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REVIEW

Octreotide and enterocutaneous fistula closure in neonates and children

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Abstract Enterocutaneous fistula and its conservative management still pose a challenge for the surgeon. The use of octreotide and somatostatin in neonates and children as adjunctive therapy in the conservative management of this condition, leads to major controversy regarding its efficacy. Therefore, we conducted an extensive literature review of published articles regarding the use of somatostatin and its analogues in the treatment of enterocutaneous fistula in neonates and children. Our review is then presented together with a case vignette and discusses the different practical aspects of the treatment with these drugs.

Conclusion: The major diversity in treatment regimens among published studies makes outcomes difficult to compare. However, given the results of the different cases reported in the literature and of our own experience, we suggest a possible beneficial effect of octreotide and somatostatin on closure of enterocutaneous fistula in these patients.

What is Known:

- *Enterocutaneous fistula in neonates and children is a very challenging condition.*
- *Treatment of enterocutaneous fistula still remains controversial.*

What is New:

- *Octreotide and somatostatin may play a role in the closure of enterocutaneous fistula.*
- *Our review will provide an updated source of information to guide management.*

Keywords Enterocutaneous fistula · Neonate · Octreotide · Somatostatin

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Abbreviations

ECF	Enterocutaneous fistula
GH	Growth hormone
NEC	Necrotising enterocolitis
O	Octreotide
Pat	Patient
SC	Subcutaneous
S	somatostatin

Introduction

Enterocutaneous fistula (ECF) is a surgical complication with significant morbidity and a mortality rate in adults of 5 to 30 % [10, 24], mainly related to sepsis, malnutrition, dehydration, electrolyte imbalances and metabolic disturbances [4, 16]. The cornerstone of ECF management lies in conservative

treatment, that usually includes bowel rest, parenteral nutrition, antibiotics and local wound care, which will lead to a fistula healing rate of 60 to 75 % [37]. Somatostatin and its analogues have been commonly used in adults as an adjuvant treatment to achieve closure of ECF in addition to other gastrointestinal fistulas, with uneven results, so there is understandable controversy about its success rate [1, 3, 9, 15, 23, 30, 32, 37]. Enterocutaneous fistula is a very rare disease in children, and, therefore, there is limited experience with both conservative and surgical management. Paediatric series of ECF patients managed with conservative treatment without somatostatin or its analogues report a healing rate of 54 %, mortality rate of 8 to 24 %, and time reported to healing of the fistula varies between 6 and 107 days, with an average of 30 days [12, 39]. We report our experience in the treatment of ECF with octreotide in a newborn, and we set out a literature review [4, 8, 17–19, 40], summarised in Table 1.

Case vignette

A 32-week-gestation, premature male newborn weighing 1978 g presented bilious nasogastric drainage and failure to pass meconium shortly after birth. Abdominal X-ray revealed a "double-bubble" sign with absence of air more distally in the gastrointestinal tract (Fig. 1a), and contrast enema revealed a small calibre colon, a "microcolon of disuse" (Fig. 1b). During the surgical procedure, a high jejunal multiple intestinal atresia was found (Fig. 2a), with type II atresia in the first jejunal loop (Fig. 2b), and type IIIb or apple-peel atresia (Fig. 2c), with the reduced intestinal length entailed by this atresia. The atretic segments were resected, the duodenum was tapered, and finally, an end-to-end anastomosis was performed and a transanastomotic tube was placed. Four days after the surgery abdominal distention and crepitus in the surgical wound were observed, and an abdominal X-ray confirmed the presence of pneumoperitoneum (Fig. 3a). At the time of emergency surgery, a tube perforation of the bowel was found, located distal to the anastomosis and intense diffuse peritonitis (Figs. 3b and 3c). The perforation was successfully sutured and a jejunostomy with separated stomas was constructed. Six weeks later, the jejunostomy was closed due to high stoma output. On postoperative day 8, bilious and gas drainage from the surgical wound was observed (Fig. 4a), with a minimal dehiscence and a normal plain film of the abdomen. Medical therapy of the ECF was begun at that time: bowel rest, total parenteral nutrition, broad spectrum intravenous antibiotics (meropenem and vancomycin), and octreotide

Table 1 Use of octreotide and somatostatin in paediatric patients with ECF [4, 8, 16–18, 38]

	Diagnosis	Gestational age, weeks	Age	Weight, g	Drug	Route	Starting day from ECF	Initial dose, μg/kg/day	Maximum dose, μg/kg/day	Days to closure	Total days
Pat 1 [18]	Meconium peritonitis	34	7 days	2350	O	IV cont	2	1	6	10	10
Pat 2 [8]	Duodenal perforation	30	10 days	1200	O	SC bid	22	1.4	4.8	7	7
Pat 3 [4]	NEC	29	24 days	1400	O	IV cont	NA[a]	36	72	NA[a]	NA[a]
Pat 4 [38]	NEC	FT	55 days	2290	O	SC bid	9	1.4	6	5	30
Pat 5 [17]	NEC	27	57 days	1030	S	IV cont	4	36	72	3	9
Pat 6 [18]	NEC	34	68 days	1876	O	IV cont	3	1	1	21[b]	21[b]
Pat 7 [4]	NEC	24	6 months	635	O	SC bid	NA	1.4	2	8	>8[c]
Pat 8 [16]	Duodenal perforation	NA	6 years	NA	O	SC tid	NA	50	300	4	12
Our patient	Polyatresia	32	53 days	1978	O	IV cont	0[d]	12	72	7	23

Doses are expressed in micrograms/kilogram/day

We know the dose regimen for octreotide or somatostatin used in our case (day 1, 12 μg/kg/day; day 2, 24 μg/kg/day; day 3–6, 48 μg/kg/day; day 7–14, 72 μg/kg/day; day 15, 48 μg/kg/day, day 16–23, 24 μg/kg/day), in case 1 (day 1–8, 1.4 μg/kg/day; day 8–10, 6 μg/kg/day), in case 4 (day 1–2, 1.4 μg/kg/day; day 3–5, 2.8 μg/kg/day; day 6–8, 4 μg/kg/day; day 9–14, 6 μg/kg/day; day 15–30, 3 μg/kg/day) and in case 5 (day 1–2, 36 μg/kg/day; day 3–7, 72 μg/kg/day; day 7–9, NA). In the other patients, there is no information available about the dose regimens

In our patient, the treatment was gradually tapered until it was finally suspended (day 15, 48 μg/kg/day; day 16–23, 24 μg/kg/day), as well as in patients 5 and 7 (no information is available about these dose regimens). For the other patients ($n = 6$) treatment was withdrawn without previous tapering

Oral feeding was resumed after fistula closure and drug withdrawal (patients 1, 2, 5, 8 and our case), after fistula closure but during octreotide treatment (patient 4), or with the fistula still open, during treatment (patient 6)

bid twice daily,, *FT* full term, *g* grams, *IV cont* intravenous continuous infusion, *NA* not available, *NEC* necrotizing enterocolitis, *O* octreotide, *Pat* patient, *S* somatostatin, *SC* subcutaneous, *tid*. three times a day

[a] The exact number of days is not reported in the article; octreotide was administered for 14 days. The fistula closed and the treatment was discontinued four days later. The fistula reopened and octreotide was resumed. The patient presented a pulmonary hypertension crisis leading to definitive discontinuation of octreotide

[b] Three weeks; in the article the exact number of days is not reported

[c] The dose was gradually tapered and eventually stopped; in the article the exact number of days is not reported

[d] Treatment was begun at diagnosis of enterocutaneous fistula

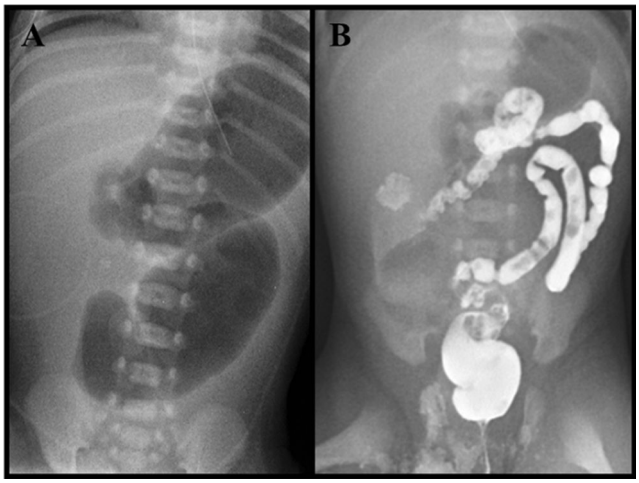

Fig. 1 Abdominal X-ray shows the double-bubble sign **a**. Barium enema reveals disuse microcolon **b**

infusion, commenced at 12 μg/kg/day, and gradually increased to 72 μg/kg/day on day 7 (Table 1). The fistula output quickly decreased and ceased on the seventh postoperative day (Fig. 4b), and the upper gastrointestinal series on the fourteenth postoperative day showed fistula closure and absence

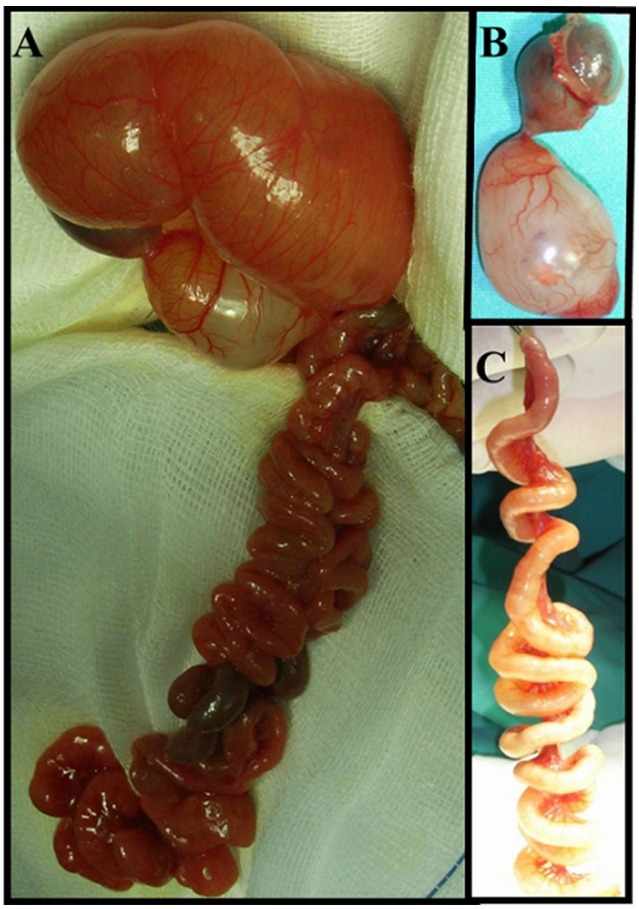

Fig. 2 High jejunal multiple intestinal atresia **a**. Type II atresia **b**. Type IIIb or apple-peel atresia **c**

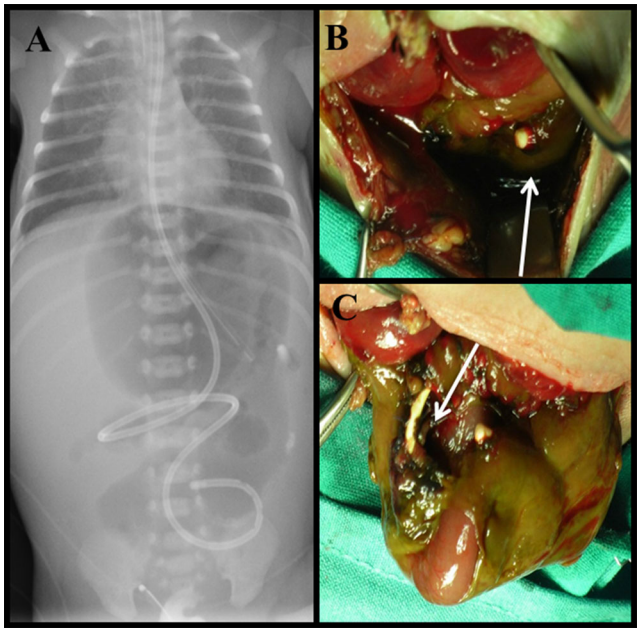

Fig. 3 X-ray of the abdomen demonstrating pneumoperitoneum **a**. Exteriorization of transanastomotic tube through intestinal perforation (*white arrows*) and intense diffuse peritonitis **b**, **c**

of stenosis (Fig. 4c). Enteral feeding was then resumed, and the dose of octreotide was gradually decreased to 24 μg/kg/

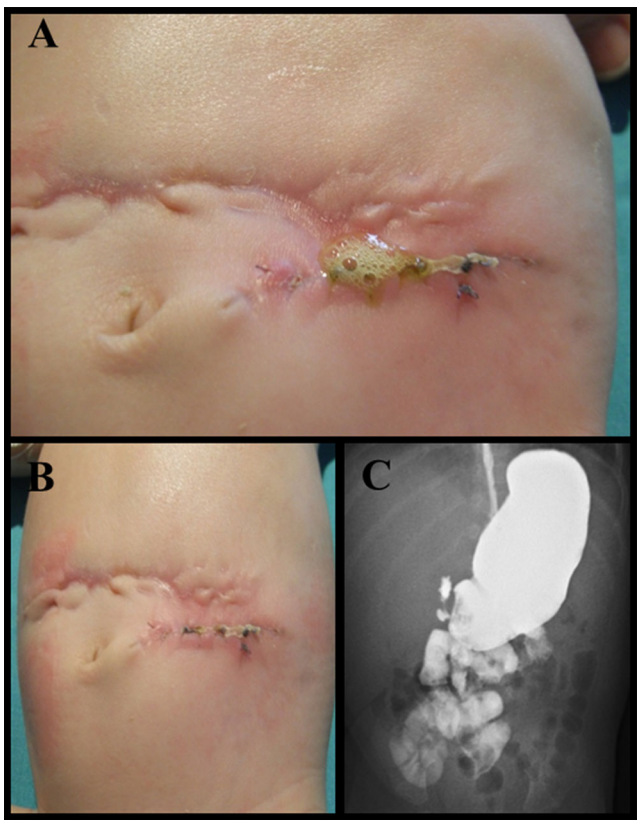

Fig. 4 Bilious and gas content flowing through the surgical wound **a**. Surgical wound healed **b**. Normal upper gastrointestinal barium study **c**

day up until day 23, when it was completely discontinued. During treatment with octreotide only isolated episodes of abdominal cramping and transient hyperglycaemia were detected. There was a favourable outcome, exclusive enteral nutrition was tolerated, and the patient was discharged from hospital after three months. During three years of follow-up the patient has remained asymptomatic, a regular diet was tolerated and there was appropriate growth and development.

Literature review

Enterocutaneous fistula in children

Enterocutaneous fistula in children is a major surgical complication, most often related to necrotising enterocolitis (NEC) surgery, among other conditions, such as meconium peritonitis, intestinal atresia or volvulus. The main goal of treatment is to achieve early closure of the fistula, thereby reducing morbidity and mortality resulting from the effects of ECF, and reducing hospital stay. Different treatments have been used to shorten the fistula closure time, such as drugs that reduce intestinal motility or decrease secretions, and, more recently, octreotide and somatostatin [4, 8, 17–19, 40].

Somatostatin and its analogues: mechanism of action

Somatostatin

It was first isolated in 1973 [6], and since the eighties it has been used to treat pancreatic, intestinal and biliary fistulas in adults. Somatostatin is a naturally occurring tetradecapeptide found in the hypothalamus, pancreas, gastrointestinal tract, salivary glands, thyroid gland and the heart. Its functions are generally inhibitory, via an endocrine, paracrine or autocrine mechanism, or acting as a neurotransmitter [26], and its main targets are the endocrine system and the gastrointestinal tract. In the hypothalamus somatostatin inhibits the release of growth hormone (GH) and thyrotropin and in the pancreas and gastrointestinal tract endocrine and exocrine secretion is reduced.

This tetradecapeptide also reduces splanchnic blood flow and slows down gastrointestinal motility in addition to gallbladder contraction, thereby increasing water and electrolyte absorption [11, 13, 14, 16, 21, 40]. It also limits growth and cellular division in the gastrointestinal tract [21]. The therapeutic use of somatostatin is limited by its short half-life, only 2–3 min, which makes continuous intravenous administration mandatory and associates a rebound effect after withdrawal (especially GH, insulin and glucagon) [22].

Octreotide (SMS 201-995)

This is a synthetic octapeptide somatostatin analogue with similar effects but with a greater potency and a half-life of 45 min after intravenous administration or 60–120 min after subcutaneous injection [14, 21, 26, 27, 29]. The longer half-life of octreotide enables intermittent intravenous or subcutaneous administration, making it more useful in the clinical setting than somatostatin. Although bioavailability is 100 % when administered by the subcutaneous route in healthy subjects, it may be limited in patients with obesity, oedema or poor peripheral perfusion [21].

In the extensive literature published concerning adults there is considerable controversy regarding the usefulness of somatostatin or its analogues for the treatment of ECF [1, 3, 9, 15, 23, 30, 32, 37], in contrast to the favourable outcomes reported in paediatric patients. So far, it has not been proven whether the effects of continuous intravenous infusion are comparable to those of subcutaneous injection every 8 to 12 h. Intermittent subcutaneous dosing could produce some fluctuations in the effects, which would affect treatment efficacy. Furthermore, it is unclear whether the effects of octreotide are equivalent to those of somatostatin, because among the five somatostatin receptors (SSTR 1–5), octreotide has a similar affinity to SSTR 2 and 5, moderate affinity to SSTR 3 and void affinity to SSTR 1 and 4. Scientific evidence actually suggests that the beneficial effect of somatostatin is greater than that of its analogues [15]. Stevens P et al. concluded in their review that somatostatin, octreotide and lanreotide shorten the time to fistula closure, but only somatostatin increases the rate of spontaneous closure, and none of them have been shown to significantly affect mortality rate [37]. In the meta-analysis of Rahbour et al. it was concluded that both somatostatin and its analogues (octreotide and lanreotide) increase the rate of fistula closure and decrease time to closure, but have no effect on mortality, and it is suggested that somatostatin could be better in achieving both objectives [32].

Clinical use of octreotide and somatostatin in children

Based on the functions of somatostatin and its analogues, and on the experience in adults, these drugs have been used in a wide range of medical and surgical diseases in children [2, 4, 5, 7, 8, 14, 17–19, 28, 29, 35, 36, 38, 40, 41] (Table 2).

Use of octreotide and somatostatin in enterocutaneous fistulas in children

The use of octreotide and somatostatin for this condition is related to its physiologic effects; they tend to decrease the volume and enzyme content of gastrointestinal, biliary and pancreatic secretions, and also prolong gastrointestinal transit

Table 2 Uses of somatostatin and its analogues in children

Uses in medical pathology [2, 13]		Uses in surgical pathology [4, 8, 38, 18, 17, 16, 28, 37, 5, 27, 35, 39, 34, 7]
Congenital hyperinsulinism		Postoperative chylothorax
Overgrowth syndromes		Postoperative chyloperitoneum
Congenital chylothorax		Enterocutaneous fistula
Intestinal lymphangiectasia		Intestinal fistula
Gastrointestinal bleeding		Pancreatic fistula
Portal hypertension		Pancreatic ascites
Pancreatitis		Pancreatic pseudocyst
Gastroesophageal reflux		Biliary fistula
Dumping syndrome		High stoma losses
Constipation/intestinal pseudo-obstruction		Diarrhoea secondary to short bowel syndrome
Idiopathic secretory diarrhoea		
Diarrhoea secondary to other disorders	Human immunodeficiency virus	
	Carcinoid syndrome	
	Microvillus inclusion disease	
	WDHA syndrome[a]	

[a] Watery diarrhoea, hypokalaemia, achlorhydria (WDHA) syndrome, associated with vasoactive intestinal peptide secreting tumours (ganglioneuromas or ganglioneuroblastomas most commonly in childhood)

time, increasing hydroelectrolytic absorption. All these mechanisms accelerate fistula closure [4, 21, 41].

After performing an extensive literature review of the PubMed and Cochrane Library databases we have only found eight patients with ECF treated with either octreotide or somatostatin (Table 1). The sex distribution was males ($n=5$), women ($n=2$) and unreported ($n=1$), and the age distribution was neonates ($n=4$), all premature babies born between 27 and 30 weeks gestational age, infants ($n=3$) of which two were previously preterm babies, and children ($n=1$). All patients developed ECF after abdominal surgery, mainly for NEC ($n=5$), among other causes such as duodenal perforation ($n=2$) and meconium peritonitis ($n=1$).

Conservative management with bowel rest ($n=8$), nasogastric decompression ($n=8$), parenteral nutrition ($n=6$) and antibiotics ($n=4$) was started. There are no data on parenteral nutrition and antibiotics in two and four patients, respectively. Treatment with octreotide ($n=7$) or somatostatin ($n=1$), was not begun on the day of diagnosis of ECF in any patient (median = day 4, range = 2–22) and this information is lacking in three patients. Somatostatin was administered intravenously as a continuous infusion ($n=1$). Octreotide was given by continuous intravenous infusion ($n=3$), or subcutaneously as two or three daily doses ($n=4$). The most common initial dose varied between 1–1.5 μg/kg/day (range 1–50 μg/kg/day) and was gradually increased to a maximum dose between 3 and 6 mg/kg/day (range 1–300 μg/kg/day). The drug was then discontinued ($n=6$) or tapered and then discontinued ($n=2$).

Oral feeding was resumed after closure of the ECF and cessation of the drug ($n=4$), after closure of the ECF but during treatment ($n=1$), or with the ECF still open, during treatment ($n=1$). These data are not available for two patients.

The fistula closed in seven of the eight patients treated with octreotide ($n=6$) or somatostatin ($n=1$), with time to closure ranging from three days to three weeks (median = 7 days); the total number of days treatment varied between 7 and 30 days (median = 10 days). In case 3, octreotide was given for 14 days and the fistula closed; octreotide was discontinued four days later, and the fistula reopened. After recommencing treatment with octreotide the patient developed pulmonary hypertension, and, therefore, it was suspended indefinitely.

Following the administration of octreotide, the only reported side effect was pulmonary hypertension (cases 3 and 7); this has not been previously reported in the literature, and only in case 3 did this lead to cessation of treatment [4]. Patient 3 was a 29-week-gestation male neonate who presented ECF when he was 24 days old, after surgery for NEC. He received continuous intravenous octreotide in a dose range of 36–72 μg/kg/day, which had to be discontinued because of the onset of moderate pulmonary hypertension. Patient 7 was a 24-week-gestation male newborn, who developed an ECF at age 6 months, during the postoperative period of intestinal continuity re-establishment after NEC. He was given subcutaneous octreotide in a dose range of 1.4–2 μg/kg/day, split into two daily doses and the fistula closed on day 8. The patient presented oxygen desaturation related to the administration of octreotide, and severe pulmonary hypertension was confirmed. Tolerance of octreotide or somatostatin was excellent in the other patients ($n=6$).

Side effects of octreotide and somatostatin in children

The most common side effects reported in children are transient gastrointestinal symptoms, mainly abdominal pain after commencing treatment [2, 4, 14, 20, 25, 31, 33, 34] (Table 3). From now on we will highlight those most important side effects.

Side effects reported in patients with enterocutaneous fistula

Pulmonary hypertension

Pulmonary hypertension has been reported in two premature babies with ECF who were receiving treatment with octreotide, subcutaneously twice daily (dose range, 1.4–2 μg/kg/day) and intravenously as a continuous infusion (range, 36–72 μg/kg/day), respectively [4]. Arevalo et al. suggest that preterm infants with bronchopulmonary dysplasia and high pulmonary vascular resistance are a risk group for pulmonary hypertension and, therefore, they propose monitoring the oxygen saturation of these patients with continuous pulse oximetry, and they also recommend performing an echocardiogram in order to enable an early diagnosis of this potential adverse event.

Side effects reported in patients with other diseases

Necrotizing enterocolitis

Eight cases of NEC have been communicated in patients treated with octreotide (subcutaneous in 6 patients, with a dose range of 15–27 μg/kg/day, intravenous in two cases, with a dose range of 96–192 μg/kg/day), six because of congenital hyperinsulinism, and the other two as a result of chylothorax [20, 25, 33]. Laje et al. proposed that the pathophysiological mechanism could be accounted for by the reduction in the celiac and mesenteric arteries flow caused by octreotide, and they advise keeping all neonates receiving treatment with octreotide closely monitored [20].

Table 3 Side effects of somatostatin and its analogues in children [2, 4, 13, 19, 24, 30, 32, 33]

Gastrointestinal	Endocrinometabolic	Cardiovascular
Abdominal pain	Hyper/hypoglycaemia	Arrhythmias
Abdominal distension	GH deficiency[b]	Hypertension
Vomiting		
Diarrhoea, steatorrhoea		
Cholelithiasis		
Necrotizing enterocolitis		
Vitamin B12 deficiency[a]		
Helicobacter pylori gastritis[a]		

[a] Vitamin B12 deficiency and *Helicobacter pylori*-associated gastritis have been reported in acromegalic patients with long-term octreotide treatments, although this association has not been clearly demonstrated [25]

[b] Long-term use of octreotide does not appear to slow down growth, despite inhibiting the release of GH; both normal growth during treatment with octreotide, and growth recovery after discontinuing treatment have been reported. This is probably because of the fact that, at usual doses, the nocturnal growth hormone peak, necessary for normal growth, is not suppressed [13, 37]

Cholelithiasis

This side effect has been disclosed primarily in patients with long-term octreotide treatment, over a month [14, 22, 31, 34, 38]. Biliary stasis because of slow gallbladder emptying and sphincter of Oddi dysfunction, together with the decrease in hepatic bile secretion and the modification in its composition constitute the pathophysiological mechanism postulated [25, 26]. Performing ultrasound before commencing treatment and every six months in those patients requiring prolonged treatment with octreotide is therefore recommended.

Other

Other relevant side effects are cardiovascular, although only two cases have been reported in the literature. Al-Hussaini et al. [2] published a case of ventricular fibrillation and another case of arterial hypertension in two patients treated with octreotide for gastrointestinal bleeding (octreotide in perfusion at 96 μg/kg/day) and dumping syndrome (subcutaneous octreotide at 2 μg/kg/day bid) respectively, underlining the need to undertake an electrocardiogram before commencing therapy with octreotide and to monitor blood pressure during treatment. In those patients who present either arrhythmias or long QT syndrome, octreotide treatment should be contraindicated.

Given the reported side effects, it is advisable to clinically and biochemically monitor in an intensive care unit those patients suffering from ECF during treatment with octreotide or somatostatin. Surveillance should be maximal in neonates and patients receiving high doses and/or long-term treatments.

Discussion

ECF is still a very serious complication which remains associated with high morbimortality. For this reason, for our patient we considered using early octreotide, to maximise conservative treatment, given that this treatment appears to speed up closure of the ECF and it is possible for the closure rate to increase [15, 32, 37]. The aim of this treatment regimen was to avoid new surgery, with the morbimortality this would entail in our patient, with the history of a diffuse peritonitis

secondary to intestinal perforation (Fig. 3b, c), and with the reduced intestinal length in regard to the apple-peel atresia (Fig. 2c).

During the course of our literature search we did not find any other review article on the use of octreotide or somatostatin in paediatric patients with ECF. Our patient represents the ninth case in over a 25-year period (1989–2014) and fistula closure was attained in eight of the nine patients (Table 1). Octreotide has been used more than somatostatin, in eight cases since it is easier to administer. This drug could be given subcutaneously intermittently because of its longer half-life, although four out of eight patients were administered intravenous continuous infusion. In those cases we reviewed in addition to the case we report, we have been able to observe a temporal correlation between the onset of treatment with either octreotide or somatostatin and the decrease in ECF debit, up until closure, even though patients are not comparable and treatment patterns are different in all of them (Table 3). The treatment was started early in our case and in case 5, the fistula closed on the seventh and third day of treatment, respectively, suggesting that perhaps commencing treatment early could contribute to earlier closure of the fistula. In our patient, we used intermediate doses (starting dose 12 μg/kg/day, maximum dose 72 μg/kg/day) in regard to the previously reported doses (1–50 μg/kg/day as starting dose and 1-300 μg/kg/day as maximum dose), and the fistula healed on the seventh day of treatment. In the review performed, for those patients treated with intermediate to high doses (6 to 300 μg/kg/day), regardless of administration route, fistula closure also occurred in a shorter time, ranging from 3 to 5 days (cases 4, 5 and 8). Treatment was gradually discontinued in our case and only in two of the eight cases revised (cases 5 and 7), without fistula relapse, while in case 3, in which the treatment was stopped without prior tapering dose, the fistula recurred. Therefore, a gradual decline in octreotide or somatostatin dose might be appropriate to avoid the rebound effect withdrawal of these drugs can produce, as this could lead to reopening of the fistula.

Finally, we believe it is useful to add somatostatin or octreotide to conservative treatment of the ECF because it appears to speed up closure of the fistula and it is possible for its closure rate to increase [15, 32, 37]. Furthermore, somatostatin and its analogues reduce the fistula debit, controlling hydroelectrolytic losses and improving local control of the wound, thereby finally enabling earlier removal of parenteral nutrition and venous access; the morbidity associated with these is thus minimised.

Given our patient's results and the results of all the cases reviewed, we believe that the treatment regimen most consistent physiologically among the multiple regimens published would include the following points: early onset to try and speed up closure of the fistula. The use of intermediate to high doses (6–300 μg/kg/day) compared to those published, given that it is with these doses that an earlier closure is reported and because there is no clear correlation between the doses used and the reported complications. Continuous intravenous administration and recommendation for gradual withdrawal, to avoid or minimise the rebound effect reported with intermittent regimens and treatment discontinuation.

In light of the variability in the reported dose of octreotide or somatostatin, it is necessary to establish the minimum effective dose, the maximum tolerated dose, and the optimal administration route for somatostatin and its analogues in children, and standardise the treatment regimens, to make the outcomes comparable. We should note that the effect of octreotide is likely to be dose-dependent; low doses may be insufficient while excessive doses may decrease splanchnic flow too much, leading to an overall worsening of the situation [20]. This may be of greater importance in preterm infants, in which the dose should perhaps be lower [4].

Conclusions

From our experience and from the literature review we conclude that the initial management of ECF should be conservative, and octreotide and somatostatin should be part of such treatment. These two drugs have shown the capacity to shorten the time to fistula closure, allowing earlier withdrawal of parenteral nutrition. This effect can be crucial in neonates and even those patients who will ultimately require surgery, facilitating treatment prior to surgery and optimising the patient's condition.

Owing to the low incidence of enterocutaneous fistula and its high morbimortality, it could be necessary to perform a multicentre, double-blind, randomised, placebo-controlled trial to determine the efficacy of octreotide and somatostatin and the most suitable treatment regimen to optimise conservative management of this complex condition.

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Authors' contribution Noela Carrera Guermeur: Dr. Carrera designed the study, drafted the initial manuscript, and approved the final manuscript as submitted.

Rosa M. Martín-Crespo Izquierdo, Hilda J. Ramírez Velandia, Ángel Pantoja Bajo: Dr. Martín-Crespo, Dr. Ramírez, and Dr. Pantoja treated the patient reported and provided the images presented, performed the extensive literature search in adult and child literature both from the medical and surgical points of view, reviewed and accepted the text we are submitting.

Rafael Luque-Mialdea: Dr. Luque-Mialdea coordinated and reviewed the entire process from design of the work to submission to the journal.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent The patient's parents gave their informed consent prior to his inclusion in the study.

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