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Case and Review

Subcutaneous Magnesium Sulfate to Correct High-Output Ileostomy-Induced Hypomagnesemia

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Keywords
Magnesium • Subcutaneous infusions · Hypodermoclysis · Radiation enteritis · Ileostomy

Abstract
Fluid and magnesium abnormalities are common in patients with high-output stomas. Subcutaneous magnesium administration may be more feasible for long-term management in ambulatory patients, but magnesium sulfate is approved only for intravenous or intramuscular injection. We describe the management of chronic hypomagnesemia and dehydration secondary to a high-output ileostomy following radiation and chemotherapy for anal squamous cell carcinoma with intermittent home-based subcutaneous magnesium infusions in a 61-year-old female with a history of Crohn's disease and multiple bowel resections. Despite aggressive management with intravenous magnesium sulfate and oral magnesium glucoheptonate over 8 months, 49% of her magnesium concentrations were <0.60 mmol/L (mean 0.61 ± 0.09) necessitating 4 emergency, 1 hospital, and 4 infusion clinic visits. After initiation of subcutaneous magnesium sulfate, all magnesium concentrations were >0.60 mmol/L (mean 0.79 ± 0.08 mmol/L over 9 months). The patient tolerated the infusions well, only developing one minor

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episode of infusion-related cellulitis. A systematic review of the literature identified 14 reports where subcutaneous magnesium sulfate was effective and treatment for adults or children with hypomagnesemia was safe. Home-based intermittent administration of subcutaneous magnesium may be a helpful and safe intervention to temporarily prevent and treat select patients with recurrent symptomatic hypomagnesemia.

Introduction

Patients with intestinal failure secondary to a short bowel commonly experience hypomagnesemia, salt and water depletion, undernutrition, and vitamin/mineral deficiencies [1]. Sodium and water depletion may be severe in patients with high-output stomas and may necessitate restriction of hypotonic fluids, drinking an oral glucose-saline solution, antimotility drugs, and proton pump inhibitors or octreotide [2]. Hypomagnesemia secondary to high ostomy output may be treated by correcting water and sodium depletion, oral or intravenous doses of magnesium, or occasionally oral 1-alpha hydroxycholecalciferol [1, 3]. While intravenous and oral magnesium supplements are recommended in patients with high-output stomas [2], replacement with oral magnesium supplements is difficult as most magnesium salts are poorly absorbed, and they may cause diarrhea [4, 5].

In some patients with high-output stomas, intravenous or subcutaneous saline may be needed to maintain fluid and sodium balance [1]. Clinical practice guidelines have suggested that 4 mmol magnesium sulfate may be added to 500–1,000 mL of saline and be given subcutaneously 1–3 times a week if needed [1, 6]. While other narrative reviews also support this practice if the oral, intravenous, or intramuscular routes are not available [7, 8], in Canada and other jurisdictions, magnesium sulfate is approved for intravenous or intramuscular administration only [9].

We report a case of successful correction and maintenance of normal magnesium concentrations with home-based intermittent subcutaneous magnesium infusions in a 61-year-old female with severe symptomatic hypomagnesemia secondary to a high-output ileostomy for Crohn's disease exacerbated by chemoradiation therapy for anal squamous cell cancer. Additionally, we systematically review the literature describing the use of subcutaneous magnesium supplementation to correct hypomagnesemia in patients with short bowel syndrome or other gastrointestinal conditions as well as hypomagnesemia of other causes.

Case Report

A 61-year-old female with colonic and perianal Crohn's disease, a chronic nonhealing wound in the perineum, a 4-month history of anal squamous cell carcinoma treated with combination chemoradiation presented to her family physician with a 10-day history of diffuse paresthesia and numbness on October 6, 2016, approximately 5 weeks following discharge from the local cancer center.

Originally diagnosed with Crohn's disease at 19 years of age, she had undergone 4 previous bowel resections with the last one at the age of 49. She presented with a perineal mass on

May 6, 2016 and began outpatient mitomycin C and 5-fluorouracil with daily radiation treatments directed to the pelvis and anal canal on June 27. She completed 18 of 30 radiotherapy fractions as an outpatient but was admitted to the local cancer center on July 23 for management of pain associated with radiation desquamation and significant metabolic abnormalities including dehydration, hypotension, and hypomagnesemia related to a high-output ileostomy. Her radiotherapy was completed on August 10 and at discharge on August 30, she was using loperamide 2–4 mg orally b.i.d. and psyllium b.i.d. p.r.n. to regulate her ostomy output, was on morphine 15 mg orally every 4 h and 10 mg orally every 1 h p.r.n. for pain control and a variety of oral supplements (vitamin D 2,000 IU daily, zinc 50 mg daily, selenium 50 mg daily, calcium 1,000 mg daily, centrum multivitamin b.i.d.).

After presenting on October 6, she was found to have several electrolyte and fluid imbalances including hypomagnesemia (0.41 mmol/L), hypokalemia (3.1 mmol/L), elevated serum creatinine (123 mmol/L; estimated glomerular filtration rate [eGFR] 41 mL/min/1.73m^2), total calcium 1.82 mmol/L (albumin 37 g/L), and her symptoms were successfully managed in the emergency department with a 2-g intravenous bolus dose of magnesium sulfate (Fig. 1). There she was prescribed 75 mg (3 mmol) of elemental magnesium orally twice daily as magnesium glucoheptonate 1,500 mg/15 mL b.i.d. and calcium carbonate 500 mg b.i.d. Subsequent monitoring indicated an increase in her magnesium concentrations over the course of the next month, but she continued to empty her ostomy approximately 12 times per day and her serum creatinine (151 mmol/L; eGFR: 32 mL/min/1.73m^2) indicated prerenal renal insufficiency.

On November 8, home subcutaneous normal saline infusions (1 L over 8–12 h overnight) were started and her psyllium and loperamide therapy were increased to 4 mg q.i.d, while she continued magnesium glucoheptonate 1,500 mg magnesium orally b.i.d. Over the next 10 weeks, her eGFR improved, stabilizing in the 40–50 mL/min/1.73m^2 range, her magnesium glucoheptonate was titrated up to 3,000 mg (150 mg [6 mmol] orally t.i.d. in response to dropping magnesium concentrations [0.49 mmol/L on November 22]), and Codeine Contin was added and titrated up to 100 mg b.i.d. Despite this, over the next month, her magnesium concentrations showed a downward trend and on January 23, 2017, her magnesium was 0.46 mmol/L and she received a 2-g intravenous bolus dose of magnesium sulfate in the emergency department on January 25. She continued to have high ostomy output (i.e., 300–400 mL every 2–3 h) and on February 1, pantoprazole 40 mg daily was added, cholestyramine was prescribed in place of psyllium, stool cultures were collected (subsequently *Clostridium difficile* negative), and she was booked for upper endoscopy/ileoscopy to evaluate for recurrence of Crohn's disease.

While her family physician was arranging intermittent intravenous magnesium sulfate boluses at the hospital-based infusion clinic, her magnesium level continued downward to 0.43 mmol/L and she received 2 g of magnesium sulfate intravenously in the emergency department on February 24 and 26. After receiving a third dose of 2 g magnesium sulfate intravenously at the infusion clinic on March 2, she was electively admitted to the Inpatient Gastroenterology Service to expedite the investigation of her high-output ileostomy/hypomagnesemia and there received another dose of intravenous magnesium sulfate. Endoscopy showed mild gastritis, ileostomy and computed tomography enterography ruled out recurrent Crohn's disease, and her urine magnesium level was <0.40 mmol/L ruling out renal losses. Radiation enteritis was the presumed diagnosis on discharge (March 6) and no changes

were made to her medications except pantoprazole was discontinued. Three weeks later (March 27), her magnesium was 0.55 mmol/L and another dose of magnesium sulfate 2 g was administered at the infusion clinic. On April 21, a consultant nephrologist suggested adding magnesium sulfate to her home subcutaneous fluid. While the feasibility of this recommendation was being explored, the patient had an emergency department visit on June 2 for general weakness and required two further 2-g bolus doses of magnesium sulfate at the infusion clinic on May 24 and July 5.

On July 19, 2017, the patient returned to the family medicine clinic to discuss initiating home subcutaneous magnesium sulfate supplementation. The patient agreed and was instructed to add magnesium sulfate 1 g (i.e., 4 mmol elemental Mg^{2+}; 5 mL 200 mg/L magnesium sulfate) to her 500 mL normal saline infusion on 2 consecutive days, take 1 day off, then repeat the dose on the following 2 consecutive days. The clinic registered nurse instructed the patient on how to prepare and administer the infusion overnight. One week later, on July 25, her magnesium level was 0.88 mmol/L. She tolerated the infusions well with only a minor burning sensation and no significant side effects. After 2 more doses, her next magnesium level on July 31 was 0.87 mmol/L. During the following week, she took 2 serial doses followed by 3 days off and her next magnesium level on August 8 was maintained at 0.86 mmol/L. As shown in Figure 1, subsequent subcutaneous magnesium infusions on 2 days on a 3-days-off schedule were successful in maintaining magnesium concentrations >0.7 mmol/L for the next 6 weeks.

Due to a continued high output from her ileostomy (i.e., 300 mL, 12–15 times per day), the patient was assessed at the GI Malnutrition Clinic on September 22. Tethering of the bowel secondary to radiation, abnormal motility related to multiple previous surgeries, and bacterial overgrowth were suspected. She was started on a course of cyclical ciprofloxacin 500 mg b.i.d. and metronidazole 500 mg b.i.d., 2 weeks on and 1 week off, and restarted pantoprazole 40 mg twice daily. Her other therapies were unchanged.

The patient continued to tolerate the subcutaneous magnesium infusions well. However, on October 10, during a preoperative medical treatment for perineal wound closure, she complained of a 1-day history of pain and erythema on the left side of her abdomen where she last had her infusion, chills, and had a temperature of 38.0°C. She was treated for a presumed early cellulitis with a 7-day course of oral cephalexin.

In follow-up at the Malnutrition Clinic on November 3, the patient reported emptying her ileostomy less frequently and was advised to continue the cyclical antibiotics. As her magnesium was 0.67 mmol/L and renal function was stable (eGFR = 50 mL/min/1.73m^2), she continued subcutaneous magnesium infusions but switched to oral magnesium glycinate 2,000 mg (200 mg [8 mmol] elemental magnesium) 2 tablets three times daily from magnesium glucoheptonate. Between November 21 and December 7, the patient was admitted to hospital for elective closure of her perineal wound. At her third visit to the Malnutrition Clinic (January 12, 2018), her weekly magnesium concentrations were noted to be between 0.73 and 0.92 mmol/L and she was advised to reduce the frequency of magnesium infusions to 2 days on 4 days off and to start a trial of cutaneous magnesium lotion.

On follow-up, at the Malnutrition Clinic on May 18, her subcutaneous magnesium infusions were stopped as her ileostomy output was <2 L per day and her magnesium levels were consistently >0.7 mmol/L. For the next 4 months, she consistently maintained magnesium levels above 0.7 mmol/L with oral magnesium glycinate therapy. However, she still required

ongoing subcutaneous parenteral saline 500 mL daily to maintain fluid status. As of the time of writing in March 2019, her most recent magnesium was 0.77 mmol/L and she remains off subcutaneous magnesium supplementation.

Discussion

Our case report adds to the existing literature, which suggests that subcutaneous magnesium sulfate is safe and effective in normalizing serum magnesium levels and reversing symptomatic hypomagnesemia in patients with severe refractory hypomagnesemia secondary to gastrointestinal, congenital, or medication induced causes. A systematic literature search (online suppl. Appendix 1; for all online suppl. material, see www.karger.com/doi/10.1159/000501121) to identify original research describing subcutaneous administration of magnesium (sulfate) in adults or children yielded 14 publications meeting our inclusion criteria [10–23] (Fig. 2; Table 1, Table 2, Table 3, Table 4). A total of 5 case reports [10–13, 17] and 3 publications reporting 2 retrospective case series [14–16] described experiences of patients with gastrointestinal conditions using subcutaneous magnesium supplementation. Seven case reports were identified in nongastrointestinal conditions [18–24] but one was excluded as there was no English language abstract and the full text was only available in German [24]. We excluded reports describing the use of subcutaneous magnesium for other conditions including tetanus [25, 26], hydrofluoric acid burns [27, 28], and pain [29–32].

Reports in Patients with Gastrointestinal Conditions

The 7 available reports detailed in the tables (Table 1, Table 2, Table 3, Table 4) describe administration of subcutaneous magnesium to correct refractory hypomagnesemia to 63 adults with a variety of gastrointestinal conditions leading to gastrointestinal failure. They were published between 1991 and 2018 with the majority of reports from the UK (n = 4). In 5 of the 7 reports, subcutaneous magnesium was prepared in a bag of intravenous fluids and infused intermittently. For the intermittent subcutaneous infusions, the dose of magnesium ranged from 2 to 12 mmol of magnesium per bag but most commonly was in the 2 to 8 mmol/L range. The duration of the infusions was between 6 and 12 h and they were typically given overnight. The frequency of infusion ranged between 2 and 7 days per week. In the 2 publications that reported typical weekly doses, the ranges were 8–28 mmol magnesium sulfate/week [11] and a mean of 21 ± 9.8 (range 8–40) mmol per week [14]. Two reports addressed duration of therapy. McDermott et al. [10] reported a total of 24 months of therapy, while Small et al. [14] noted average treatment durations of 17.4 ± 34 and 10 ± 8.5 months for those receiving 4 and 8 mmol of magnesium per infusion, respectively.

In two cases, subcutaneous magnesium was administered via a syringe pump [10, 17]. In one, a microinfusion pump was used and 14 mmol (8 mL) of magnesium sulfate was added to 7 mL of sterile water and infused over 10 h overnight [10]. In the second, a CME T34 (McKinley syringe pump) with one 50-mL syringe daily was used to deliver 8 mmol magnesium sulfate (i.e., 4 mL of magnesium sulfate 50% injection) made up to 32 mL with water for injection to provide an isotonic solution. The success of treatment in normalizing serum magnesium concentrations was reported in all 7 publications and only 2 individual cases of unsuccessful

response to subcutaneous magnesium supplementation were reported. Symptomatic improvement was reported in 3 out of the 7 papers [10, 11], while the remaining 5 did not report this outcome. Local or systemic adverse effects were discussed in 5 out of the 7 reports, with superficial skin abscesses, transient local edema that resolved with reducing the rate of infusion, and cellulitis at the needle insertion site noted.

Reports in Other Conditions

The 6 included case reports describe administration of subcutaneous magnesium to 5 adults and 1 child with a variety of medical conditions necessitating magnesium supplementation including congenital causes of hypomagnesemia [18, 19, 21, 22], in the hospice/palliative care context [20], and in cisplatin-induced hypomagnesemia [23] (Table 1, Table 2, Table 3, Table 4). These were published between 2000 and 2017, with 2 reports from Germany [18, 19], 2 from the United States [20, 21], and 1 each from Switzerland [22] and the Netherlands [23]. Continuous infusions via an infusion pump were used in 5 of the 6 reports [18, 20–23], and in the remaining report it was unclear how magnesium was delivered [19]. Dosing information for the continuous infusions were only reported in 3 of the 5 cases and are detailed in the tables (Table 1, Table 2, Table 3, Table 4). The duration of therapy was reported in 3 cases as 2 days [20], at least 6 months [22] and 2 years [23]. The effect on serum magnesium concentrations was reported in 4 of 7 cases and success in normalizing levels was reported in all 4 cases [18, 21, 22]. Impact on symptoms was reported in 4 cases and in all cases most symptoms were deemed to be improved or resolved [18, 19, 22, 23]. In 1 case, no skin irritation was reported [20], while in 2 reports, subcutaneous infections [22] or mild skin lesions and nonpainful indurated areas [23] were noted at the insertion site.

While we were unable to definitively establish that subcutaneous magnesium therapy corrected our patient's hypomagnesemia, 20 out of 41 (49%) of her routine magnesium levels were <0.6 mmol/L (mean ± SD = 0.61 ± 0.09 mmol/L), and she had 4 emergency visits, 1 hospital admission, and 4 infusion clinic visits related to hypomagnesemia during treatment with oral and intravenous bolus magnesium. In contrast, she had no concentrations <0.6 mmol/L (mean 0.79 ± 0.08 mmol/L) and 1 minor episode of infusion-related cellulitis during 10 months of home-based subcutaneous therapy, while her eGFR was similar in both periods (50.4 vs. 49.1 mL/min/1.73 m^2). However, improved magnesium levels could be explained by better management of her ostomy output with cyclic antibiotic therapy and dietary counselling, which led to the eventual ability to stop parenteral magnesium therapy altogether. The use of oral magnesium glycinate rather than oral magnesium glucoheptonate in addition to optimization of her antimotility therapy, codeine, and proton pump inhibitor may also have contributed.

Notably, our use of a home compounded magnesium solution is not consistent with new USP 797 standards for pharmaceutical compounding and we would recommend preparation by a compounding pharmacy using an ISO 5 environment. In this context, 500 mL normal saline bags may be stored refrigerated for 9–14 days after the magnesium is added [33, 34].

In conclusion, the intermittent administration of subcutaneous magnesium sulfate in conjunction with hydration fluid administered at home may be a helpful and safe but underrecognized intervention to maintain serum magnesium levels in patients with high-output ostomies and recurrent hypomagnesemia in clinical practice. In appropriate patients, this strategy

may help to avoid repeated emergency department visits, hospital admissions, and infusion clinic visits for intravenous magnesium supplementation.

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Statement of Ethics

The patient has provided written informed consent to publish this case.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Contributing to the conception and design: M.J. Makowsky, P. Bell. Analysis and interpretation of data: M.J. Makowsky, L. Gramlich. Drafting of initial manuscript: M.J. Makowsky. Critical revision of manuscript for intellectual content: M.J. Makowsky, P. Bell, L. Gramlich. Approval of the final manuscript: M.J. Makowsky, P. Bell, L. Gramlich.

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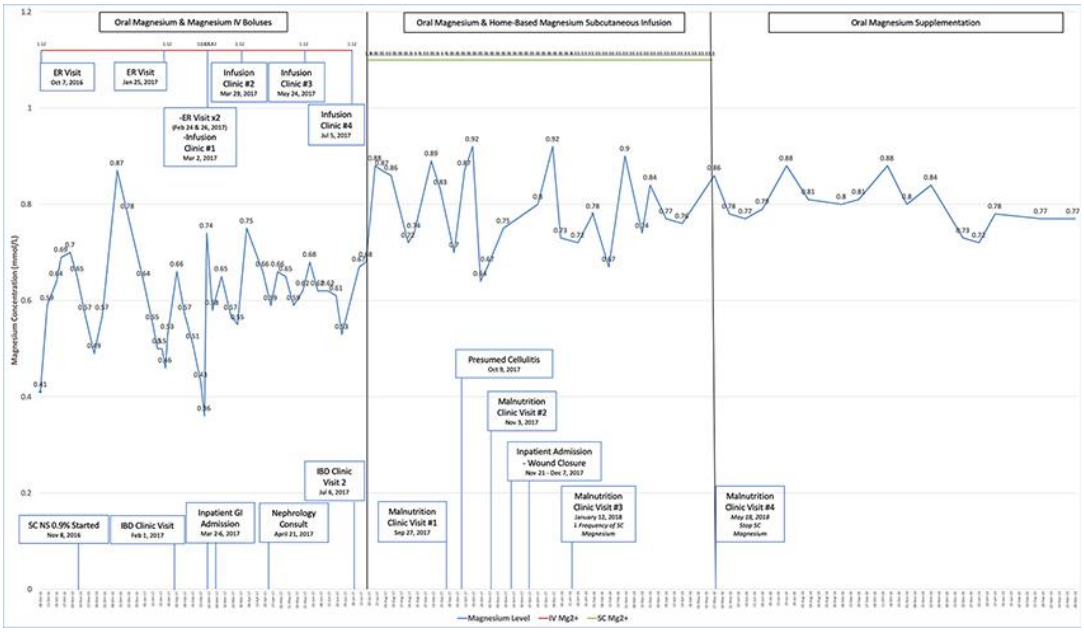

Fig. 1. Magnesium concentrations over time. Analysis of the mean difference in magnesium concentrations between the period on intravenous magnesium boluses (mean ± SD pre: 0.61 ± 0.09 mmol/L) versus on subcutaneous home-based magnesium infusions (mean ± SD post: 0.79 ± 0.08 mmol/L) using a bayesian single subject autoregressive approach (i.e., JZS + AR model) indicated that there was a true difference as a result of the intervention (bar = 8.903 e−05) [35]. ER, emergency room; IV, intravenous; SC, subcutaneous; NS, normal saline; IBD, inflammatory bowel disease; GI, gastrointestinal.

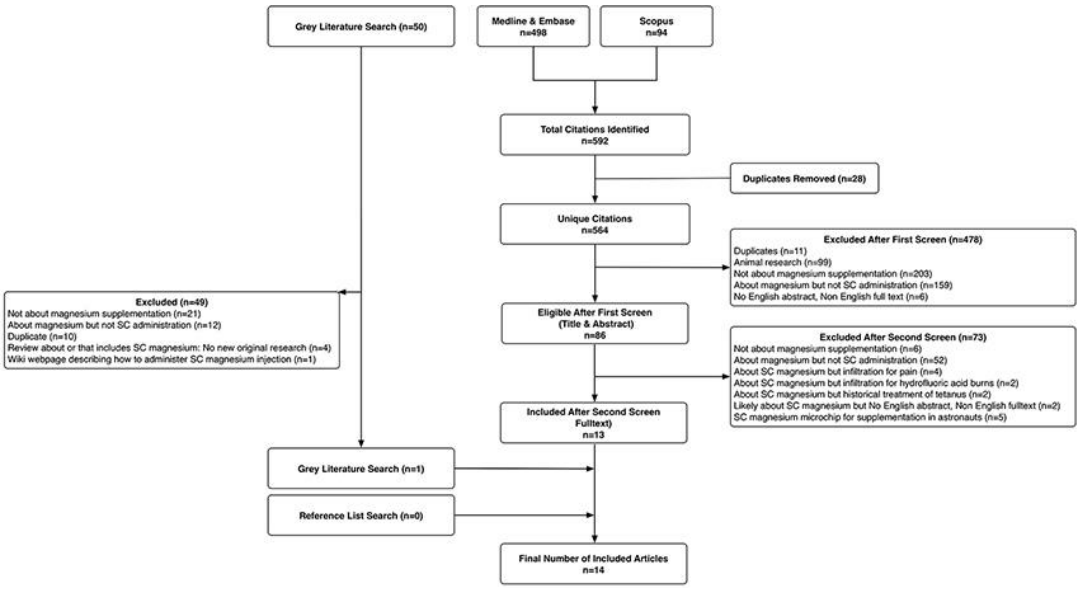

Fig. 2. Flow diagram. SC, subcutaneous.

Table 1. Summary of included reports describing subcutaneous magnesium administration

Search	Author, year of publication	Design	Patients	Magnesium dose	Influence on Mg^{2+} and symptoms	Adverse effects	Country
Gastrointestinal conditions							
M/E	McDermott et al. [10], 1991	Case report	*n* = 1; 63 yrs old Total regional pancreatectomy	The final dose was magnesium sulfate 14 mmol (8 mL) and 7 mL of sterile water administered subcutaneously via microinfusion pump (Walkmed pump (Medfusion, Duluth, GA, USA); 10 h overnight Duration: 24 months	*Mg^{2+}*: serum magnesium levels kept within a low normal range *Symptoms:* improved	On one occasion two 1-cm dark colored superficial skin abscesses were reported	United States
M/E	Martínez-Riquelme et al. [11], 2005	Case series	*n* = 10 (mean age: 65.3 ± 13.5 yrs) with GI failure and adequate micronutrient status who could not maintain a positive salt, water and magnesium balance; *n* = 8 received magnesium sulfate supplementation	500–1,000 mL of NS or D5W with between 2 and 4 mmol of magnesium sulfate subcutaneously by gravity drip over 6–12 h (overnight) 3–7 days per week (total dose 8–28 mmol magnesium sulfate/week	*Mg^{2+}*: normal serum Mg concentrations were achieved within 2 weeks *Symptoms:* mild paresthesia's resolved in 2 patients and several reported improved vigor and strength	Three patients developed transient local edema that resolved with reducing the rate of infusion No patient suffered local infection or other complications	United Kingdom
M/E	Tsao et al. [12], 2005	Case report	*n* = 1 56-year-old female with Crohn's disease and multiple bowel resections; hypomagnesemia despite 24 mmol/day oral magnesium oxide	Magnesium 4 mmol per 1 L normal saline, twice weekly	*Mg^{2+}*: she maintained her hydration and serum Mg^{2+} levels on this regimen *Symptoms:* not reported	Not reported	United Kingdom
M/E	Alfaro Martínez et al. [13], 2009	Case report	*n* = 1 71-year-old male; rectal carcinoma, with recurrent severe hypocalcemia secondary to hypomagnesemia and prerenal renal failure after colectomy and terminal ileostomy; previous oral and IV magnesium	*In hospital treatment:* initial IV magnesium infusion; on the second day he was transferred to subcutaneous administration of saline solution with magnesium sulfate (12 mmol of magnesium sulfate in 1,000 mL of saline solution during 12 h) via a butterfly needle *Outpatient treatment:* Self-administered subcutaneous infusion of 500 mL of saline solution with 6 mEq of magnesium sulfate during 6 h per day; co-treatment with oral calcium gluconate, calcitriol, and codeine He was advised to increase saline administration to 1,000 mL per day if diuresis diminished or ileostomy losses increased	*Mg^{2+}*: levels of serum calcium, magnesium and PTH normalized *Symptoms:* patient whose daily activities were very limited, has resumed a normal life	Not reported	Spain

Mg^{2+}, magnesium; M/E, Medline/Embase; S, Scopus; G, Google; yrs, years; PTH, parathyroid hormone.

Table 2. Summary of included reports describing subcutaneous magnesium administration (continued)

Search	Author, year of publication	Design	Patients	Magnesium dose	Influence on Mg^{2+} and symptoms	Adverse effects	Country
M/E	Small et al. [14], 2015 Small et al. [15], 2015 (update)	Retrospective review 10 years Intestinal failure database at St. Mark's Hospital, Harrow, United Kingdom	*n* = 26 (19 female; 7 male) patients from an intestinal failure database using home subcutaneous fluid *n* = 21 had magnesium in their infusions Initial inpatient assessment; patients taught to self-administer fluids via gravity subcutaneously into the upper leg or abdomen *n* = 32 (22 female; 10 male) *n* = 24 had magnesium in their infusions	Mean of 21 ± 9.8 (range 8–40) mmol per week Sixteen had 4 mmol magnesium per infusion (Treatment duration: 17.4 ± 34 (3–139) months Five had 8 mmol magnesium added/ infusion. (treatment duration: 10 ± 8.5 (2–24) months	*Mg^{2+}*: in 2 patients the treatment did not correct magnesium levels *Symptoms:* not reported *Mg^{2+}:* in 3 patients the treatment did not correct magnesium levels	Most patients (*n* = 20; 77%) had no complications Problems were leaking at the infusion site and the infusion taking too long (>14 h)	United Kingdom
G	Adgey et al. [16], 2016	Retrospective chart review Intestinal failure unit of the Belfast Trust (9 years)	*n* = 35 patients who used home subcutaneous fluids over a 9-year period *n* = 30 (median age: 56.5 yrs; 53% female) had magnesium replacement in their fluids 87% of patients had Crohn's disease, ischemia and post-operative complications	Magnesium 4 mmol per bag (with the volume of the bag varying per patient)	*Mg^{2+}*: median magnesium concentrations increased pre to 1-month post: pre: 0.57 mmol/L (IQR: 0.52–0.62) Post: 0.78 mmol/L (0.73–0.86) ($p < 0.001$) *Symptoms:* not reported	Two patients experienced cellulitis at the needle site 4 other patients required admission for dehydration 1 required home parenteral nutrition	Northern Ireland
M/E	Fenning et al. [17], 2017	Case report	*n* = 1 66-year-old female Recurrent symptomatic hypomagnesemia, on the background of advanced ovarian cancer and high-output ileostomy	Inpatient initial treatment with 20 mmol magnesium sulfate IV; the next day she started daily continuous subcutaneous magnesium (8 mmol magnesium sulfate [4 mL of magnesium sulfate 50% injection] made up to 32 mL with water for injection to provide an isotonic solution; delivered in a 50 mL syringe via a CME T34 (McKinley syringe pump) Outpatient therapy: continued continuous subcutaneous magnesium infusion; blood levels checked weekly then less frequently *Duration:* patient died 2 months after discharge	*Mg^{2+}*: magnesium remained stable throughout her inpatient stay (0.83 mmol/L on discharge, 6 days after admission) *Symptoms:* not reported	There were no acute complications with delivering magnesium via syringe pump	United Kingdom

Mg^{2+}, magnesium; M/E, Medline/Embase; S, Scopus; G, Google; yrs, years; PTH, parathyroid hormone.

Table 3. Summary of included reports describing subcutaneous magnesium administration (continued)

Search	Author, year of publication	Design	Patients	Magnesium dose	Influence on Mg^{2+} and symptoms	Adverse effects	Country
Other medical conditions							
S	Aries et al. [18], 2000	Case report	28-year-old male with abnormal intestinal magnesium absorption; presenting with recurrent cerebral seizures. Hypomagnesemia (0.48 mmol/L) despite daily IV magnesium infusion Treated with continuous magnesium infusion via indwelling subcutaneous *infusion pump*	Not specified *Duration:* not reported	*Mg^{2+}*: "normal serum magnesium concentrations were attained" *Symptoms:* "all symptoms disappeared"	Not reported	Germany English abstract full text in German
S	Weinbrenner and Besser [19], 2006	Case report	27-year-old female with generalized tonic clonic seizures and hypomagnesemia with secondary hypocalcemia (HSH syndrome) on oral magnesium supplementation	Treated with "parenteral application of magnesium 82.5 mmol/d)" Unclear if dose provided is IV or SC *Duration:* not reported	*Mg^{2+}*: not reported *Symptoms:* magnesium stopped her seizure and normalized her cerebellar signs except for slight dysarthria, and that subcutaneous magnesium supplementation kept her durable free of her neurologic symptoms	Not reported	Germany English abstract, full text in German
M/E	Pirrello et al. [20], 2007	Retrospective case series	*n* = 32 hospice patients treated with hyaluronidase for facilitation of hypodermoclysis and medication infusion *n* = 1 patient received subcutaneous potassium and magnesium supplementation added to their hydration fluid for 2 days	Potassium 20 mEq/L and magnesium 1 g/L *Duration:* 2 days	*Mg^{2+}*: not reported *Symptoms:* not reported	No skin irritation noted	United States
S	Sanda et al. [21], 2008	Case report	*n* = 1 2-year-and-8-month-old female child with severe hypocalcemia and hypomagnesemia secondary to activating calcium sensor receptor mutation Treatment with teriparatide and continuous subcutaneous magnesium sulfate via *infusion pump*	Not specified *Duration:* not reported	*Mg^{2+}*: she responded well to adjunctive therapy with continuous subcutaneous magnesium *Symptoms:* not reported	Not reported	United States

Mg^{2+}, magnesium; M/E, Medline/Embase; S, Scopus; G, Google; yrs, years; PTH, parathyroid hormone.

Table 4. Summary of included reports describing subcutaneous magnesium administration (continued)

Search	Author, year of publication	Design	Patients	Magnesium dose	Influence on Mg^{2+} and symptoms	Adverse effects	Country
M/E	Bock and Roth [22], 2013	Case report	27-year-old with severe refractory hypomagnesemia to oral and IV magnesium Required almost weekly IV magnesium infusions to keep her plasma magnesium levels ≥0.3 mmol/L below which she developed paresthesia and cramps Continuous infusion of subcutaneous magnesium via portable *insulin pump*	Insulin pump; 3 mL pump reservoir filled with undiluted 50% magnesium sulfate solution; infusion rate 0.1 mL/h to deliver 4.8 mmol magnesium per day Catheter replaced q2-3 days *Duration:* at least 6 months	*Mg^{2+}*: serum magnesium increased and remained at mean 0.52 mmol/L over 6 months (±0.06 SD) *Symptoms:* paresthesia, cramps and diarrhea secondary to oral magnesium supplements subsided	2 episodes of subcutaneous infection	Switzerland conference abstract
S	Vermeulen et al. [23], 2017	Case report	*n* = 1 39-year-old female Severe uncontrolled and irreversible hypomagnesemia secondary to cisplatin treatment in childhood; unresponsive to oral therapy, IV and IM therapy also trialed Also had trials of low-salt diet, acetazolamide, amiloride, hydrochlorothiazide) The cause was identified to be irreversible damage to the distal tubules as the site of magnesium loss Continuous subcutaneous magnesium via *insulin pump*	Inpatient therapy: magnesium sulfate 50% was combined with lidocaine 2% (2:1 ratio) resulting in 5 g Mg sulfate/24 h Outpatient therapy: 10 mL magnesium sulfate 50% with 3 mL lidocaine 2% running at 0.6 mL/h Lidocaine was used to prevent pain at the insertion site, and the subcutaneous needle insertion site was switched regularly *Duration:* >2 years of follow-up	*Mg^{2+}*: magnesium values normalized *Symptoms:* most but not all symptoms were reported to have responded well to therapy Level of energy, muscle cramps, paresthesia, hyperventilation, agitation, painful bones and fainting improved remarkably Palpitations, light headedness, rigid muscles and insomnia did not show an apparent improvement	Inpatient therapy: well tolerated by the patient with acceptable local and no systemic side effects *Long-term outpatient therapy:* mild skin lesions at the insertion site and non-painful indurated areas	Netherlands

Mg^{2+}, magnesium; M/E, Medline/Embase; S, Scopus; G, Google; yrs, years; PTH, parathyroid hormone.