and American Association of Clinical Endocrinologists. Endocr Pract. 2011;17:456–520.
4. Suwansaksri N, Preechasuk L, Kunavisarut T. Nonthionamide drugs for the treatment of hyperthyroidism: From present to future. Int J Endocrinol. 2018;2018:1–10.
5. Ozdemir Baser O, Cetin Z, Catak M, Koseoglu D, Berker D. The role of therapeutic plasmapheresis in patients with hyperthyroidism. Transfus Apher Sci. 2020;59:1–5.
6. Schwartz J, Padmanabhan A, Aqui N, Balogun R, Connelly-Smith L, Delaney M. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the Writing Committee of the American Society for Apheresis: The seventh special issue. J Clin Apher. 2016;31:149–338.
7. Muller C, Perrin P, Faller B, Richter S, Chantrel F. Role of plasma exchange in the thyroid storm. Ther Apher Dial. 2011;15:522–31.
8. Garla V, Kovvuru K, Ahuja S, Palabindala V, Malhotra B, Abdul Salim S. Severe hyperthyroidism complicated by agranulocytosis treated with therapeutic plasma exchange: Case report and review of the literature. Case Rep Endocrinol. 2018;2018:1–6.
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.

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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

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

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 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.

Bibliografía

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.

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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

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

El uso de la monitorización continua de la glucosa (MCG) en la diabetes tipo 1 (DT1) ha demostrado reducir algunas complicaciones agudas, mejorar el control glucémico y la satisfacción de uso por parte de los pacientes[1–3]. Recientemente, aquellos países que han introducido la financiación pública de estos dispositivos de manera masiva han publicado los resultados disponibles en el Reino Unido[4], Bélgica[5], Suecia[6] o Francia[7], confirmando en vida real resultados positivos en términos de reducción de HbA1c, ingresos hospitalarios por complicaciones agudas y una mejora en la satisfacción de los pacientes en comparación con la determinación habitual de glucemias capilares.

En España, la financiación pública de la MCG se ha abordado de manera diferente dependiendo del ámbito autonómico donde aplicarla. En Cataluña, dicha financiación se estableció en diferentes fases y la última contemplaba la financiación general para todos los pacientes con DT1[8]. El gran número de pacientes que incluía esta última fase de implantación nos llevó a evaluar la viabilidad y efectividad de un algoritmo de decisión (fig. 1) dirigido a la implantación masiva de la MCG en personas con DT1 atendidas en nuestra Unidad de Diabetes en el menor tiempo posible. En nuestro caso, se priorizó el uso del dispositivo de MCG de tipo *flash* Freestyle Libre[9]. Un profesional administrativo, con soporte del personal sanitario, contactó con las personas candidatas y las incluyó en el programa según sus competencias digitales. Los nuevos usuarios recibieron información del dispositivo, un teléfono de contacto y un enlace a un seminario formativo web. Los menos familiarizados con la tecnología y con menores competencias digitales recibieron formación presencial en grupos reducidos.

En un período de 3 meses y medio, comprendido entre el 1 de marzo y el 15 de junio de 2021, se contactó telefónicamente con 1519 candidatos (52% mujeres, edad media de 43,82 ± 15,29 años, HbA1c media del 7,71% ± 1,19, 19% usuarios de infusor subcutáneo de insulina). Un total de 1045 pacientes (69%) iniciaron el uso de la MCG financiada, de los cuales 320 (21%) se autofinanciaban el uso de la MCG previamente; 331 personas (22%) rechazaron el uso del dispositivo y no se consiguió contactar con 143 personas (9%). En los seminarios web dirigidos por una enfermera educadora en diabetes, se incluyeron 292 pacientes (29%), mientras que solo 39 (3%) requirieron formación presencial. La mayoría de pacientes que rechazaron el inicio de MCG manifestaron su falta de interés en el uso del dispositivo (45% de los casos) y un 17% de los pacientes prefería tomar una decisión tras la visita con su endocrinólogo habitual. No se registraron complicaciones agudas destacables ni problemas clínicos relevantes. Observamos un discreto incremento del número de consultas sobre el dispositivo (se registraron un total de 190 llamadas y 11 visitas presenciales no planificadas).

Recientemente se ha publicado en esta revista un trabajo en España que demuestra que la incorporación de un programa educativo en formato grupal y telemático sobre el uso de dispositivos de MCG de tipo *flash*, dentro de las estrategias de implantación de estos sistemas, es una opción efectiva y con beneficios asociados en calidad de vida y miedo a hipoglucemias, implementable en la práctica clínica habitual en pacientes adultos con DT1[10]. Nuestro trabajo añade nueva información al respecto y demuestra que la implantación masiva de la MCG financiada en la población con DT1 en un breve período de tiempo es factible, segura y efectiva mediante el uso de estrategias coordina-