CASE REPORT

Gastroesophageal Reflux possibly associated with Verapamil

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INTRODUCTION

The target site of action of the calcium channel antagonists is cardiac and vascular smooth muscle. However, other sites of smooth muscle are not immune to the effects of calcium channel blockers, since all types of smooth muscle cells require the influx of calcium to effect a muscle contraction. In the smooth muscle of the gastrointestinal tract, blocking influx of calcium could cause a decrease in gastric motility and lower esophageal sphincter pressure. This effect has been reported with nifedipine[1] but not with diltiazem or verapamil. We report the case of an 83-year-old female patient who developed reflux esophagitis and decreased gastric motility possibly associated with verapamil taken to control hypertension.

CASE

An 83-year-old female was admitted to a rural hospital with a three-day history of nausea, vomiting, and uncontrolled hypertension, possibly secondary to inadequate absorption of medication with the vomiting. Her past medical history was remarkable only for a history of heartburn postprandially and at night, with pain often causing her to awaken. She had no previous history of peptic ulcer disease. She had been taking verapamil 240 mg slow-release daily for hypertension for six weeks prior to admission. Treatment in the rural facility with prochlorperazine, verapamil, and hydrochlorothiazide/triamterene did not control her symptoms and she was transferred to Foothills Hospital six days later.

On the first day of admission the patient was extremely confused (not oriented to time, place or person) and nauseous with periodic episodes of vomiting. Her blood pressure was 220/95, with no postural drop. Mild epigastric tenderness was noted, but there were no other gastrointestinal findings. Volume depletion with prerenal azotemia was present, with a BUN of 12.0 mmol/L and a serum creatinine of 119 mmol/L. Her creatinine clearance was calculated to be 29 mL/min, based on an estimated weight of 50 kg. Medications ordered on day one were nifedipine 10 mg PO Q6H and SL Q3H PRN if systolic blood pressure was over 200 mm Hg, as well as dimenhydrinate 50 mg IV/IM/PO Q4H PRN for nausea. Verapamil was not prescribed during this admission.

The working diagnosis was bowel obstruction, possibly a pyloric stricture, although the possibility of a dysmotility problem related to verapamil was raised. Endoscopy on day three of admission revealed multiple small erosions on the lower one-third of the esophagus and decreased gastric motility, suggestive of esophageal relfux with esophagitis. Sucralfate slurry 1 g four times a day (made by mixing 1 g tablet in water), and domperidone 10 mg one half hour before meals and at bedtime were then started to treat the esophagitis and decreased gastric motility, respectively. When nifedipine did not adequately control the blood pressure, it was stopped on day four of admission and captopril 12.5 mg three times a day was started.

The patient's nausea and vomiting continued through admission days four to nine although with decreased severity and frequency. The medical staff believed that these symptoms were slowly resolving and that complete resolution could be expected

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with time. It is also possible that the change from one calcium channel blocker, verapamil, to another, nifedipine, delayed resolution of her symptoms. Her volume status returned to normal as did her BUN. Once the CNS depressive antiemetics were discontinued on day six, her mental confusion began to resolve. The dose of captopril was increased gradually to control the hypertension. She was transferred back to the rural facility on admission day 10, with instructions to switch to cisapride if the nausea and vomiting did not resolve with domperidone. Follow-up revealed that nausea and vomiting were not noted to be a problem during her recovery in the rural hospital.

DISCUSSION

Adverse gastrointestinal effects of the calcium channel antagonists include constipation, nausea and vomiting, and abdominal discomfort including heartburn.[2] The incidence of nausea and heartburn with nifedipine is 10% when data from both controlled and uncontrolled trials are combined.[3] Constipation is the most common gastrointestinal side effect of verapamil.[4,5] These findings suggest that there is an antagonistic action of calcium-channel blockers on gastrointestinal smooth muscle contraction.

Calcium channel antagonists, particularly nifedipine, are recognized as a treatment for some disorders of gastrointestinal motility in which the lower esophageal shincter (LES) pressure is abnormally increased, such as achalasia.[6] Studies in normal adults have shown that nifedipine, 20 mg sublingually, can decrease LES pressure by as much as 32%.[7,8,9] It has also been shown that verapamil may decrease LES pressure. In a study involving eight normal adults and seven patients with achalasia, verapamil 0.15 mg/kg IV over two minutes resulted in a decrease of LES of up to 31% in both groups.[10] Although it is recommended to avoid calcium channel blockers in the prevention and treatment of GER,[11] only one case of a calcium channel blocker, nifedipine, causing GER could be found.[1] Published case reports implicating verapamil could not be found, however, G.D. Searle and Co. has at least one unpublished report on file.[12]

The effects of calcium channel antagonists on the gastrointestinal tract are not well understood. Since the possibility exists that these agents can cause GER they should be used with caution in patients with GI motility disorders. Calcium channel blockers should be considered as a potential contributing factor if GER develops in patients taking these agents.

CONCLUSION

This patient's gastrointestinal symptoms cannot be unequivocably attributed to verapamil. However, the slow resolution of symptoms after verapamil was stopped and the well documented effects of calcium-channel blockers on lower esophageal sphincter tone, are suggestive of a causative relationship. We feel it is important to recognize that verapamil may cause or exacerbate GER in some patients.

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