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Case report

Acute lactic acidosis as a complication of thiamine-free parenteral nutrition in two neutropenic children

Acidose lactique compliquant une alimentation parentérale non supplémentée en thiamine chez deux enfants neutropéniques

Myriam Razgallah Khrouf [a,c], Habib Besbes [b,*], Mohamed Ali Soussi [a], Monia Ben Khaled [b], Manel Turki [c], Selima Zaouali [a], Monia Ouederni [b], Fethi Mellouli [b], Mohamed Bejaoui [b]

[a] *Service de pharmacie, Centre national de greffe de moelle osseuse, 1029 Tunis, Tunisia*
[b] *Service d'hémato-immunologie pédiatrique, Centre national de greffe de moelle osseuse, rue Jebel-Lakhdar, Bab Saadoun, 1029 Tunis, Tunisia*
[c] *Laboratoire de pharmacologie, faculté de pharmacie, 5000 Monastir, Tunisia*

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Abstract

Following a national out-of-stock of pharmaceutical speciality made with multivitamins formula for intravenous infusion, two hospitalized children with immuno-hematological disorder receiving vitamins-unsupplemented total parenteral nutrition (TPN), had acute lactic acidosis associated with neurological and respiratory symptoms. Clinical and biological signs had quickly resolved after the intravenous administration of thiamine. The thiamine deficiency is an uncommon complication of TPN. This complication remains unrecognized especially in patients with serious diseases in which acidosis could be multifactorial.

Keywords: Total parenteral nutrition; Thiamine deficiency; Lactic acidosis

Résumé

Suite à une rupture de stock à l'échelle nationale d'une spécialité pharmaceutique à base de multivitamines pour administration intraveineuse, deux enfants hospitalisés ayant un trouble immuno-hématologique et recevant une nutrition parentérale non supplémentée en vitamines, ont présenté une acidose lactique associée à des symptômes respiratoires et neurologiques. Les signes cliniques et biologiques ont été rapidement résolus après l'administration intraveineuse de thiamine. Le déficit en thiamine est une complication rare de la nutrition parentérale. Cette complication reste méconnue, en particulier, chez les patients atteints de maladies graves dans lesquelles l'acidose pourrait être multifactorielle.

Mots clés : Nutrition parentérale ; Déficit en thiamine ; Acidose lactique

1. Introduction

Total parenteral nutrition (TPN) is an artificial feeding technique developed since 1968, whose purpose is to cover the patient's nutritional and energetic needs [1]. Reported complications of TPN, especially infections, are not rare [2]. However, acute severe lactic acidosis secondary to thiamine-unsupplemented TPN is an unusual complication. This

* Corresponding author.
E-mail addresses: myriam.khrouf@gmail.com (M. Razgallah Khrouf), hbib.toubib@gmail.com (H. Besbes), mohamedalisoussi@yahoo.fr (M.A. Soussi), moniabkhaled@yahoo.fr (M. Ben Khaled), manel_turki@yahoo.fr (M. Turki), selima.zaouali@gmail.com (S. Zaouali), moniahasan@yahoo.fr (M. Ouederni), melloulif@yahoo.fr (F. Mellouli), mohamed.bejaoui@rns.tn (M. Bejaoui).

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metabolic disorder can be fatal and must be known by practitioners who prescribe TPN. We report two cases of children with immuno-hematological disorder, who are fed exclusively by TPN, illustrating this rare condition. It's noteworthy that parenteral nutrition in our centre is prepared manually and aseptically under laminar flow hood in pharmacy department. TPN formula contains proportion of glucose, lipids, amino acids (Primene®) without sulfites, and added vitamins, electrolytes and oligoelements. Following a national shortage of multivitamins formula for intravenous infusion, the two patients received vitamins-unsupplemented TPN.

2. Case 1

A 4-year-old boy weighing 15 kg suffering from acute B-cell lymphoblastic leukaemia was hospitalized for allogenic geno-identical hematopoitic stem cell transplantation indicated in his second complete remission, 2 months after an intensive chemotherapy (EORTC protocol). A conditioning regimen by etoposide (600 mg in one dose), cyclophosphamide (1800 mg as total dose in 2 days) and busulfan (288 mg as total dose in 4 days) which was prescribed had led to bone marrow suppression. TPN was prescribed on the day-1 of the graft, administrated in his subcutaneous implantable port. Three weeks from the beginning of TPN, partially offset metabolic acidosis occurred and laboratory tests showed pH at 7.34, a high anionic gap at 19.73 mmol/L (normal range < 16 mmol/L) and lactic acid level at 2.9 mmol/L (normal range < 2 mmol/L). When the acidosis occurred, the child received three antibiotics (ciprofloxacin, vancomycin, tazobactam-piperacilline), anti-viral agent (ganciclovir) and prophylactic anti-fungal agent (fluconazole) as well as omeprazol and cyclosporin. The glucose intake in TPN was 22 g/kg/day representing 80% of the total energy intake. Serum glucose was 5.5 mmol/L, urine glucose and urine ketones were negative.

3. Case 2

An 18-month-old girl weighing 8 kg was admitted in the intensive care unit for primary immune deficiency (combined immunodeficiency) with severe auto-immune neutropenia (neutrophils at 0/mm^3) resistant to G-CSF. The infant had caught serious bacterial infections and CMV reactivation. She was also colonized by multiple resistant bacteria. She received a broad-spectrum antibiotics, antiviral agent and antifungal agent. In her special nutritional and metabolic condition, TPN was prescribed after putting a central venous catheter (Broviac™). The aim was not only to prepare the child for allogenic hematopoitic stem cell transplantation but also to minimize nutritional consequences of both conditioning regimens as well as complications resulting from the graft. Three weeks under TPN and before conditioning regimen, the infant developed a metabolic acidosis, pH at 7.21, and anion gap at 28.73 mmol/L and serum lactic acid level at 3.6 mmol/L. When acidosis occurred, the patient received imipenem, targocid, colymicin, ciprofloxacin, ganciclovir, itraconazole and G-CSF. The glucose intake was at 23 g/kg/day (75% of total energy). Serum glucose was 4.4 mmol/L, urine glucose and urine ketones were negative.

Both patients developed clinical signs which were more marked in case 2 with drowsiness and lethargy, sine materia dyspnoea, and unexplained vomiting. A part from tachycardia, the hemodynamic status was stable and no other signs were observed. It is important to note that 24 hours prior to this acute biological disorder, both patients were asymptomatic. On the basis of laboratory tests, infectious causes were excluded: markers of inflammation, blood culture and the microbiological analysis of the different collected samples from TPN were negative. Exogenous acids and diabetic ketoacidosis were also excluded. For both patients, no liver dysfunction was noticed and the renal function was normal. Another suspected cause of lactic acidosis was thiamine deficiency. This hypothesis was supported by the rapid resolution of clinical signs within 8 hours after intravenous (IV) administration of 100 mg of vitamin B1. The IV administration had been conducted for 3 days then relayed by oral multivitamins solution. This measure was generalised for all hospitalised patients under TPN and no recurrence of lactic acidosis was noticed.

Table 1 shows the biological modifications of our patients before IV thiamine administration and 8 hours after.

4. Discussion

Both patients who had hemato-immunological disorder with neutropenia and receiving TPN developed acute symptomatic acidosis in the third week from the beginning of TPN. The most frequent causes in the clinical context of our patients were infections, renal failure and metabolic acidosis induced by some drugs. Those diagnoses were easily excluded by the lack of biological arguments supporting infections, a normal renal function and the drugs used did not lead to acidosis. However, the occurrence of metabolic acidosis at the same period in the two patients, who were under TPN, supports a complication of this feeding technique such as an exogenous excess of unmetabolized acids; this hypothesis is unlikely to be true because the anionic gap and serum lactic level would be in normal range. Another less known and indirect complication of TPN is the accumulation of lactic acids [3,4]. This complication should at first refer to thiamine deficiency which is an extremely rare condition because vitamins supplementation is usually done systematically. The national out-of-stock of multivitamins formula for IV infusion and the scarcity of this complication, making it unrecognized by physicians, explain thiamine deficiency in our cases.

The physiopathological mechanism is that TPN leads to a state of hypercatabolism. Thus, excessive caloric load and a rapid use of thiamine from hepatic reserves induce a deep depletion of thiamine with an exaggerated production of lactate. In fact, the thiamine pyrophosphate (TPP), active form of thiamine, is a catalytic cofactor necessary for the transformation of pyruvate to acetyl CoA in the mitochondrion citric acid cycle [5]. In the lack of TPP, pyruvate is deflecting to another metabolic pathway and leading to anaerobic glycolysis stimulation. This