Chyme reinfusion or enteroclysis in nutrition of patients with temporary double enterostomy or enterocutaneous fistula

Ronan Thibault[a] *and Denis Picot*[b]

Purpose of review
Patients with double temporary enterostomy or enterocutaneous fistula may suffer from intestinal failure. Parenteral nutrition is the gold standard treatment until surgical re-establishment of intestinal continuity, but serious complications may arise. Chyme reinfusion or enteroclysis are indicated.

Recent findings
Chyme reinfusion corrects the intestinal failure by restoring intestinal absorption, allowing parenteral nutrition weaning in 91% of patients. Chyme reinfusion contributes to improve nutritional status and reduce plasma liver test abnormalities. Chyme reinfusion is feasible at home without any serious complications in selected patients. Mechanisms underlying chyme reinfusion effectiveness on intestinal function, such as restoration of ileal brake, are suggested but most remain to be demonstrated. When the downstream small bowel is exposed, enteroclysis of enteral nutrition or hydration could be helpful to reduce parenteral nutrition needs, or in case of insufficient food intake during chyme reinfusion.

Summary
Chyme reinfusion or enteroclysis are less expensive, well tolerated, and easy-to-use nutrition support techniques, which may allow reducing parenteral nutrition-related healthcare costs. The latter remains to be demonstrated in the setting of a prospective randomized controlled trial. This review may contribute to improve the awareness of intensivists, digestive surgeons, and gastroenterologists involved in intestinal failure management to spread the use of chyme reinfusion or enteroclysis.

Keywords
enteral nutrition, fistuloclysis, gastrointestinal surgery, intestinal failure, parenteral nutrition

INTRODUCTION

In the course of an intestinal surgery procedure, several clinical situations lead the surgeon to undertake a double temporary enterostomy (small bowel resection, peritonitis, fistulae, anastomosis protection, ...) or could be complicated of enterocutaneous fistula (ECF) (peritonitis, anastomosis leakage, digestive adherences, ...). These conditions could constitute a type 1 short bowel syndrome and are often complicated with intestinal failure, especially when the stoma output is equal or higher than 1500 ml/24 h. These lead to serious complications resulting in hospital readmissions, such as acute or chronic dehydration, renal failure, electrolyte disturbances, micronutrients and mineral deficiencies, and malnutrition, thus increasing healthcare-related costs and affecting patients' quality of life [1]. Intestinal failure was recently defined by the European Society for Clinical Nutrition and Metabolism (ESPEN) as 'the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth' [2▪▪]. In case of temporary double enterostomy or ECF, the intestinal failure is type 2, and defines as a prolonged acute condition, often in metabolically

[a]Nutrition Unit, Department of Endocrinology, Diabetology and Nutrition, Home Parenteral Nutrition Centre, CHU Rennes, Université de Rennes 1, INSERM U991 and [b]Department of Nutritional and Digestive Rehabilitation, Clinique Saint Yves, Rennes, France

Correspondence to Professor Ronan Thibault, MD, PhD, Unité de Nutrition, CHU Rennes-Pontchaillou, 2, rue Henri Le Guilloux, 35000 Rennes, France. Tel: +33 2 99 28 96 46; fax: +33 2 99 28 96 47; e-mail: ronan.thibault@chu-rennes.fr

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KEY POINTS

- In case of intestinal failure secondary to high output temporary enterostomy or ECF, chyme reinfusion is an efficient and reliable technique of enteral nutrition which corrects intestinal failure by restoring intestinal absorption, allowing parenteral nutrition weaning in almost all patients.
- Chyme reinfusion contributes to improve nutritional status and to reduce plasma liver test abnormalities, and is feasible at home in well selected patients.
- Chyme reinfusion allows preparing efferent small bowel and colon to the surgical re-establishment of intestinal continuity.
- In patients with exposed efferent small bowel, enteroclysis of hydration, and/or enteral nutrition solutions could allow improving hydration and nutritional status, as well as reducing parenteral nutrition needs.
- Multicentre prospective randomized controlled trials are needed to determine the impact of chyme reinfusion compared with parenteral nutrition on the incidence of complications, healthcare costs, and quality of life, as well as feasibility of home chyme reinfusion, in intestinal failure patients with temporary high-output double enterostomy or ECF.

unstable patients, requiring complex multidisciplinary care, and intravenous supplementation over periods of weeks or months [2▪▪]. At this time, the current gold standard therapy indicated until the surgical re-establishment of digestive continuity (SIRC), with a mean duration of 3–6 months, is home parenteral nutrition [3]. However, home parenteral nutrition has its own morbidity and, in the absence of expertise, the risks of infectious, hepatic dysfunction, mechanical, and metabolic complications are increased [1,3]. Therefore, the availabilities of low-cost, safer, and easy-to-use nutrition support techniques could be of high added value in these type 2 intestinal failure patients. Chyme reinfusion [4▪▪,5▪,6▪,7–9] and enteroclysis [5▪,6▪,10] could be these techniques. The scope of this review is to describe the technical principles of chyme reinfusion and enteroclysis, to give practical details for their use, review their clinical benefits in clinical practice, and, because of the lack of data, to hypothesize the mechanisms related to their clinical benefits.

DEFINITIONS

The interruption of the small bowel by a double enterostomy or an ECF separates the small bowel into an upstream afferent segment and a downstream efferent segment (Fig. 1). Enteroclysis is an enteral nutrition technique consisting in the administration of enteral nutrition or hydration solutions in the downstream efferent small bowel through efferent enterostomy or ECF exposed to the abdomen wall, chyme from the afferent small bowel being thrown out. The term 'fistuloclysis' [2▪▪,6▪,10] wrongly used as a synonym of 'enteroclysis' should be abandoned as it is medically inappropriate, referring to a technique of fistula irrigation or washing and not to an enteral nutrition technique which could be only delivered in the intestine through the fistula, but not in the fistula; it is linguistically inappropriate: one Latin prefix followed by one Greek suffix. Chyme reinfusion [4▪▪] (or refeeding enteroclysis [2▪▪,5▪] or succus entericus reinfusion [8,9]) is an enteral nutrition technique which artificially re-establishes the small bowel continuity by an extracorporeal circuit of the chyme and mimics the definitive gastrointestinal function; the chyme, composed of digestive secretions, and nutrients from oral food and/or tube feeding, is collected from the afferent small bowel, and reinfused via the enterostomy or the ECF into the efferent diverted small bowel segment. Chyme reinfusion could be, at best, in our experience, continuous, through a portable or not automated pump, or, as reported by others [5▪], sequential by manual chyme decanting.

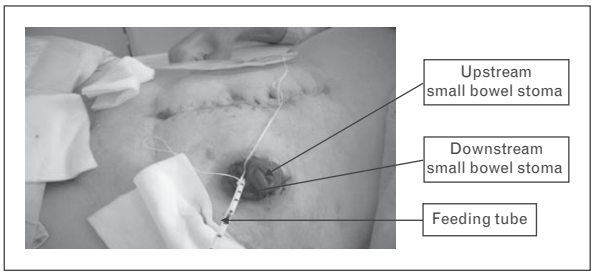

FIGURE 1. Example of a temporary double enterostomy. The small bowel continuity is disrupted with two small bowel segments exposed to the abdominal wall: the upstream afferent segment, with impaired digestive and absorptive function, and a downstream efferent segment, totally deprived of digestive secretions, bowel flow and succus entericus. The feeding tube is inserted in the downstream small bowel, and is ready for enteroclysis or chyme reinfusion.

THE PRINCIPLE OF CHYME REINFUSION WITH AUTOREGULATED PUMPS

Although first described in 1977 by Etienne Levy, and recently suggested as an alternative therapy in intestinal failure patients [2▪▪], chyme reinfusion is

rarely used, underrecognized, and not endorsed by most health insurances. This is partly because of the fact that the materials used for chyme reinfusion were not specifically dedicated to the technique. Indeed, in most centres where it is used, chyme reinfusion is performed by diverting from their first use enteral nutrition pumps and tubulures, or dialysis material... These techniques must be abandoned: chyme was collected in a bag thanks to gravity, sometimes refrigerated, often sieved to remove the largest food particles; chyme is then transferred every 3–4 h in an enteral nutrition bag to be reinfused with an autoregulated enteral nutrition pump into the downstream efferent small bowel. Others directly reinfused the chyme with a syringe. All these handlings were associated with uncomfortable odours and dirt making the chyme reinfusion technique very unpopular. Spreading the use of autoregulated pumps dedicated to chyme reinfusion would help to increase chyme reinfusion acceptation and use in intestinal failure-specialized centres. At Clinique Saint Yves, Rennes, France, we perform continuous chyme reinfusion using the Entéromate II system (Labodial, Les Clayes-sous-Bois, France), marketed since 1998 (Fig. 2). Entéromate II autoregulates continuous chyme reinfusion without any adjustment or nurse's intervention, and no uncomfortable odour. The dead space volume of the extracorporeal circuit is lower than 50 ml and does not cause any volemic deprivation. The tubulures are closed and prevent from outside infectious contamination. The automaton has two peristaltic pumps. The left pump works permanently and aspirates the jejunal effluent toward a 30-ml disposable plastic container, which is hung on an electronic steelyard. The weight of the container is continuously and electronically monitored. When the minimal volume of approximately 10 ml is exceeded, the second pump starts and the contents are infused into the diverted downstream small bowel until the return to minimal volume. The downstream small bowel is intubated through the efferent enterostomy or ECF with a simple lumen polyurethane nasogastric 14-16 French (Fr) caliber, Levine-typed tube, without balloon, into the first 15–20 cm of the small bowel (Fig. 1). We advise that polyurethane nasogastric tubes must be preferred to Foley's because of their higher internal diameter (for a given 'ch' calibre) and the absence of balloon, that could injure the small bowel when inflated too much. Ideally a radiologic opacification with water-soluble contrast agents checks the tube position and controls the anatomy and the length of the downstream small bowel until the colon.

INDICATIONS OF CHYME REINFUSION

In our experience, the patients eligible for chyme reinfusion fulfil the following criteria: intestinal failure defined as a theoretical indication to parenteral nutrition, plus a stoma output nihil per mouth of at least 1200 ml/24 h; existence of a double enterostomy or at least two orifices of ECF visible on the abdominal wall; theoretical temporary nature of the stoma or ECF in the expectancy of SIRC; presence of efferent small bowel between the stoma and the colon, or a terminal ileostomy; absence of obstruction of digestive fistula between the mouth

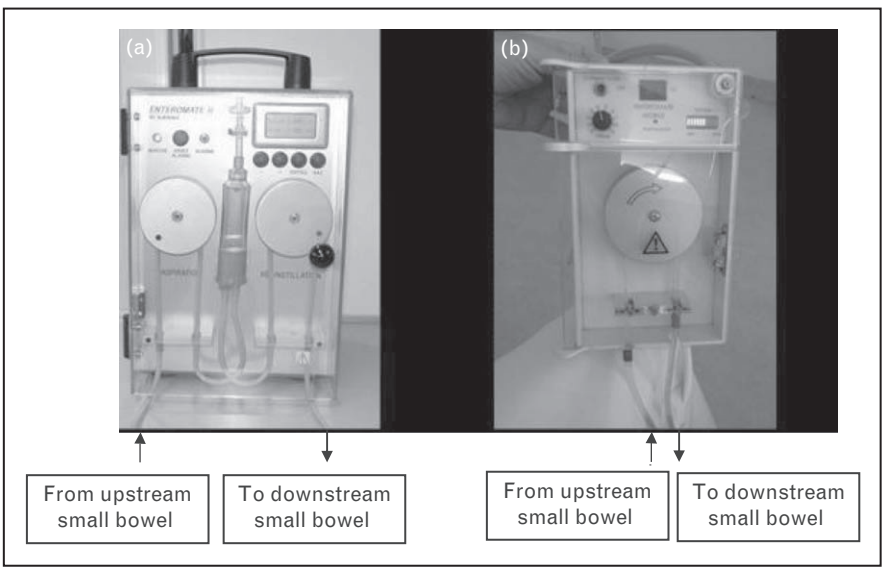

FIGURE 2. Chyme reinfusion technique with the automated pump Enteromate II (a) and the portable Enteromate Mobile (b) (Labodial, Les Clayes-sous-Bois, France).

and the afferent stoma, and in the efferent intestinal tract; ability to catheterize the efferent stoma with a feeding tube on more than 15 cm; absence of progressive peritoneal carcinosis; age more than 17 years; full agreement of the patient to carry out chyme reinfusion and accept the food constraints of ingesting smooth puree meals.

CHYME REINFUSION AND ENTEROCLYSIS IN DAILY PRACTICE

Chyme reinfusion and enteroclysis should be integrated in a global approach of intestinal rehabilitation. Patients require complex management of opened abdominal wounds, high intestinal outputs, and need a multidisciplinary nutrition team, including specially trained nurses and nutritionist gastroenterologists or surgeons. During the 2 days before chyme reinfusion initiation, enteroclysis is initiated by instilling 1 litre of oral rehydration solution, together with laxatives in case of faecal residues or faecaloma in the colon. At the same time, antimotility drugs, for example, loperamide, are stopped to prevent ileus. Antispasmodic agents could be useful in case of abdominal pain, and cholestyramine is given by enteroclysis in the event of diarrhoea during the first days. In case of persisting diarrhoea, loperamide is used. Antisecretory gastric drugs are used in all patients before and during chyme reinfusion. Octreotide is never used. Once the patient has been adequately trained and is capable of correctly adjusting the rate of reinfusion, portable nonautoregulated Enteromate Mobile pump (Labodial, Les Clayes-sous-Bois, France), marketed since 2010, is used secondly to give autonomy to the patient at hospital or at home. This pump is autonomous thanks to batteries. During chyme reinfusion, to avoid tube obstruction, patients are mandatorily orally fed ad libitum with smooth puree meals. In case of insufficient food or hydration intake during chyme reinfusion, enteral nutrition and additional hydration solutions could be administered classically through a nasogastric feeding tube, gastrostomy or jejunostomy, or, in some cases, by 'en Y' enteroclysis in the reinfusion tube into the downstream small bowel [6▪,8,9].

CLINICAL BENEFITS OF CHYME REINFUSION AND ENTEROCLYSIS

Only a few studies have reported the beneficial effects of chyme reinfusion or enteroclysis in intestinal failure patients with temporary double enterostomy or ECF. Only one [4▪▪] was published within 18 months and none was prospective randomized controlled trials. These studies are monocentric case series, having included only a low number of patients, and did not report post-SIRC clinical outcomes. In adult patients, chyme reinfusion could restore intestinal absorptive capacities [4▪▪,7]. This could allow parenteral nutrition discontinuation a few days after its initiation [4▪▪,5▪], and the improvement of frequently observed liver test abnormalities [4▪▪]. Plasma liver test improvement seems greater in patients treated by enteroclysis coupled with chyme reinfusion than by enteroclysis alone [6▪]. In neonates and premature infants with double enterostomies, chyme reinfusion reduces parenteral nutrition dependence and corrects plasma liver tests abnormalities [9]. Chyme reinfusion improved nutritional status [4▪▪,6▪,7]. The larger monocentric (Clinique Saint Yves, Rennes, France) prospective cohort assessing the efficacy of chyme reinfusion in 212 patients with a temporary double enterostomy (86% of patients) or ECF (14%) waiting for SIRC is under publication and confirms these findings, and suggests the feasibility of home chyme reinfusion [4▪▪]. Double enterostomy or ECF were mainly because of peritonitis (44%) and cancer (34%). Chyme reinfusion corrects the intestinal failure by restoring intestinal absorption: reduction in intestinal losses by 85%, strong improvement in nitrogen and fat digestive absorption coefficients, and strong reduction in the proportion of patients with plasma citrulline less than 20 μmol/l [4▪▪]. As a result, parenteral nutrition and/or IV hydration could be stopped in 91% of patients, within a median ± interquartile of 2 ± 9 days after chyme reinfusion initiation [4▪▪], or in 100% of cases within 20 days in the little case series of 20 patients reported by Coetzee *et al.* [5▪]. In addition, nutritional status improved. With chyme reinfusion, the number of patients who had one or several plasma liver test abnormalities decreased from 87 to 51% ($P < 0.001$) [4▪▪].

COMPLICATIONS AND SIDE-EFFECTS OF CHYME REINFUSION

The management of chyme reinfusion-related complications and side-effects requires dedicated healthcare staff education. In our case series of 232 patients [4▪▪], eight patients (3%) were excluded because of chyme reinfusion early complications, including one lethal: anal incontinence, $n = 2$; ischaemic colitis, $n = 1$; newly developed fistulas, $n = 3$; cancerous colic stenosis, $n = 1$; letal mesenterical infarction, $n = 1$. Wu *et al.* [6▪] reported diarrhoea, vomiting, nausea, abdominal pain, and abdominal distension that could affect 14% of patients, but were all relieved later during chyme reinfusion course. In other case series [4▪▪,5▪], the prevalence of chyme reinfusion-related technical problems (e.g. tube

disinsertions or obstructions, chyme leaks, stoma care problems, ...) and gastrointestinal side-effects was not collected. In our experience, the most frequent side-effects of chyme reinfusion are: the difficulty to accept the food constraints of ingesting smooth puree meals that could impact on mood, quality of life, and nutritional status; obstruction or displacement of the chyme reinfusion tube; spasmodic pains during the resumption of normal downstream intestine function; severe constipation, especially if antidiarrheal drugs are used (this is the reason why loperamide has to be stopped before chyme reinfusion initiation).

One considerable advantage of chyme reinfusion is, by using the whole remnant small bowel, to prefigure the post-SRIC intestinal function. Indeed some symptoms occurring during chyme reinfusion, such as pain, faecal incontinence, diarrhoea, would have occurred after SRIC. Thus chyme reinfusion should allow anticipating and even preventing situations that would have occurred after the SRIC with potentially more serious consequences and sometimes would have required a second surgery. For example, in case of faecal incontinence, anal biofeedback could be prescribed before the SRIC.

FEASIBILITY OF HOME CHYME REINFUSION

In 59 (28%) patients of our French case series [4▪▪], chyme reinfusion was feasible at home in selected patients after specific training and education, where they must have acquired total autonomy for chyme reinfusion and basic stoma care. The median duration of home chyme reinfusion was 36 ± 40 days, accumulating 7.4 patient-years. For home chyme reinfusion, we have elaborated a dedicated clinical pathway, including a thesaurus of solutions facing well defined technical problems. As a result, no patient had to stop chyme reinfusion, only a few were readmitted for minor problems, and none had to go back to parenteral nutrition. Unfortunately, at this time, home chyme reinfusion is not yet recognized by health insurances as a nutrition support technique. More studies, noteworthy multicentric, are needed to demonstrate safety and clinical benefits of home chyme reinfusion.

MEDICOECONOMICS BENEFITS OF CHYME REINFUSION

At this time, parenteral nutrition remains the gold standard therapy until the patients underwent the SRIC. Parenteral nutrition costs are much higher than those of enteral nutrition and increase with complications [1]. The quick parenteral nutrition weaning with chyme reinfusion could have avoided 26.6 patient-years with parenteral nutrition [4▪▪]. As a great part of the costs of type 2 intestinal failure patients' therapies resulted from parenteral nutrition-related complications [11], chyme reinfusion could be associated with substantial cost savings. The prospective randomized controlled trial efFiciency of Reinfusion of chYme (FRY), supported by the French National Clinical Research Program, will determine the impact of chyme reinfusion compared with parenteral nutrition on the incidence of complications, healthcare costs, and quality of life in intestinal failure patients with temporary high-output double enterostomy until a follow-up of 1 month post-SIRC. Thanks to an additional ESPEN Technology grant 2015, the FRY trial will allow determining feasibility of home chyme reinfusion in a multicentric setting.

HYPOTHESES UPON THE MECHANISMS OF THE CLINICAL BENEFITS OF CHYME REINFUSION AND ENTEROCLYSIS

In case of small bowel disruption, the absence of the ileal brake results in a noninhibition of gastric emptying, gastric hypersecretion, and accelerated intestinal motility, contributing to impaired absorption. Supposed mechanisms of chyme reinfusion-induced improvement of intestinal function are the reabsorption of digestive secretions (gastric, pancreatic, and biliary succus) and the restoration of the ileal brake. The latter was first suggested by Lévy *et al.* [12] who showed that proximal stoma output was broken down by hydration solution enteroclysis into the downstream small bowel (−20%) and mainly by chyme reinfusion (−33%). Plasma citrulline normalization is the result of the increase in the functional enterocyte mass and of the better extraction of intraluminal glutamine [7]. In case of terminal ileum resection, the enterohepatic cycle of bile acids is disrupted leading to bile salt malabsorption. This results in an increase in bile acid synthesis by the liver which, in turn, enhances hepatic lipogenesis and intrahepatic cholestasis, resulting in plasma liver test abnormalities. At physiological state, bile salts activate the intracellular Farnesoid X Receptor (FXR) in the small intestine and liver epithelium [13▪]. FXR activation is in part mediated by endocrine-acting fibroblast growth factor (FGF) 19, a bile salt-induced enterokine. The release of the FGF19 subsequently inhibits bile salt synthesis from cholesterol. In case of intestinal failure-induced enterohepatic cycle disruption, bile salts synthesis is not inhibited, resulting in overproduction and liver accumulation that could have a direct toxicity on hepatocytes. Chyme reinfusion could act by

restoring bile salt enterohepatic cycle and bile salts signalling, decreasing liver inflammation, and plasma liver tests. A study is ongoing to demonstrate this hypothesis. Other mechanisms such as changes in intestinal microbiota or prevention of bacterial overgrowth deserve further investigation.

CONCLUSION

Chyme reinfusion or enteroclysis are well tolerated and easy-to-use nutrition support techniques. In case of intestinal failure secondary to high output temporary enterostomy or ECF, chyme reinfusion is an efficient and reliable technique of enteral nutrition which corrects intestinal failure by restoring intestinal absorption. Chyme reinfusion contributes to improve nutritional status and to reduce plasma liver test abnormalities, and is feasible at home in well selected patients. By allowing the parenteral nutrition weaning within a short period, chyme reinfusion could be associated with substantial cost savings. The prospective randomized controlled trial FRY, supported by the French National Clinical Research Program, will determine the impact of chyme reinfusion compared with parenteral nutrition on the incidence of complications, healthcare costs, and quality of life in intestinal failure patients with temporary high-output double enterostomy. This review may contribute to improve the awareness of intensivists, digestive surgeons, and gastroenterologists involved in intestinal failure management to spread the use of chyme reinfusion and enteroclysis.

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Conflicts of interest

D.P. declares advisory activities without any financial retribution with Labodial, Les Clayes-sous-Bois, France. The remaining author has no conflicts of interest.

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- ■■ of outstanding interest

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