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CALCIUM CHANNEL BLOCKERS AS A ETHIOLOGICAL FACTOR FOR GASTROESOPHAGEAL REFLUX DISEASE

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Abstract: Gastroesophageal reflux disease is the most common visceral manifestation of chronic calcium channel blockers use, resulting in impaired esophageal clearance and retention of ingested food. Progression of gastroesophageal reflux disease and the damaging effect of due to esophageal dysmotility is clearly understood . Nifedipine is a widely prescribed calcium antagonist in a significant percentage of ischaemic heart disease patients in order to inhibit coronal vasospasm. We describe the case of severe exacerbation of gastroesophageal reflux disease in a 76-year-old female with Gastroesophageal refluxe disease who was treated with oral nifedipine for Ischaemic heart disease.

Key Words: Esophagus, Ischaemic heart disease, Nifedipine, Gastroesophageal reflux disease.

Introduction

Gastrointestinal dysmotility is not uncommon in patients suffering from gastroesophageal reflux disease, with a reported incidence even up to 80% [1]. Esophagus stands for the most frequently invaded organ in cases of gastrointestinal involvement, with gastroesophageal reflux disease (GERD) [2]. The main mechanisms of nifedipine that cause gastroesophageal reflux disease is impaired efficacy of peristalsis and clearance, reduction of the pressure of the lower esophageal sphincter (LES), high incidence of hiatal hernias due to the gradual shortening of the organ, and delay of gastric emptying [3].

Concerning Ischaemic heart disease and Gastroesophageal reflux disease, their firm association is well established. Patients suffering from ischaemic heart disease and taking nifedipine are likely to develop Gastroesophageal reflux disease . [4].

These patients who are suffering from Gastroesophageal reflux disease and taking nifedipine for their ischaemic heart disease should avoid treatment with any drug that could enhance GERD development. Recent studies suggest that calcium channel blockers (CCBs), and particularly nifedipine, increase the risk of GERD by significantly reducing the tone of the LES, increasing esophageal exposure to gastric acid and reducing the amplitude and duration of esophageal peristalsis [6–8]. According to these findings, the administration of CCBs should be avoided, if possible, in patients with GERD. We report a very interesting case of gastroesophageal reflux disease developing in a 76-year-old female suffering from ischaemic heart disease and taking nifedipine , after a 6-month period of receiving oral nifedipine for treating ischaemic heart disease. Our case underlines for the first time the urgent need of considering the potential effect of CCBs as an exaggerator of gastroesophageal reflux disease in patients with nifedipine-derived GERD, through enhancing esophageal acid reflux due to progression of esophageal LES dysmotility.

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Case Report

Our patient was a 76-year-old never-smoker female who presented to the emergency department complaining of retrosternal discomfort, after a chocking episode which had awakened her during the night. Physical examination revealed limited thickness of the fingers, presence of ulcers in the oral cavity, palmar telangiectasias and slightly audible crackle sounds bilaterally in the lower respiratory fields. Her vital signs were as follows: blood pressure 160/95 mm Hg, heart rate 70 bpm, temperature 36.3°C, respiration rate 20/min and SatO2 97%.. Electrocardiogram reveal ischaemic heart disease. Blood tests at admission demonstrated leukocytosis (4,800/mm3), slight thrombocytosis (280,000/mm3), C-reactive protein levels of 1.8 mg/dl and serum lactic dehydrogenase of 412 IU/l. The rheumatological patient's medical history included presence of Sjögren's syndrome, rheumatoid arthritis and GERD (under anti-secretory treatment). In addition, she reported that approximately 6 months before she had been diagnosed with ischaemic heart disease and arterial hypertension and since then she had been receiving oral nifedipine (40 mg) daily. The patient mentioned that after the initiation of treatment with nifedipine, arterial hypertension was controlled and she did not experience any other ischaemic heart disease symptoms; nevertheless, she reported exacerbation of GERD symptoms, despite receiving anti-secretory treatment with proton pump inhibitors.

The initial management of our patient in the emergency department consisted of intravenous administration of hydrocortisone and omeprazole. After 2 h, the patient's clinical condition had improved, The patient was referred to the Department of Gastrointestinal Medicine for further hospitalization and was discharged after 9 days in excellent clinical condition. It was decided that nifedipine treatment for ischaemic heart disease should be replaced with diltiazem, which has proven to affect less esophageal dysmotility and lower sphincter pressure, compared to other CCBs [9]. Moreover, the daily dose of anti-secretory therapy with omeprazole was doubled. Nearly 12 months after her admission to the emergency department, the patient has not experienced similar severe GERD symptoms or respiratory complications, with both arterial hypertension and ischaemic heart disesa efficiently controlled.

Discussion

CCBs, which are considered to be the gold standard in confronting ischaemic heart disease, have proven to be associated with impaired esophageal motility by various studies, with nifedipine so far dominating the researchers' interest. This adverse effect is mediated by the inhibition of calcium influx into the smooth muscle cells, which is essential for adequate contraction and thus maintenance of efficient pressure of the LES, in order to prevent gastroesophageal reflux [10]. Moreover, CCBs tend to increase esophageal exposure to gastric acid and to reduce the amplitude and duration of esophageal peristalsis [6–8], implying the existence of multiple effects of these drugs on esophageal motility. These findings are collected , which suggested that over the 10-year period of the study, treatment with CCBs was an independent factor for GERD-related physician visits [11]. Consequently, it is evident that CCBs should be prescribed with extreme caution in patients with potentially life-threatening GERD, such as patients with systemic sclerosis, particularly in cases of pre-existing lung invasion of the disease, as chronic aspiration may lead to rapid progression of lung fibrosis.

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It is reasonable to assume that treating patients with esophageal dysmotility with CCBs, e.g. for hypertension or angina pectoris, may resemble a serious risk factor of further impairment of GERD and GERD-related diseases, such as chronic inflammation of the respiratory tract. In patients with esophageal sclerosis, this vicious circle of aspiration and lung inflammation, apart from further enhancing fibrosis, is associated with an increased probability of sleep apnea, another life-threatening condition, which is consistent with the feeling of chocking that awakened our patient during the night [13]. Also, the absence of long-term beneficial effect of CCBs in progressive gastroesophageal reflux disease further highlights the importance of their cautious prescription in patients with esophageal dysmotility. On the other hand, it is suggested that not all CCBs have to the same extent the adverse effects described above; it appears that diltiazem affects less esophageal dysmotility and lower sphincter pressure, compared to other CCBs [9]. Diltiazem was an attracting alternative, providing minimal damaging effect on GERD and the concomitant aspiration risk. Nevertheless, its administration was accompanied by doubling of the daily proton pump inhibitor dose.

Up to now, there are no solid data that can shed light on this therapeutic challenge. So far, the skepticism regarding the use of CCBs in patients with gastroesophageal reflux disease mainly focuses on investigating the consequences of their administration in esophagus function itself. Although the up-to-date findings are undoubtedly impressive, the final effect of CCBs on GERD-related disorders remains unknown. Consequently, further prospective studies should be conducted in order to assess the short- and long-term effects of CCBs in patients with disease complicated by esophageal dysmotility, GERD and serious GERD-related conditions, such as interstitial lung disease.

Conclusions

CCBs have been proven to be associated with a higher risk of developing gastroesophageal reflux. We report a case of rapid progression and exacerbation of gastroesophageal reflux symptoms in a 76-year-old non-smoker female with ischaemic heart disesa , after a 6-month period of receiving oral nifedipine. The patient finally addressed the emergency department with symptoms of gastroesophageal reflux disease. After 9 days of hospitalization the patient was discharged in excellent clinical condition and nifedipine was switched to diltiazem, along with increasing the daily dose of anti-secretory therapy. Nearly 12 months later, the patient has not experienced similarly severe GERD symptoms and seems to tolerate the new therapeutic approach well. Our case report highlights the necessity of further investigation of the long-term effects of CCBs in GERD-related complications, particularly those imposing a significant risk of mortality.

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