of intact small bowel plus distal colon	High-output losses	PN	202

*High-output losses were classified as minimum 1200 ml/day. DJ, duodenojejunal; IPAA, ileal pouch–anal anastomosis; PN parenteral nutrition; ECRP, endoscopic retrograde cholangiopancreatography.

Feasibility study enrolment

A total of ten patients were recruited into the feasibility study between April 2018 and January 2019, with data captured until September 2019. One patient declined to participate. The baseline characteristics for the ten recruited patients, including indications for CR are summarized in *Table 1*. The cohort consisted mainly of patients with complex intestinal failure, eight of whom had high-output losses in the context of proximal enterostomies, EAF, or ileostomy with surgically shortened gut. Five patients required PN at baseline. The median time elapsed between enterostomy/fistula creation and enrolment was 66·5 (range 6–656) days. Median patient age was 66 (range 28–84) years and there were seven men.

Device use and performance

The feasibility trial encompassed over 740 patient-days of device installation and testing (median 39·5 (range 1–234) days); some patients did not always use the pump every day it was installed, depending on competing medical needs or device update cycles. Six of ten patients transitioned to outpatient device use once trained. One patient (no. 7) who had radiation strictures was diagnosed with a bowel obstruction soon after consenting and was removed from the study after 1 day. Another patient (no. 10), who had

an EAF, used the pump multiple times per day for several months, then had two pumps installed simultaneously (operated using a single driver) for 3 weeks before reversal surgery. This patient had a complex EAF following surgical complications, with a disconnected loop of small bowel over 1 m in length between two jejunal openings (*Fig. 4a*,*b*). A pump was inserted down each fistula limb to rehabilitate the entire bowel by CR, including the disconnected segment, before successful reversal with two anastomoses (*Fig. 4c*).

The device was progressively improved over the study based on technical evaluations, usability testing and patient feedback. The centrifugal pump underwent four design revisions including the addition of inlet shields to reduce clogging, tighter tube connectors, increased size and upgraded magnetic force. The driver underwent three design revisions to optimize magnetic coupling, and to improve efficiency and ergonomics. *Fig. 4d*,*e* shows the device in use in a regular ileostomy appliance, and *Fig. 4f* shows a close-up view of the pump.

All eligible patients elected to continue device use after the initial 3-week feasibility period. The endpoint for device use was restorative surgery in seven patients, withdrawal from the study owing to bowel obstruction in one, and natural reduction in fistula outputs in one patient. The remaining patient (no. 2), who had gut ischaemia, underwent a long period of testing before ultimately declining reversal and electing for a permanent ileostomy.

Usability

The iterative technical improvements throughout the study corresponded to progressive increases in device usability scores, with scores decreasing from a median of 9 to 2 between the first and final designs, on a Likert scale ranging from 1 (very easy to use) to 10 (very difficult to use).

The most common patient concern, reported by all patients to varying extents, was pump inlet blockages and reduced CR efficiency due to pump congestion. This was partly mitigated when the inlet shields were added, and by incorporating a flow-reversal feature activated when cycling the mode button. However, this problem could be eliminated completely only by requiring patients to eliminate stringy or highly fibrous dietary items (such as pineapple, celery, broccoli, carrots and corn). Lack of dentition and therefore complete mastication in two patients contributed to pump blockages. With dietary instructions implemented, the final device iteration could freely reinfuse approximately 150–200 ml low-viscosity chyme in 30–60 s without blockages.

Difficulties encountered with other components of the system were uncommon. The feeding tube exacerbated peristomal skin irritation in three patients, and became dislodged at least once in three patients. Displaced tubes were reinserted and retained by slightly increasing the volume of the retention balloon (for example to 4 ml). Three patients commented that the pump reduced the speed and efficiency of changing stoma appliances.

Twelve nursing staff who interacted with the final version of the device also provided usability feedback. The median score for staff usability was 2·5 on a scale ranging from 1 (very easy to use) to 10 (very difficult to use). Acceptance was high, with 11 of 12 nurses reporting very low levels of disgust associated with device use on a five-point Likert scale, 11 commenting that infusion was valuable clinically, and nine reporting that their workload did not increase or was simplified when managing patients with the device.

Clinical outcomes

A range of clinical outcomes was evaluated across the cohort on a case-series basis.

Nutrition, fluid balance, renal function and biochemistry

Of five patients receiving PN at baseline, four were able to resume an oral diet sufficient to stop PN. One of these patients (no. 8) experienced naturally declining fistula losses and would most likely have ultimately ceased PN regardless of pump use; all others continued to experience high outputs necessitating regular CR until surgical stoma reversal. The patient with a mid small bowel stoma (no. 4), who did not wean from PN, reduced PN volumes by 50 per cent and spent days each week out of hospital until stoma reversal. Patients gained a median of 2·6 (range 0–7) kg in bodyweight over the CR period (excluding the patient who was removed from the study).

Four of the patients receiving PN exhibited deranged (cholestatic) liver enzymes at baseline, which demonstrated recovery within 3 weeks of initiating CR (alkaline phosphatase: mean difference −123 units/l, $P = 0{\cdot}050$; γ-glutamyltransferase: mean difference −290 units/l, $P = 0{\cdot}268$). An example of liver enzyme improvements is shown in *Fig. 5*, in a patient (no. 5) with a high-output proximal jejunostomy who had small bowel perforation with ischaemia and sepsis. After initiating CR, the patient resumed an oral diet and stopped PN within 1 week, and this was maintained until surgical stoma reversal on day 48 of CR.

Across all patients, there was no significant change in serum creatinine level at baseline compared with after 3 weeks of pump use (median 81 *versus* 88 μmol/l; $P = 0{\cdot}135$) or eGFR (median 93 *versus* 97 ml per min per

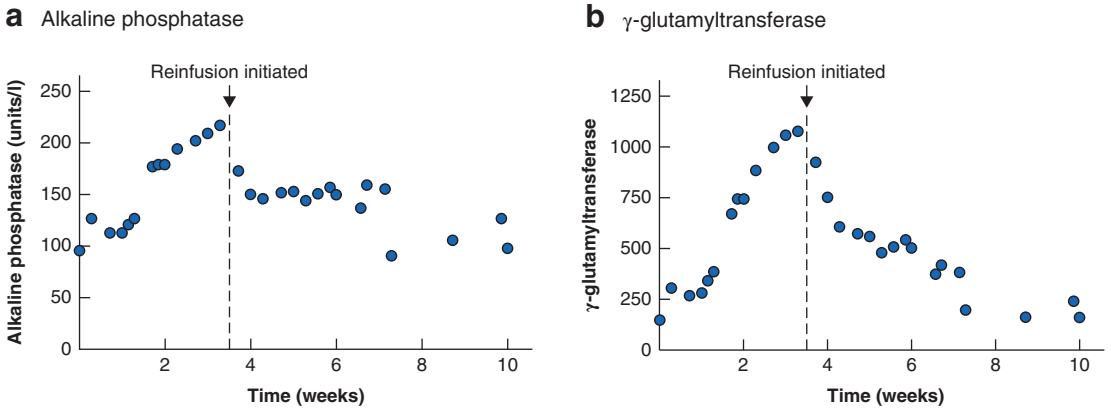
Fig. 4 Images of chyme reinfusion device in use

a Example of a complex enteroatmospheric fistula treated by chyme reinfusion (CR) during the feasibility study. The patient was transferred to the author's unit after an unsuccessful attempt at fistula repair, and had been nil by mouth and receiving parenteral nutrition, for 6 months. CR was initiated successfully into the distal limb, allowing resumption of oral diet, cessation of parenteral nutrition and hospital discharge. **b** A large stoma appliance with window access was employed to enable access for pump maintenance, with bag changes performed weekly. **c** Before surgical stoma reversal, a second pump was added into a second jejunal fistula opening, to rehabilitate a 1-m segment of disconnected gut. **d**,**e** Example of pump in place and driver application in a standard ileostomy appliance. **f** Front view of injection-moulded centrifugal pump attached to a feeding tube.

1·73 m^2; $P = 0·343$), indicating that fluid management was adequate with or without pump use. During the study, one patient (no. 10) developed an episode of acute renal injury within the 181-day period of pump use, with serum creatinine rising to twice the baseline level; this was managed by initiating periodic clinic visits for intravenous fluid administration. This patient averaged an ongoing jejunal output exceeding 4 litres per day once CR and oral diet had been initiated, with PN stopped. This episode of renal injury occurred despite consistent reinfusion of almost 100 per cent of daytime losses, and was attributable to persistent high residual nocturnal losses (over 1 litre per night). The patient declined the proposal of waking overnight to reinfuse chyme.

Serum electrolyte levels did not show any overall change across the whole cohort at baseline compared with at

Fig. 5 Feasibility series data for liver enzyme improvements



Serum levels of **a** alkaline phosphatase and **b** γ-glutamyltransferase in a patient (no. 5) with a distal jejenostomy who was successfully weaned from parenteral nutrition following initiation of chyme reinfusion and resumption of oral diet.

least 3 weeks of therapy (sodium: $P = 0{\cdot}940$; potassium: $P = 0{\cdot}672$; calcium: $P = 0{\cdot}068$; phosphate: $P = 0{\cdot}130$; magnesium: $P = 0{\cdot}880$). One patient (no. 1), with a jejunostomy after iatrogenic small bowel injury, had persistent hypomagnesaemia requiring regular intravenous replacement at baseline, which normalized after initiating CR (*Fig. 6a*). This patient had been admitted for 8 days before enrolment for intravenous fluids in the context of refractory high outputs, and after enrolment was able to reinfuse the majority of their chyme (*Fig. 6b*), allowing successful discharge from hospital without need for further supportive fluids.

Testing viability of stoma reversal

For two patients, CR served as a method of testing distal bowel function before stoma reversal. For one patient (no. 2), who had bowel ischaemia after aortic dissection, and had undergone small bowel resections and subtotal colectomy, concern centred on the adequacy of anorectal function after prolonged diversion (1 year, 9 months). This patient used the device intermittently for gut rehabilitation and functional evaluation for over 200 days, while undergoing serial dilatations of a strictured rectum, before declining reversal in view of refractory continence concerns that failed to improve. Use of the pump facilitated this patient's decision-making.

The second patient (no. 3), who had ulcerative colitis and had undergone construction of an ileal pouch–anal anastomosis, previously experienced persistent pouch fistula and sepsis requiring reversion to defunctioning ileostomy. CR served as a robust functional test of pouch integrity after initial radiological exclusion of ongoing leak. This patient underwent 100 days of therapy, regularly passing bowel motions via the pouch before undergoing reversal surgery with confidence.

Recovery after stoma removal

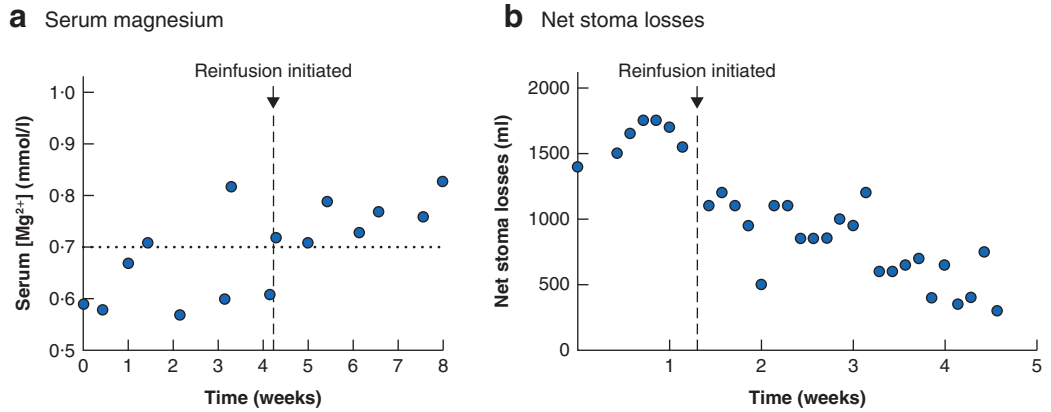
One of seven patients who underwent reversal surgery experienced postoperative ileus. This patient (no. 10) had complex EAFs requiring prolonged adhesiolysis; time to GI2 was 10 days. Recovery of gut function in all other patients was rapid, with median time to GI2 of 2 (range 1–4) days and median duration of hospital stay of 2 (1–5) days. One patient (no. 3) was readmitted with sepsis related to pneumonia, which was managed conservatively.

Safety and side-effects

CR was well tolerated by all patients once established. The most common side-effects were abdominal discomfort (7 of 10 patients), bloating (4) and nausea (4). In general, these side-effects were prominent only for the first week of therapy, but could recur if chyme was infused too rapidly or in excessive volumes. These symptoms always improved or resolved after reducing infusion volumes or speed, and patients quickly learned to titrate bolus dosing to a personal threshold to ensure comfortable ongoing use.

Three patients developed constipation after CR containing loperamide, and were treated with laxatives and loperamide cessation. Effects from increased medication absorption were noted in two patients after initiation of CR. One patient (no. 5) had longstanding severe trigeminal neuralgia, usually well controlled by carbamazepine, which flared after stoma creation. On initiation of CR, the symptoms subsided, presumably owing to recovery of oral

Fig. 6 Feasibility series data for improvements in serum electrolytes



a Serum magnesium and **b** net stoma losses in a patient (no. 1) with a high-output jejunostomy. After initiation of chyme reinfusion, intravenous fluids and electrolyte replacements could be stopped and the patient was discharged until the time of reversal surgery. The dotted line represents the normal lower range for magnesium. *Intravenous replacements.

carbamazepine absorption. A second patient, who had an EAF (no. 10), had increased drowsiness after initiation of CR, presumed to be due to increased absorption of regular analgesic and anxiolytic medications; these doses were titrated down, with recovery of alertness.

One patient (no. 10) suffered a serious adverse event requiring invasive intervention during the feasibility study. This patient had been nil-by-mouth with total PN for more than 180 days after failed fistula repair, before transfer to the author's unit. Soon after initiating pump use, the patient was able to resume an oral diet and wean from PN, but then developed severe cholecystitis that was not responsive to conservative therapy, necessitating percutaneous cholecystostomy.

No device-related serious adverse events or microbiological complications occurred during the study.

Discussion

This study describes a novel CR device for double/loop enterostomies and EAF, including validation in a first-in-human study with over 2 patient-years of testing. The design incorporates an innovative magnetically coupled centrifugal pump, thereby avoiding physical or electrical contact with chyme, and enabling use with any standard stoma appliance. This design was shown to allow successful, safe and acceptable use by patients and staff, facilitating CR of high volumes of stoma output over time frames of up to 6 months. In addition, microbiological safety was confirmed in a laboratory study, demonstrating that bacterial overgrowth or adverse microbial selection were not risks.

CR has historically been applied by isolated clinical groups, with the largest experience in France[17,18]. A recent systematic review[7] of 24 adult studies showed numerous clinical benefits in patients with high-output losses, intestinal failure, and fluid/electrolyte imbalance, and with minimal complications. In a recent large report[5] of 212 patients, CR led to reduction in high outputs from 73 to 4 per cent of patients, PN cessation in 90·6 per cent (126 of 139), and demonstrable benefits in nutritional status, gut rehabilitation and liver enzymes. This large series was enabled by a peristaltic roller pump (continuous CR device) called Enteromate® (Labodial, Clayes-sous-Bois, France)[19,20], which has since been discontinued.

In the present feasibility study, the observed clinical benefits similarly encompassed remediation of high-output losses, PN and intravenous fluid cessation, improvement of electrolyte and liver enzyme abnormalities, resumption of oral diet, discharge from hospital, and gut rehabilitation with rapid recovery after surgical stoma reversal. Although data for the novel device are currently feasibility level and without controls, the historical data on CR achieved by a variety of methods add weight to the potential benefits. An RCT of the novel device is planned.

CR has historically failed to gain clinical traction owing to lack of acceptable techniques, available technologies or palatable workflows[7,9]. Other than the sporadic use of custom devices, manual solutions for CR have often been applied (such as straining and syringing), including in settings where PN is too costly or not widely available[11,21];

however, these manual strategies are time-consuming and unpleasant[9]. Similarly, a 10-year review[8] of CR in children cited labour-intensive procedures as well as the need for multidisciplinary coordination as limitations. The authors anticipate that an effective, efficient and easy technical solution for chyme recycling has the potential to become the standard of care for patients with high-output enterostomies and EAFs, when distal limb access is safe and possible.

To achieve this, however, any new technology must undergo the challenging transition to commercialization, including manufacturing at scale and regulatory clearance. To this end, the device has now been transferred to a commercial company (Surgical Design Studio, Auckland, New Zealand), and is undergoing CE Mark. The device has also recently achieved Breakthrough Device Designation from the US Food and Drug Administration, an expedited pathway for devices offering more effective treatment, or diagnosis of life-threatening or irreversibly debilitating human diseases or conditions[22]. It is anticipated that the device will be cleared for clinical use in the USA and Europe during 2020, but clinicians interested in trialling the device sooner may contact the authors to request access.

Some centres have shown promising results using the alternative strategy of fistuloclysis (installation of enteral feed to the distal stoma limb), rather than CR[23,24]. However, fistuloclysis physically attaches the patient to an enteral feeding pump, and necessitates customized interfaces of feeding tubes through a stoma appliance. The CR device used in the present study introduces a potentially superior workflow, by efficiently and intermittently recycling natural chyme within the stoma appliance itself. It would be of interest to formally compare fistuloclysis and CR in future.

Despite the potential advantages of the new CR device, several important limitations and training points were noted during the feasibility study. CR volumes must be titrated to tolerance to avoid gastrointestinal side-effects such as bloating, discomfort, nausea and diarrhoea. Patients (or carers) must be willing to engage with device maintenance, including driver recharging and regular pump changes, timed with stoma appliance changes. Dietary modifications are required so that the pump does not become clogged with fibrous residues. The transition to CR may require the weaning or cessation of antidiarrhoeal medication to avoid constipation, and potentially titration of other medications owing to greater absorption. In addition, patients can still become dehydrated if they are not consistent or compliant with CR and device use, or if high nocturnal losses are not reinfused, which can lead to renal impairment. It remains to be seen whether high volumes of output (for example more than 2·5 l/day) can be bolus-reinfused consistently in a larger cohort of patients. Further advances in pump design may help to mitigate or reduce such limitations in future.

A potential limitation of the bacterial study was that the bacterial content of new effluent entering the stoma appliance was not measured constantly over the study period. However, given that the first chyme entering the bag was already consistently rich in bacteria, and these concentrations then remained static for several hours, the authors made the reasonable assumption that no significant growth occurred in the bag during the observed window.

Another area of potential future application of the device is in reinfusing chyme in patients with defunctioning loop ileostomies. Readmission rates in patients with an ileostomy are up to 10–15 per cent, with high outputs and dehydration the most common reason[25,26]. New onset of renal impairment has been observed in up to 19 per cent of patients with an ileostomy[27]. Ileostomy CR is likely to be safe as early as 8–13 days after stoma creation, so long as anastomotic integrity is first verified[28], and could substantially reduce these events. Such an intervention could also facilitate the completion of chemotherapy, which is more commonly interrupted by chemotherapy-associated diarrhoea in patients with an ileostomy[29], while also potentially reducing the severity of low anterior resection syndrome by eliminating the negative consequences of prolonged colonic diversion and microbiome starvation[30,31].

There is developing interest in stimulation of the efferent limb before stoma reversal surgery, which may improve time to postreversal gut recovery, reduce rates of postoperative ileus, and decrease hospital stay[32,33]. These improvements were also supported in the present feasibility study, in which all patients undergoing simple enterostomy closure, including jejunostomy, recovered rapidly (median hospital stay 2 days); however, these results must be confirmed in a larger clinical trial.

This study has described a novel device for CR, and shown that the device is effective, safe, user friendly and clinically acceptable. Broad clinical benefits are suggested, which now await further evaluation. CR has the potential to become the standard of care for high-output double enterostomies and EAFs.

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.