Annals of Medicine and Surgery 60 (2020) 327–329

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Case Report

Hypocalcemia secondary to hypomagnesemia in a patient on liraglutide

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ARTICLE INFO

Keywords:
Hypomagnesemia
Hypocalcemia
Parathormone (PTH)
Liraglutide
Diarrhea
PTH

ABSTRACT

A 73-year-old man with type 2 diabetes on Liraglutide with a history of coronary artery disease. Admitted to emergency for abdominal pain, severe diarrhea and episodes of tetany attacks. Laboratory workup reveals hypomagnesemia, hypocalcemia and normal parathormone (PTH).

After intravenous administration of magnesium and calcium, the blood ionogram quickly normalized. In addition, plasma levels of intact parathyroid hormone increased immediately after magnesium administration.

Strongly suggests that hypocalcemia resulted from a disruption of adequate parathyroid hormone secretion caused by hypomagnesemia which in turn was caused by severe diarrhea under treatment with Liraglutide.

1. Introduction

Serum magnesium concentration is determined by the interaction of intestinal absorption and renal excretion. Hypomagnesemia may occur following an insufficient intake of magnesium, an increase in renal or gastrointestinal losses, especially in the case of chronic disorders of the digestive tract, associated with diarrhea, malabsorption, steatorrhea or redistribution of extracellular to intracellular compartments [1]. Several drugs are known to cause hypomagnesemia, including proton pump inhibitors (PPI).

This report describes the case of a patient suffering from tetany attacks with hypocalcemia probably due to hypomagnesemia secondary to diarrhea on Liraglutide.

1.1. Case presentation

A 73 year old man who presented for an imbalance of his type 2 diabetes with anorexia, weight loss estimated at 8kg over 2 months, diarrhea and attacks of tetany.

The patient was initially on an inhibitor of DPP4, Metformin and Glimipiride. During his stays in cardiology he underwent an adjustment of his treatment with Abasaglar and Liraglutide, three months later the patient reported the appearance of abdominal pain, diarrhea with episodes of tetany attacks.

Upon admission the conscious, normocardial, normotensive and eupnetic patient Apyretic at 36.7 °C, weight: 84kg, Height: 1.69 m, **BMI**: 29.13. The sign of Chvosteket and sign of keychain were negative, the rest of the physical examination is without distinction. The initial **ECG** did not show signs in favor of hypocalcemia.

Subsequent examinations revealed a normal parathyroid hormone (PTH) plasma concentration of 21.51ng/l (15–65) ng/l and a low vitamin D (D2+D3) level of 53.7 nmol/l. Urinary excretion of magnesium was 7.53 mEq/24h (3-5mEq/24h) on a limit of one dose made after 3 days of IV magnesium supplementation (Table 1).

Intravenous electrolyte supplementation was initiated with ECG monitoring. The patient received in 500 cc of 5% glucose serum: 8 g of calcium gluconate and 4 g of magnesium sulfate 2 g of potassium chloride in 24 hours. At the end of 48 hours, this correction led to normalization of serum calcium, magnesia, kalaemia and an elevation of PTH as well as an improvement of the glycemic cycle. Oral magnesium intake was maintained in the form of Magnesium Pidolate.

Liraglutide therapy was discontinued. At the time of discontinuation of Liraglutide treatment, there was a clear improvement in digestive disorders and the balance sheet remained stable, confirming the absence of hypoparathyroidism and the causal link incriminating Liraglutide is suspected.

2. Discussion

The main etiologies of hypomagnesemia are the lack of intestinal

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https://doi.org/10.1016/j.amsu.2020.10.052
Received 17 July 2020; Received in revised form 20 October 2020; Accepted 21 October 2020
Available online 29 October 2020

Table 1
Initial blood test results showed multiple electrolyte abnormalities.

Biology	Interval	Value
Sodium	139 mmol/l	(136–145)
Potassium	3,2 mmol/l	(3,5-5,1)
Cl	98 mmol/l	(98–107)
Co2	24 mmol/l	(22–29)
Glycemia	6,80 mmol/l	(4,11–6,05)
Urea	5,20 mmol/l	(0,50–11,90)
Creatinine	73 µmol/l	(59–104)
Clairance ckdepi	88 ml/min/1,73 m^2	>90
Calcium mmol/l	1,52	(2,20–2,55)
Albumine	37	(35–52)
Prealbumin g/l	0,17 g/l	>0,20
Calcium corrected	1,60 mmol/l	(2,20–2,55)
Phosphorus mmol/l	1,22	(0,81–1,45)
Mgnesiummmol/l	<0,1	(0,66–1,07)

absorption (malabsorption, diarrhea, fistule, by-pass …) and/or an excess of renal loss (diuretics, polyuria, hypercalcemia, nephrotoxic drugs …)[2]. A number of cases of severe drug-induced hypomagnesemia have been reported with long-term use of PPIs, the exact mechanism of which is not yet elucidated. The most likely etiology is intestinal malabsorption secondary to disruption of active transport through the intestinal wall by acting on the function of the TRPM6 channel[3]. There are also rarer genetic causes, usually found in young children.

In our patient it is suspected that the symptomatic and profound hypomagnesemia is caused by a malabsorption syndrome following his chronic diarrhea.

The digestive absorption of magnesium (Mg) occurs through two transport mechanisms: active transcellular transport, which occurs mainly in the colon, and passive paracellular transport, which occurs in the small intestine [4,5], which is governed by electrochemical gradients and water flow [6], so that in diarrhoeal states Mg can be secreted in the lumen of the intestine with water and electrolytes [7].

As in the case of dehydration, activation of the renin-angiotensin-aldosterone system stimulates the secretion of aldosterone and resulting in an increase in extracellular volume, which inhibits the tubular reabsorption of magnesium and thus the loss of magnesium in the urine [8].

Hypomagnesemia is not the only biochemical abnormality in our patient, we also have hypocalcemia and hypokalemia, in reports by (Whang et al., 1984; Whang and Ryder, 1990), it was demonstrated that the major electrolyte change associated with hypomagnesemia is hypocalcemia followed by hypokalemia and hypophosphatemia.

The mechanism of hypocalcemia is due to the fact that Mg interferes with PTH secretion and its action on target organs [9,10]. In many studies reported in the literature, only the administration of Mg causes an immediate normalization of serum Ca concentrations and an increase in plasma PTH concentrations.

In addition, the low plasma concentrations of 1.25 (OH) 2D, which improved after normalization of plasma Mg concentrations, suggested an alteration in target organ reactivity to PTH caused by hypomagnesemia [11].

Low magnesium content is a strong independent predictor of the development of type 2 diabetes (Kao et al., 1999). The decrease in magnesium has a negative impact on glucose homeostasis and insulin sensitivity in diabetic patients (Nadler et al., 1993). as well as on the development of complications such as retinopathy, thrombosis and hypertension (Nadler et al., 1992), our patient perfectly normalized his blood glucose levels after balancing his magnesium levels.

The therapeutic management of hypomagnesemia is judged by severity; patients with symptomatic hypomagnesemia should receive intravenous magnesium supplementation, and oral intake should be reserved for asymptomatic patients.

No studies have been conducted to determine the optimal treatment regimen describing the modalities of magnesium supplementation. However, consensus statements recommend the administration of 8–12 g of magnesium sulfate within the initial 24 hours, followed by 4–6 g/d for 3–4 days to replenish body reserves [12]. For the maintenance infusion, an infusion of 1–2 g/h of magnesium sulfate can be administered for 3–6 hours, then reduced to a rate of 0.5–1 g/h as a maintenance infusion [13]. The objective is to achieve serum magnesium concentrations of 0.8 mEq/L as quickly as possible. Maximum infusion rates should generally remain at 2 g/h, Since plasma magnesium concentration is the primary determinant of magnesium reabsorption in Henle's Cove, an abrupt rise in plasma magnesium concentration decreases the stimulus for magnesium retention. When the renal threshold for magnesium is exceeded, up to 50% of the infused magnesium will be eliminated in the urine. If measured immediately after a magnesium infusion, serum magnesium levels may be higher than expected; however, this does not mean that the body's magnesium stores are replicating, and additional oral magnesium salt supplementation is often required (4).

3. Conclusion

Deep hypomagnesemia disrupts the secretion of PTH, responsible for hypocalcemia associated with a potential severity of electrolyte disorders, it is imperative to mention the drug origin following the broad prescription of Liraglutide in diabetics with obesity and cardiovascular field.

Discontinuation of Liraglutide and parenteral substitution by magnesium infusion rapidly corrects the clinical and biological disorders. Regular monitoring of renal function is necessary to avoid iatrogenic hypermagnesemia.

Provenance and peer review

Not commissioned, externally peer reviewed.

Author's contributions

Dr. EJ, Dr. IJ, and Dr. CB analysed and performed the literature research, Pr. HL performed the examination and performed the scientific validation of the manuscript. Issam Jandou was the major contributors to the writing of the manuscript. All authors read and approved the manuscript.

Declarations

Ethical approval and consent to participate. This study has been approved by the ethics committee of UHC Ibn-Rochd Casablanca, Morocco.

Consent to publication

The consent to publish this information was obtained from study participants. We confirm that the **written** proof of consent to publish from study participants are available when requested and at any time.

Availability of data and material

The datasets in this article are available in the repository of the urology database, Chu Ibn-Rochd Casablanca, upon request, from the corresponding author.

Annals of medicine and surgery

All authors disclose any conflicts of interest

Ethical approval

The study committee of the jura sud hospital center approves the favorable opinion to publish this work.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Registration of research studies

1 Name of the registry:
2 Unique Identifying number or registration ID:
3 Hyperlink to your specific registration (must be publicly accessible and will

be checked):

Guarantor

Dr. Jandou issam

Declaration of competing interest

The authors state that they do not have competing interests.

Abbreviation

PTH	parathormone
PPI	Proton pump inhibitors
BMI	body mass index
ECG	Electrocardiogram
ADH	Antidiuretic hormone
Mg	magnesium

Appendix B. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.amsu.2020.10.052.

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