

## Acute Pancreatitis after Therapy with GABARAN

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### Abstract

The main objective of this clinical-case-presentation is to attract attention that the therapy with Gabaran in high dosage and per long period of time without a careful control of function of pancreas (common dosage of amilasemia and amilasuria level) can develop unexpected severe acute pancreatitis and may put the patient's life in danger.

**Keywords:** Pancreatitis; Therapy; Gabaran drug

### Introduction

Acute pancreatitis is one of the most dangerous diseases from the medical practice and for this reason the name of the disease is sometimes "the big abdominal drama". The most common causes of acute pancreatitis are very well known: alcohol consumption, digestive problem like gall stones inside of the common biliary duct, postoperative causes after laparoscopic remove of the gall bladder or trauma.

Rarely, the cause could be after medications, but Gabaran is not mentioned in this list and the truth and the clinical reality shows that this drug could develop unexpected acute pancreatitis after prolong administration of therapy and needs a carefully supervise of pancreatic enzymes (amilasemia and amilasuria). This drug is use in present in therapy of the epilepsy and also in therapy of the polyneuritis of the lower limbs.

Caution should be exercised with close monitoring in patients with past acute or chronic pancreatitis, although there is documented safety even in these patients [1]. Furthermore, the causality for many drugs remains elusive and for only about thirty of these 525 drugs has a definite causality been established [2]. A retrospective study conducted in Germany concluded that the incidence of drug-induced AP is 1.4% [3]. A national survey performed in Japan in 1999 reported that 1.2% of all cases of AP were drugging induced [4].

### Materials and Methods

I am going to present the clinical case of a 48-year-old man (who is non-alcoholic) with type 2 diabetes mellitus under diet and therapy with Siofor (0-1/2-0) and a good control of the level of glycemia (glycosilate Hb level=5 g%); but in time he developed symptoms which are suggestive for sensitive polyneuritis (complication in context to type 2 diabetes mellitus). For this reason the neurologist started a therapy with Gabaran 300 mg, 6 drugs/day ( $3 \times 2$  drugs/day=1800 mg/day) for two weeks. After that 4 drugs/day= $4 \times 300$  mg=1200 mg/day for another three weeks ( $1200$  mg  $\times 21=25.200$  mg) and in the end it remained continuous with three drugs per day ( $3 \times 300$  mg/day=900 mg/day), because of severity of the symptoms. After three months of this therapeutic scheme, the patient came for consultation due to intense epigastric pain. He admitted that the symptoms started approximately three weeks ago. But instead of visiting a doctor he stayed home hoping for his pain to go.

At the objective examination everything was normal except for the sensibility of palpation in the epigastric area. An upper endoscopy was performed and was normal; therefore, gastritis, gastric or duodenal ulcers were excluded. Helicobacter pylori test was negative. EKG was normal and excluded a posterior-inferior acute myocardial infarction.

After all lab tests were performed it come up that the level of amilasuria was increased (1483 mg/dl) but the level of amilasemia was in normal range.

In this moment acute pancreatitis was suspected. Because of the fact that the patient came three weeks late for consultation, the amilasemia-level was not increased, since it gets back to its normal range in just the first days. Only the level of amilasuria was caught at an increased value.

For this reason the patient was hospitalized, the laboratory tests were repeated and amilasemia was normal as well but the level of amilasuria was=2883 UI/l so the confirmation of acute pancreatitis was sure. For this reason the patient started the standard protocol of therapy with NTG tube, saline solution with antispasmodic, antisecretory and antibiotic twice per day with amelioration of the symptoms and good evolution of the patient.

An abdominal ultrasound was performed and was normal, without any stones inside the gall bladder or common biliary duct. The pancreas looked normal as well. So a biliary cause of acute pancreatitis was excluded. Because the person was a non-alcoholic patient (also the family confirmed this), the liver blood test was in normal range as well (GOT, GPT and Gama GT were normal) and also the toxicological tests for alcohol consumption (alcholemlia) were performed and were negative, these points were precluded of being the cause of acute pancreatitis. The main problem in this moment remained to find the etiology of acute pancreatitis.

Because the only medication used was Gabaran in high doses and for a long period of time (except for Siofor therapy of type 2 diabetes mellitus with well-known hepatotoxic and nephrotoxic side effects), this drug was suspected to be responsible for the episode of acute pancreatitis, proven by the increase level of amilasuria.

In the medical literature, the possible etiology of acute pancreatitis in small percent secondary after medications was mentioned (post medicaments acute pancreatitis), but Gabaran was not mentioned in the list of these medications (drugs). This is not the only clinical case from my medical practice with this situation.

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I had also some other clinical cases with the same situation with increased level of amilasemia or amilasuria after the consumption of this drug on nonalcoholic persons and without digestive problem like gall bladder-stones or stones inside the common biliary duct and with severe acute pancreatitis, who needed the standard protocol of therapy in this direction.

## Results and Discussion

Usually the neurologist doctor recommend starting therapy with one pill Gabaran 300 mg one pill/three time/day in the first day, than one pill twice per day in the second day and one pill three time per day in the third day. After that the doctor can increase the dose after a few days at maximum 1800 mg/day, in three prizes. In case of kidney problem the dosage must be reduced comparative with these dosages.

This clinical case presented suggests that high doses of Gabaran like 300 mg, 6 drugs/day ( $3 \times 2$  drugs/day=1800 mg/day) for two weeks. After that 4 drugs/day= $4 \times 300$  mg=1200 mg/day for another three weeks ( $1200$  mg  $\times 21=25.200$  mg) and in the end it remained continuous with three drugs per day ( $3 \times 300$  mg/day=900 mg/day). After three months of this therapeutic scheme, the patient came for consultation due to intense epigastria pain.

The drug Gabaran in the medical practice has been used under carefully monitoring of the levels of amilasemia and amilasuria and the administration must be stopped if the level of these markers for acute pancreatitis starts to increase. The imbalance between the risk and benefit has to be seriously taken into account and must be reevaluated. At the clinical case mentioned before the side effects appear very serious but the benefit influence of drugs in therapy of sensitive polyneuritis was very low.

The patient continues to have *paresthesias* in both of his legs, more ascended during the night, after this complex scheme of therapy with Gabaran for a long period of time and in high dosage, and a very low influence of the symptoms appear in contrast to the severe and risky side effects. Drug-induced pancreatitis (DIP) is assumed to be a relative rare entity, and its incidence is reported between 0.1 and 2% of AP cases [5]. The incidence of DIP is still unknown since little evidence has been obtained from clinical trials, and most incidences have been documented as case reports [5].

Five-hundred and twenty-five different drugs suspected to cause acute pancreatitis are reported in the database of World Health Organization (WHO) [2]. Since 1980, azathioprine (AZA) and its metabolite 6-mercaptopurine (6-MP) were reported to be able to induce pancreatitis [6].

The mechanism of how azathioprine causes pancreatitis is not well elucidated and the development of pancreatitis did not appear to be dosing related [6]. I do not found in the medical literature reported cases of drug induce pancreatitis (DIP) after therapy with Gabaran.

## Conclusion

The most important conclusion is that the administration of the drug Gabaran in therapy of sensitive *polyneuritis* is not safe. The imbalance between the risks and benefits must be seriously taken into account and has to be reevaluated. If the dosages are more increase than 1800 mg/day and the period of administration more than three weeks exist risk for developing acute pancreatitis and the patient need carefully supervision of pancreatic enzymes level (amilasuria and amilasemia) and stop the administration in this situation.

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