

# HYPOGLYCEMIA DUE TO DRUG INTERACTION WITH CLARITHROMYCIN

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## Introduction:

Interaction between Diabetes Mellitus (DM) and an infection usually results in hyperglycemia. However, there is data describing hypoglycemia events related with the association between certain antibiotics and oral anti-diabetic drugs or insulin.

## Case Report:

I. Identification: 73 years old, male, caucasian

II. Family history: irrelevant

III. Personal history: T2DM diagnosed 13 years ago without any macro or microvascular complications so far. Under insulin therapy since 2 years, with good glycemic control (HbA1c 6,9%) with rare episodes of hypoglycemia. Hypertension, Obesity and Dyslipidemia.

IV. Medication: Detemir insulin (40+28U – 0,71U/Kg); Vildagliptin+Metformin 50/1000 2id; Sinvastatin 20mg; Valsartan+Hidroclorotiazide 160/25mg

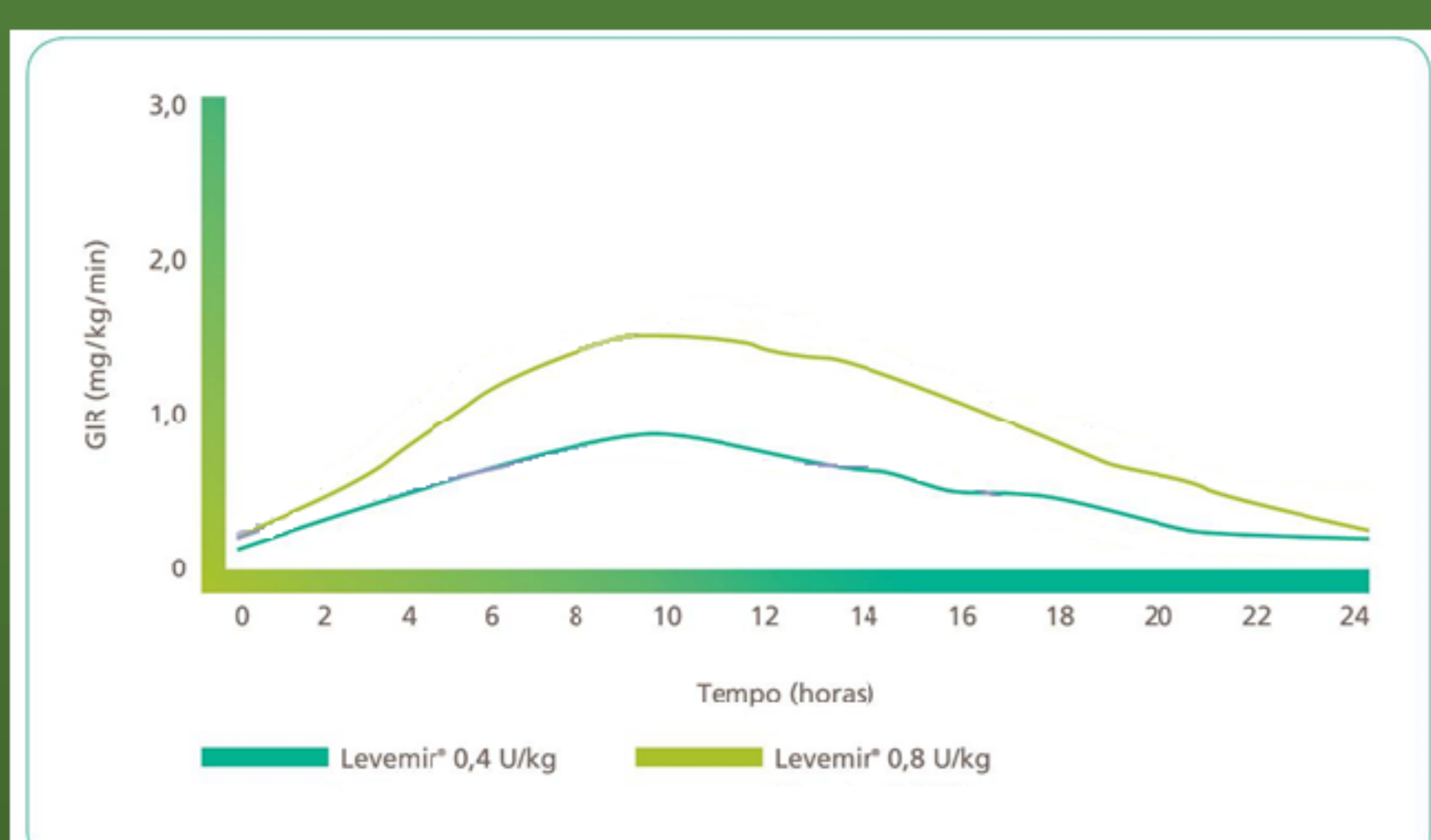
V. Case report: Due to dental abscess he started a treatment with clarithromycin 500mg 2xd. After 36 hours of taking the drug, referred two episodes of night symptomatic hypoglycaemia, on consecutive days (42 and 37mg/dl respectively), which reversed after sugar intake. In this context, he went to our clinic, and the antibiotic was changed to Amoxicillin+Clavulanic acid 850+125mg 2xd, keeping the usual therapy for DM. There weren't any more episodes of hypoglycaemia.

VI. Height: 1,70m Weight: 95,3Kg BMI: 32,96 Kg/m<sup>2</sup>

## Discussion:

In the literature there are few reports of hypoglycaemia induced by clarithromycin in combination with insulin detemir. 40-70% of clarithromycin circulates bound to proteins, which can dissociate Insulin detemir of protein binding sites (98% binds to albumin), increasing the free concentration and its pharmacological effects. This phenomenon can cause a faster beginning of action, simulating an insulin with intermediate or short-action, leading to hypoglycemia.

Fig 1. Action of insulin detemir



Graphic exposed with authorization of national NovoNordisk®

Fig 2. Insulin detemir's action simulation when administered with clarithromycin

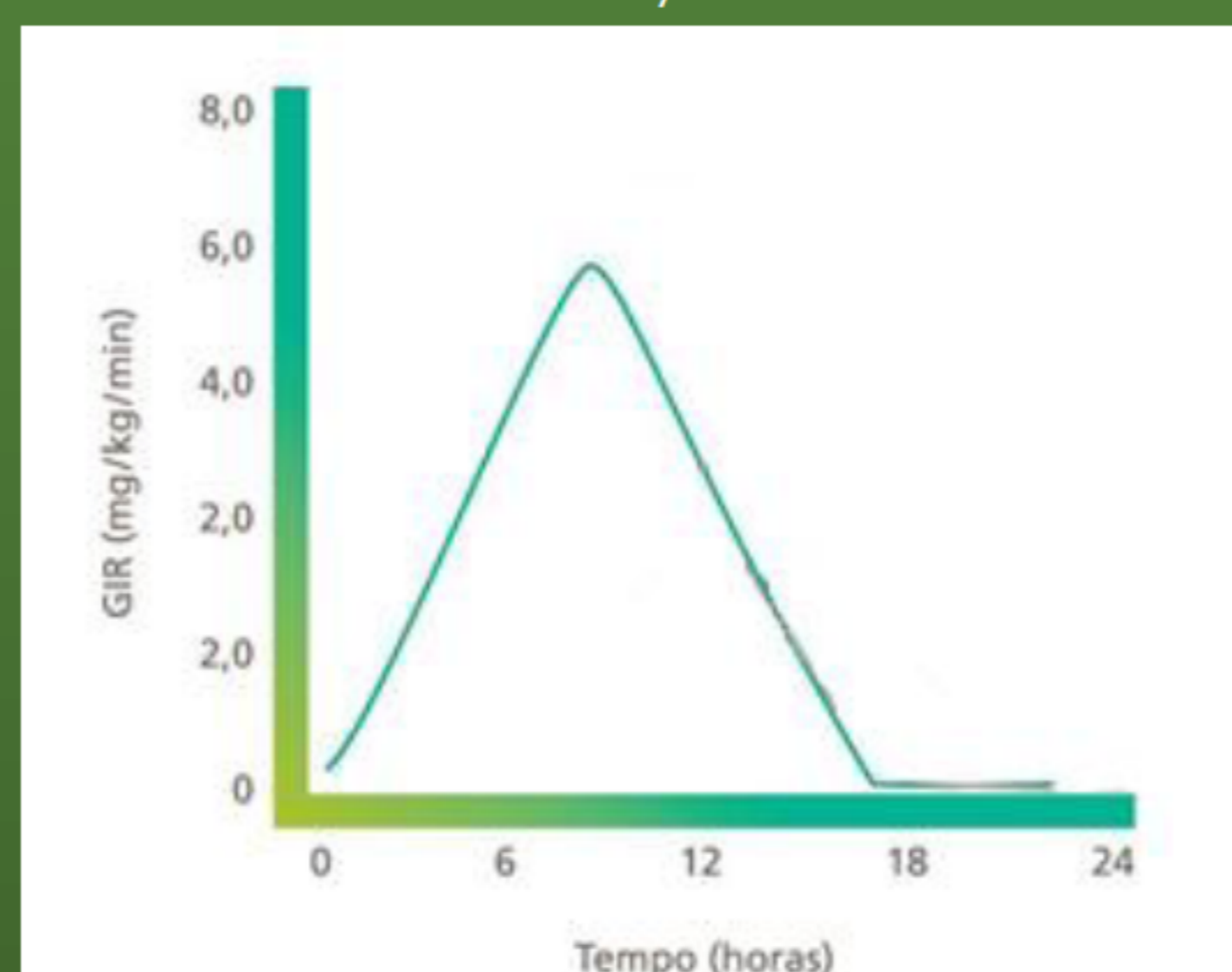
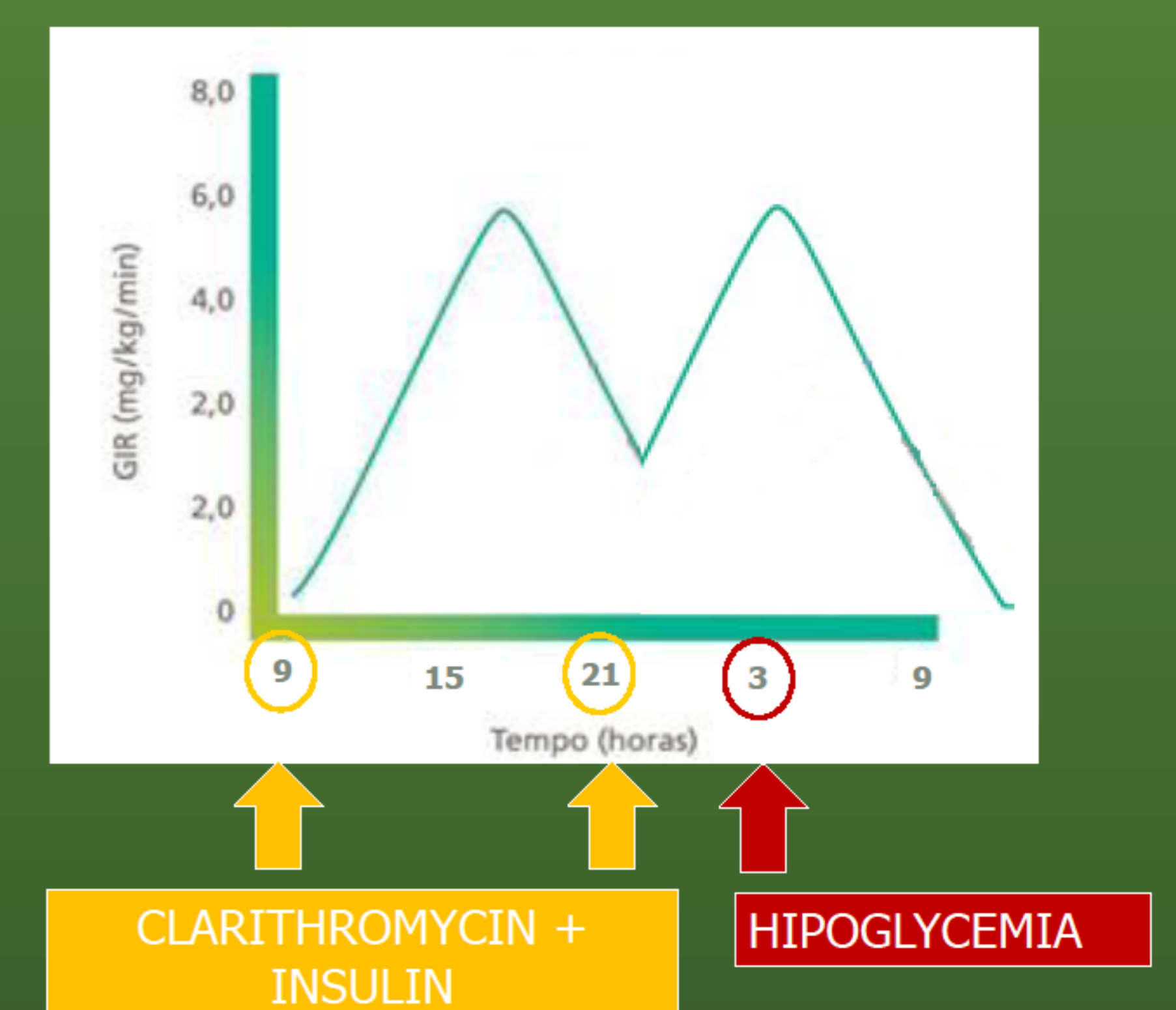


Fig 3. Insulin detemir's action simulation when administered with clarithromycin in the case report



Clarithromycin is a potent inhibitor of CYP3A4. Vildagliptin isn't a substrate of this cytochrome. Metformin is a substrate of this cytochrome's family, but there isn't any report of hypoglycaemia with this association.

Vildagliptin circulate bound to proteins in 9.3 % and metformin binding protein is negligible.

## Conclusion:

Clinicians should be aware of this drug interaction, regarding the need of adjustments of insulin doses to avoid possible adverse effects and hospitalizations. Patients who start Clarithromycin should be advised to have more frequent monitoring capillary blood glucose and must be re-educated about the signs, symptoms and treatment of hypoglycemia.

