9. Barba JR. Plasmaféresis y recambio plasmático. Rev Latinoam Patol Clin Med Lab. 2014;61:163–74.
10. Restrepo C, Márquez E, Sanz- Manizales MF. Plasmaféresis terapéutica, tipos, técnica e indicaciones en medicina interna. Acta Med Colomb. 2009;34:23–32.
11. Simsir I, Ozdemir M, Duman S, Erdogan M, Donmez A, Ozgen A. Therapeutic plasmapheresis in thyrotoxic patients. Endocrine. 2018;62:144–8.

Belén García Izquierdo[a,*], Macarena Contreras Angulo[a], Laura Armengod Grao[a], Álvaro García García[b], Pedro Iglesias[a]

[a] *Servicio de Endocrinología y Nutrición, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain*

[b] *Servicio de Hematología y Hemoterapia, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain*

* Corresponding author.
*E-mail address:* belengarciaizquierdo@gmail.com (B. García Izquierdo).



## Refeeding syndrome: What to expect when you're not expecting

## Síndrome de realimentación: qué esperar cuando no estás esperando

A 54-year-old woman in a precarious socioeconomic situation, with a history of anorexia nervosa and chronic alcoholism, with multiple episodes of acute alcohol intoxication, as well as a history of Wernicke's encephalopathy two years before, was admitted with acute alcoholic hepatitis. On admission, a prognosis score showed no severity criteria (Glasgow score 7 points [poor prognosis if score $\geq$ 9 points], Maddrey 9 points [poor prognosis if score $\geq$ 32 points] and MELDNa + 13 points [90-day mortality < 2% if score < 17 points]) and the electrolyte values were normal. She was started on fluid therapy, oral thiamine supplementation (100 mg/day) and prophylaxis of withdrawal syndrome with oxazepam (15 mg every 8 h). A mini nutritional assessment score evidenced the presence of malnutrition (score of 10 points [malnutrition if < 17 points]), confirmed as severe malnutrition, according to GLIM criteria (body mass index [BMI] of 14.5 kg/m$^2$ [weight 39.4 kg; height 165 cm] and reduced food intake).[1] In this context, oral nutritional supplementation (520 kcal) was initiated on day 4 in the ward, in addition to the hospital culinary diet, adding up to a total daily intake of 2620 kcal (66 kcal/kg/day). The day after, the patient developed gait ataxia, dysarthria and nystagmus, suggestive of Wernicke's encephalopathy, cerebrovascular event excluded. Intravenous supplementation of thiamine was started (500 mg every 8 h), and the nutritional plan maintained. However, in the following hours, the patient developed shock and ventilatory failure, requiring aminergic support and invasive mechanical ventilation. The study highlighted severe hypophosphataemia (0.07 mmol/l [0.87–1.45]), hypomagnesaemia (0.53 mmol/l [0.60–1.10]) and hypokalaemia (2.6 mmol/l [3.5–5.0]), without worsening cytocholestasis or coagulopathy. Other causes of shock, such as infection, pulmonary thromboembolism or acute coronary event were excluded. A transthoracic echocardiogram showed signs of stress cardiomyopathy. This clinical presentation was assumed in the context of refeeding syndrome and Wernicke's encephalopathy, and electrolyte replacement and organ dysfunction support were started in an intensive care unit. The electrolytes normalised and feeding was restarted at a slower rate, starting at 600 kcal per day (15 kcal/kg/day). The patient gradually improved, allowing for the suspension of aminergic and ventilatory support, with progressive resolution of the remaining condition, so she was transferred to a general ward. A progressive improvement in functional status was observed after reinforcement of motor rehabilitation, allowing her to be discharged one month after admission, under oxazepam, thiamine, pyridoxine and folic acid supplementation. She was advised to maintain a culinary diet, without enteral supplementation and to maintain alcohol abstinence. At the time of discharge, she presented a BMI of 14.5 kg/m$^2$ (weight 39 kg), with no neurological symptoms or signs, electrolyte or liver profile disorders. Two months later she had completely recovered her functional status, presenting a BMI of 15 kg/m$^2$ (weight 41 kg) and a daily caloric intake of 1100 kcal (27 kcal/kg/day), with an alcohol consumption of 10 g per day, and she was motivated to maintain a progressive weight increase.

Malnutrition is directly associated with the ability to respond to disease, leading to potential medical and surgical complications, extended hospitalisation and higher healthcare costs.[2] Therefore, nutrition screening tools have been widely adopted in order to quickly identify and intervene in patients at higher nutritional risk.[2] However, vigorous oral, enteral or parenteral refeeding in malnourished patients can be fatal.[3–5] Refeeding syndrome is a rare and potentially fatal condition, caused by the shift in fluids and electrolytes that may occur after the reintroduction of feeding in malnourished patients.[3,4] Elderly people and alcoholic, oncologic and anorexic patients are the major risk groups in developed countries.[5] The underlying mechanism of this condition rests on the rise of insulin levels caused by refeeding, promoting cellular glucose and phosphorus uptake for the production of phosphorylated compounds.[6] This leads to a sharp decline in phosphorus levels, already depleted in malnourished patients, making hypophosphataemia the hallmark characteristic of this syndrome.[6] It may also feature hypokalaemia, hypomagnesaemia and thiamine deficiency, due to underlying malnutrition and consumption of

**Table 1** Criteria for identifying patients at high risk of refeeding problems.[11]

| |
|---|
| *One or more of the following:* |
| Body mass index < 16 kg/m$^2$ |
| Unintentional weight loss > 15% in the past three to six months |
| Little or no nutritional intake for >10 days |
| Low levels of potassium, phosphate or magnesium before feeding |
| *Two or more of the following:* |
| Body mass index < 18.5 kg/m$^2$ |
| Unintentional weight loss > 10% in the past three to six months |
| Little or no nutritional intake for > 5 days |
| History of alcohol abuse or drugs, including insulin, chemotherapy, antacids or diuretics |

reserves during the carbohydrate metabolism, that begins with refeeding.[6,7] This results in multiple system disorders, including cardiovascular (myocardial contractility impairment and arrhythmias), respiratory (diaphragm contractility impairment and ventilatory failure), gastrointestinal (liver cytolysis), muscular (muscle weakness and rhabdomyolysis) and neurological manifestations (tremors, delirium, seizures or Wernicke's encephalopathy due to thiamine deficit, even in the absence of alcoholism).[7,8] The absence of diagnostic criteria makes it difficult to get accurate data on incidence rates.[7,9] However, considering the high prevalence of hospital malnutrition (approximately 30%), it is essential to be aware of this condition, which is preventable and remains relatively unknown in the medical community.[4,10] The aggressive refeeding of this malnourished woman, highly stimulating anabolism, resulted in severe metabolic changes that led to multi-organ failure with cardiogenic shock, ventilatory failure and Wernicke's encephalopathy. This extreme disorder, although rare, reinforces the importance of identifying the patients at risk (Table 1).[11]

In cases like this, it is essential to verify hydroelectrolytic status before initiating refeeding, with electrolyte and vitamin replacement, if necessary, in order to avoid the development of this syndrome.[3] According to international guidelines, refeeding should only start after electrolyte replacement and at a slow rate, starting with a maximum caloric intake of 10 kcal/kg/day, which corresponds to 16% of the provided intake in this case.[9,11,12] Moreover, a caloric intake of only 5 kcal/kg/day should be considered in extreme cases (for example, BMI less than 14 kg/m$^2$ or negligible intake for more than 15 days).[11] Additional increments should be made gradually, over three to seven days, until the target rate is reached.[11,12] Volume replacement should also be cautious, since these patients frequently have impaired cardiac and renal reserve with decreased ability to excrete an excessive volume load.[11] In the first 10 days, patients should also receive oral thiamine 200–300 mg per day, vitamin B compound tablets three times a day and a trace element supplement once a day.[11,12] In terms of surveillance, daily monitoring of renal function, blood glucose and electrolytes, especially phosphorus and magnesium, is essential, the levels of which should be stabilised before the start of refeeding.[11,12] In conclusion, this case illustrates the vulnerability of malnourished patients to refeeding syndrome. Although it is necessary to recognise and treat malnutrition, the process of refeeding should be cautious. Measures should be taken to identify the risk of refeeding syndrome and prevent this potentially fatal condition.

## Conflict of interest

The authors do not declare any conflicts of interest in relation to the work described.

## References


1. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition – a consensus report from the global clinical nutrition community. Clin Nutr. 2019;38:1–9, http://dx.doi.org/10.1016/j.clnu.2018.08.002.
2. Reber E, Friedli N, Vasiloglou MF, Schuetz P, Stanga Z. Management of refeeding syndrome in medical inpatients. J Clin Med. 2019;8:2202, http://dx.doi.org/10.3390/jcm8122202.
3. Mehanna HM, Moledina J, Travis J. Refeeding syndrome: what it is, and how to prevent and treat it. BMJ. 2008;336:1495–8, http://dx.doi.org/10.1136/bmj.a301.
4. Gariballa S. Refeeding syndrome: a potentially fatal condition but remains underdiagnosed and undertreated. Nutrition. 2008;24:604–6, http://dx.doi.org/10.1016/j.nut.2008.01.053.
5. Crook MA, Hally V, Panteli JV. The importance of the refeeding syndrome. Nutrition. 2001;17:632–7, http://dx.doi.org/10.1016/s0899-9007(01)00542-1.
6. Kraft M, Btaiche I, Sacks G. Review of the refeeding syndrome. Nutr Clin Pract. 2005;20:625–33, http://dx.doi.org/10.1177/0115426505020006625.
7. Crook MA. The Refeeding Syndrome: problems with definition and management. Nutrition. 2014;30:1448–55, http://dx.doi.org/10.1016/j.nut.2014.03.026.
8. Mehler PS, Winkelman AB, Andersen DM, Gaudiani JL. Nutritional rehabilitation: practical guidelines for refeeding the anorectic patient. J Nutr Metab. 2010, http://dx.doi.org/10.1155/2010/625782.
9. Friedli N, Stanga Z, Sobotka L, Culkin A, Kondrup J, Laviano A, et al. Revisiting the refeeding syndrome: results of a systematic review. Nutrition. 2016;35:151–60, http://dx.doi.org/10.1016/j.nut.2016.05.016.
10. van Vliet IMY, Gomes-Neto AW, de Jong MFC, Jager-Wittenaar H, Navis GJ. High prevalence of malnutrition both on hospital admission and predischarge. Nutrition. 2020;77:110814, http://dx.doi.org/10.1016/j.nut.2020.110814.
11. National Collaborating Centre for Acute Care. Nutrition support in adults, Oral nutrition support, enteral tube feeding

and parenteral nutrition. London: National Institute for Clinical Excellence; 2006.
12. Silva A, Nightingale JMD. Refeeding Syndrome: physiological background and practical management. Frontline Gastroenterol. 2020;11:404–9, http://dx.doi.org/10.1136/flgastro-2018-101065.

Francisca Marques Puga[a,*], Patrícia Baptista[b], Ana Oliveira[b], Margarida França[b]

[a] *Department of Endocrinology, Centro Hospitalar Universitário do Porto, Porto, Portugal*

[b] *Department of Internal Medicine, Centro Hospitalar Universitário do Porto, Porto, Portugal*

* Corresponding author.
*E-mail address:* francisca_puga17@icloud.com (F.M. Puga).



## Strategy and results of the massive implementation of reimbursed continuous glucose monitoring in people with type 1 diabetes

## Implantación masiva de la monitorización continua de glucosa en personas con diabetes tipo 1 en una Unidad de Diabetes de referencia bajo financiación pública: estrategia y resultados

The use of continuous glucose monitoring (CGM) in type 1 diabetes (T1D) has been shown to reduce some acute complications, improve glycaemic control and improve patient satisfaction regarding its use.[1–3] Recently, those countries that have introduced widespread public funding for these devices, such as the UK,[4] Belgium,[5] Sweden[6] and France,[7] have published their results available to date, confirming positive real-life outcomes in terms of HbA1c reduction, hospital admissions for acute complications and improved patient satisfaction compared with standard capillary blood glucose testing.

In Spain, public funding for CGM has been approached differently from one autonomous region to the next. In Catalonia, this funding was established in different phases, the latest of which included general funding for all patients with T1D.[8] The large number of patients included in this last implementation phase led us to evaluate the feasibility and effectiveness of a decision algorithm (Fig. 1) aimed at the widespread implementation of CGM in people with T1D seen at our Diabetes Unit in the shortest possible time. In our case, the use of the FreeStyle Libre *flash* CGM device was prioritised.[9] An administrative professional, supported by healthcare personnel, contacted the candidates and included them in the programme according to their technological skills. New users received device information, a contact phone number and a link to a training webinar. Those less familiar with technology and with the least technological skills received face-to-face training in small groups.

Over a period of three and a half months, from 1 March to 15 June 2021, 1,519 candidates were contacted by telephone (52% female, mean age 43.82 ± 15.29 years, mean HbA1c 7.71% ± 1.19, 19% of whom were subcutaneous insulin pump users). A total of 1,045 patients (69%) started using the funded CGM, of whom 320 (21%) had previously self-financed the use of CGM; 331 people (22%) refused to use the device and 143 people (9%) could not be contacted. In webinars led by a diabetes nurse educator, 292 patients (29%) were included, while only 39 (3%) required face-to-face training. The majority of patients who refused to start CGM reported a lack of interest in using the device (45% of cases), while 17% preferred to make a decision after consulting their regular endocrinologist. No significant acute complications or relevant clinical issues were recorded. A modest increase in the number of device inquiries was observed (a total of 190 calls and 11 unscheduled face-to-face visits).

A Spanish study was recently published in this journal that showed that the incorporation of an educational programme in group and telematic format on the use of *flash* CGM devices, as part of the implementation strategies of these systems, is an effective option with associated benefits in terms of quality of life and fear of hypoglycaemia, which can be implemented in routine clinical practice in adult patients with T1D.[10] Our study adds new information in this regard and demonstrates that the widespread implementation of funded CGM in the population with T1D in a short period of time is feasible, safe and effective through the use of coordinated strategies between healthcare and non-healthcare professionals, including face-to-face and virtual visits and online educational support.