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Vomiting as Common Adverse Event of Exenatide: A Case of Diabetic Patient with Type 2 and Duodenal Bulb and Gastric Ulcers who Showed Severe Vomiting Increased Gradually after Exenatide Injections

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Abstract

Background: Although exenatide is a valuable option of treatments for type 2 diabetes (T2DM) in obese patients, mild to moderate nausea or vomiting in a usual dose of administration is most common. The adverse event usually decreases with time.

Methods and Results: A case of 58-year-old female with T2DM and gastric ulcers is reported. Before treatment with exenatide, she had hemoglobin A1c (NGSP) 7.8% and had received oral miglitol, metformin and DPP-4 inhibitor for T2DM, oral α-blocker and telmisartan for hypertension and oral pitavastatin for dyslipidemia. Before the treatment, she had high body mass index of 44.2 kg/m^2, but no evidence of micro- and macrovascular disturbances and no symptoms of duodenal bulb and gastric ulcers. After twice daily subcutaneous injections of 10 μg/day exenatide, vomiting developed gradually. We tried to examine exact causes using endoscopy. She was diagnosed with duodenal bulb and gastric ulcers with *Helicobacter pylori*. She received bactericides drugs. After then, the bacteria were eradicated and vomiting gradually disappeared and she was re-treated with the same dosing schedule of exenatide and had a good control.

Conclusion: If the degree of vomiting gradually increases with time, they should consider another cause, as seen in this case.

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Vomiting, Exenatide, Twice daily injection, Duodenal and gastric ulcers, Type 2 diabetes melltius

Introduction

Although exenatide is a valuable option of treatments for type 2 diabetes (T2DM) in obese patients, mild to moderate nausea or vomiting in administration with a usual dose of exenatide is generally common side effect. However, the adverse event of exenatide usually decreases with time [1, 2]. We report a patient with T2DM and duodenal bulb and gastric ulcers, when she developed increased vomiting gradually after treatment with a usual dose of exenatide.

Material & Methods

A case of a 58-year-old female with height of 1.58m, with T2DM and duodenal bulb and gastric ulcers was reported. She was diagnosed with T2DM during an examination in October 2002. Before treatment with exenatide, she had a hemoglobin A1c (NGSP) of 7.8 % and had received 150 mg of oral miglitol (Seibule®, Sanwa, Japan), three times daily, 2000 mg of oral metformin (Metgluco®, Sumitomo, Japan), twice daily and 100 mg of an oral DPP-4 inhibitor, vildagliptin (Equa®, Novartis, Japan), twice daily, for T2DM. Other drugs prescribed included 1 mg of an oral a-blocker, doxazocin (Cardenalin®, Pfizer, Japan) and 80 mg of oral telmisartan (Micardis®, Astellas, Japan) for hypertension once daily at bedtime and 1 mg of oral pitavastatin (Livalo®, Kowa, Japan) for dyslipidemia once daily at bedtime. Before the treatment, she had high body mass index (BMI) of 44.2 kg/m^2 and no evidence of micro- and macrovascular disturbances and no symptoms of duodenal bulb and gastric ulcers. After changing the oral DPP-4 inhibitor to the subcutaneous injections of 10 μg/day exenatide (Byetta®, AstraZeneca, Japan) twice daily for T2D, vomiting developed gradually, and she had that the maximum degree of vomiting was 8 points on STAS-J (where 0 is no vomiting and 10 is maximally strong vomiting) [3]. Therefore, we tried to examine the exact cause using gastroscopy. She was diagnosed with duodenal bulb and gastric ulcers with *Helicobacter pylori* via nasal and oral gastroscopies. She had 20 mg of rabeprazole, 1500 mg of amoxicillin and 400 mg of clarithromycin (Rabecure PACK 400®, Eisai, Japan) daily for one week as a bacteriocide, and 6 mg of lactomin and 40 mg of clostridium butyricum with glycated bacteria (BIO-THREE®, Towa-Shinyaku, Japan) daily for one week and after which, the bacteria were eradicated. Then, vomiting (without antiemetics) gradually disappeared and she was re-treated with the same dosing schedule of subcutaneous exenatide. After then, she had good control as 6.0 % of Hb1c (NGSP) and her weight decreased as 30.0 kg/m2 in BMI. The complete recovery of duodenal bulb and gastric ulcers was demonstrated by gastroscopy.

Discussions

We first believed the patient's vomiting reflected the most commonly adverse event of exenatide administered [1, 2]. However, the degree of vomiting did not decrease with time, but gradually worsened with 8 points on the STAS-J. She revealed duodenal bulb and gastric ulcers with *Helicobacter pylori* using gastroscopy. After eliminating the bacteria, vomiting gradually disappeared along with remission of duodenal bulb and gastric ulcers confirmed by gastroscopy. The underlying reason why the gradually increasing vomiting may be

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due to, at least in part, delayed gastric emptying of exenatide effect, because that she had no autonomic dysfunction [4]. As the tip of nasal gastroscopy tube was not passed into duodenal bulb, the bulb was due to scar owing to gastric ulcer until after the eradication of bacteria, although detailed reasons for this case are not clear [5].

Conclusions

When physicians observe nausea or vomiting in patients treated with a GLP-1 receptor agonist in a usual dose of administration, the side effect generally decreases with time. However, if the degree of nausea or vomiting increases gradually, they should consider another cause, as seen in this case.

Author Contributions

Kyuzi Kamoi (KK) designed the research, conducted the experiments, collected and analyzed data, performed statistical analysis and wrote the paper.

Hideo Sasaki (HS) provided essential comments.

Conflict of Interest

There are no relevant conflicts of interest to disclosure and regarding the publication of this paper.

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