

Electrocardiographic and Arterial Blood Pressure Changes in Hypertensive Crisis After Using Sublingual Nifedipine

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Citation

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Abstract

1% of all hypertensive patients suffer from hypertensive crisis (HC). Although not the treatment of choice, in some Latin American countries is still common the use of sublingual nifedipine in the emergency room. In this study we will compare the electrocardiographic (EKG) and arterial blood pressure changes after 30 minutes of using sublingual nifedipine. Results: We included 23 patients without cardiac disease, with urgency HC and treated with 10-mg nifedipine sublingually. Most of the patients had mild to moderate changes in the EKG, such as changes in heart rate and nonspecific ST segment deviations. One patient had symmetric inverted T waves in leads V5 and V6. PR and QT intervals with no changes. The BP after 30 minutes was not the ideal. Conclusion: Sublingual nifedipine does not absorb well and does produce changes in the EKG. Patients did not achieve an optimal BP after the administration of sublingual nifedipine.

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INTRODUCTION

Hypertension (HTN) is a worldwide epidemic. It is a chronic disease that has a high morbidity, mortality and has a very high cost to society. Overall, 20% of the population in the world has HTN. In Mexico, approximately 15.2 millions of people suffer from HTN of a whole population of 97,483,412. 51% of the population (49.8 millions) is between 20 and 69 years old [1]. A hypertensive crisis (HC) occurs in about 1% of all HTN patients and they will suffer at least one event of HC in the course of the disease [2].

Before the emerging of antihypertensive drugs, the prevalence of HC was 7%. Males are affected twice than women [3]. Most of the patients that suffer from HC have been diagnosed previously with HTN. This may be caused because they do not have an adequate monitoring of BP and poor treatment compliance as well. From 1983 to 1990 the incidence of hypertensive crisis tripled from 23,000 cases per year to 73,000 cases per year in the United States. There have been some reports of few cases of post surgical hypertensive crisis with an incidence of 4-35%. Most of the patients that have suffered a HC had a past medical history of poorly controlled BP [4].

The etiology has not been shown and it is not well understood but what is known is that is secondary to a

variety of events. Some related causes are: an autonomous hyperactivity, preeclampsia, poor treatment compliance, drug cross reactivity and general anesthesia [5].

PHYSIOPATHOLOGY OF HYPERTENSIVE CRISIS

It is believed that an uprising of BP secondary to a stimulus known or unknown trigger this event. During the initial uprising of BP the endothelium releases nitric oxide. When the arteries and arterioles detect this high BP, they respond with vasoconstriction and subsequently with hypertrophy to limit that the high blood pressure reaches cellular levels. The prolonged contraction of smooth muscle causes an endothelial dysfunction, a loss of nitric oxide release and an irreversible elevation of peripheral vascular resistance. Without the response of nitric oxide, there is a major endothelial damage. The endothelial dysfunction is triggered by inflammation induced by a distention mechanism that increases the expression of inflammatory markers such as cytokines, endothelial adhesion molecules and endothelin-1. These molecular events increase the endothelial permeability, inhibit fibrinolysis and as a result, they produce an activation of the coagulation cascade. This coagulation event, plus the adhesion and platelet aggregation cause the deposition of fibrinoid material, and also an increase in arterial inflammation and vasoconstriction. In addition of the whole event, there is an amplification of the

renin-angiotensin system which contributes to vascular lesion and ischemia [67].

TYPES OF HYPERTENSIVE CRISIS

Hypertensive emergency could be potentially threatening to life and is characterized by an elevated diastolic BP of 110 mm of Hg with end organ damage manifested by lightheadedness, confusion, altered mental status, encephalopathy, malaise, intracranial or subarachnoid hemorrhage, blurry vision, blindness, and retinal hemorrhages. Other findings are left ventricular insufficiency, pulmonary edema, angina, myocardial infarction, aortic dissection and an acute renal failure. It needs to be treated shortly.

Hypertensive urgency is characterized by a diastolic BP more than 110 mm of Hg, it does not have target organ damage and it is not threatening to life. It can be treated in hours or days with oral therapy [89].

THE USE OF NIFEDIPINE

It is a drug that belongs to the dihydropyridines family or calcium channels blockers. It is a vasodilator that if it is quickly absorbed it may cause a very fast vasodilation that can produce an activation of the sympathetic system and release of catecholamines. Diltiazem and verapamil do not have these effects [9]. Nifedipine inhibits the flow of transmembrane calcium ions to cardiac and smooth muscle from arteries and arterioles. Its half-life is 2 hours. It is indicated for vasospastic angina, chronic stable angina and HTN. The FDA cardio renal advisory committee does not approve the use of sublingual nifedipine in the treatment of a hypertensive crisis. Its side effects are: cephalgia, fatigue, lightheadedness, nausea, paresthesias, somnolence, pruritus, rash, abdominal pain, dry mouth, dyspepsia, flatulence, arthralgias, tingling in lower legs, unspecific precordial pain, dyspnea, impotence and polyuria. All these side effects have an incidence of less than 3% [112].

Its sublingual use has been debatable the last years. A reason of his sublingual administration is because the sublingual area is richly capillarized and after squeezing one nifedipine capsule it would be absorbed very quickly than if it is swallowed. There is no evidence to support this, though. There was a study that included 11 patients and they were asked to bite one 10-mg nifedipine capsule and kept all the contents in their mouths for a short period of 20 minutes without swallow. Blood samples were withdrawn and it was found that nifedipine plasma levels were low (10 nm/dl).

Subsequently, the same group was asked to bite the capsule and immediately swallow it. This time, the absorption was much better and they found plasmatic levels of nifedipine more quickly (82 mg/dl). The authors concluded that the oral mucosa was a deficient barrier for the absorption of nifedipine [13]. In other study, patients underwent general anesthesia with an inflated nasogastric tube. They received the content of one 10-mg nifedipine capsule in the sublingual mucosa. In the meanwhile the investigators were measuring the plasmatic levels of nifedipine, and found that this was low. When the investigators deflated the nasogastric tube, they registered high plasmatic levels of nifedipine. They concluded that the contents of one nifedipine capsule were mixed with saliva and flow down through the esophagus to be absorbed in the gastric mucosa [14].

REPORTED SIDE EFFECTS OF NIFEDIPINE

Watcher et al [15] reported 3 cases of symptomatic hypotension in which patients developed tachycardia, lightheadedness, nausea, and chest pain after multiple nifedipine doses and none of the patients had past medical history of cardiac disease. O' Malia et al [16] reported 3 cases of patients without a past medical history of cardiac disease and developed marked hypotension after receiving one 10 mg-nifedipine capsule. 2 of these patients had an anterior myocardial infarction based on changes in the EKG and elevated cardiac enzymes. The authors advised that patients with a history of coronary artery disease and left ventricular hypertrophy should not be taking this drug. Peters et al [17] published one case of one patient with hypotension and prolonged QT interval after nifedipine use. An hour later, the patient developed torsade de pointes and ventricular fibrillation. A metanalysis that included 19,000 patients in 28 studies found that nifedipine is direct and proportionally related to an increase in mortality with doses that are more of 60 mg daily [18]. Nifedipine has been associated to cerebrovascular accidents as well, most likely secondary to a sudden lowering of high BP [19].

SUBJECTS AND METHODS

The study was performed in the IMSS General Hospital "Lic. Benito Juárez" at Ciudad Juárez, Chihuahua, México. It was an observational, prospective study. We included 23 patients with no past medical history of cardiac disease that were going to receive one 10-mg nifedipine capsule sublingually prescribed by the emergency room doctor. All of the patients underwent a basal EKG and BP taken prior to receiving the sublingual dose, and after 30 minutes we

perform another EKG and took BP again and we compared the changes.

RESULTS

All patients had less than 5 years of being diagnosed with HTN. The most common complaint was cephalaea (29.1%), chest pain (16.6%), lightheadedness (14.5%), nausea and paresthesias of left thoracic extremity (6.2%), dyspnea and lipotimia (4.1%) and vomit, epistaxis, asthenia, phosphenes and blurry vision (2%). The youngest patient was 23 years old and the oldest was 77 years old. The mean age was 53.1 years old.

CHANGES IN THE EKG

Heart rate: 11 out of 23 patients had a mild increase in heart rate, whereas 3 patients had mild decrease in heart. 9 patients maintained the same heart rate in the basal EKG and in the one taken after.

PR segment and QT interval: There were not changes in these parameters.

ST segment: 5 patients had not changes in this parameter. In 13 patients we identified nonspecific changes of ST segment. 3 patients had nonspecific incomplete atrioventricular block. We identified one case of patient with a QS wave.

T wave: We detected one case of a female patient with peaked T-waves in leads V5 and V6.

Figure 1

Figure 1: EKGs from a female patient taken before and after one dose of sublingual nifedipine with inverted peaked T-waves in leads V5 and V6.

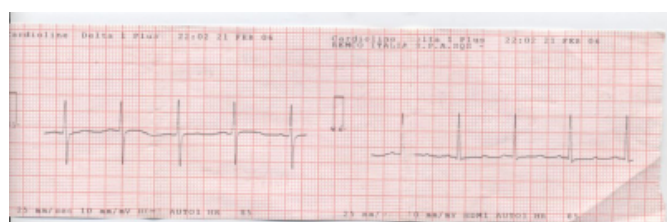
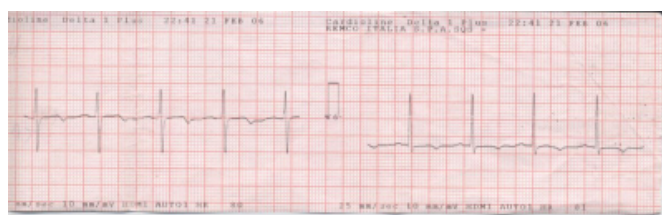


Figure 2



Changes in BP: The highest BP registered before the treatment of sublingual nifedipine was 210/140 mm of Hg and the lowest 140/110 mm of Hg. The BP taken 30 minutes after the use of sublingual nifedipine improved with an average of 24 mm of Hg for systolic BP and an average of 26 mm of Hg improvement in diastolic BP. At the end all of the patients, remained with high BP.

DISCUSSION

In some Latin American countries is still common the use of sublingual nifedipine as therapy for hypertensive crisis in the emergency room, although there have not been studies that had proven its efficacy. Patients over 65 years old seem to be the most affected group, even low doses may induce a myocardial infarction [20]. The most common side effects of nifedipine are tachycardia, negative inotropic effect and an increase of cardiac output.

The key in the diagnosis of hypertensive crisis is to differentiate between a hypertensive emergency and urgency. Taking a brief medical history and a good physical examination can lead us to make the right diagnosis, figure out the severity of the disease and the right treatment [21]. The recommended drugs in the treatment of hypertensive emergency, which requires to be lowered immediately, are: sodium nitroprusside, labelatol, fenoldopam, nicardipine, esmolol, methyldopa, and hidralazine. The main goal is to reduce BP by a maximum of 25% within minutes to 2 hours and have it below 160/100 mmHg within two and six hours unless there is target organ damage. Treatment of hypertensive urgency requires hours to days to be lowered. Such drugs are captopril, clonidine and labetalol. Even Nitroglycerin could be used in both, preferable in patients who have evidence of myocardial infarction [222324252627].

The real administered sublingual dose from one 10-mg nifedipine capsule after we squeeze it under the tongue may be close to 7-8 mg, so it is not a complete dose. A common side effect of this drug is reflex tachycardia. In our study some patients even had a decrease in heart rate, so we may conclude from this finding that the sublingual absorption

may be minimally. It has also been reported heart blocks as a rare side effect of this drug, and we had a few patients with those EKG findings. Sublingual administration works well for other drugs, but not for nifedipine. We did not perform cardiac enzymes studies because we did not find a clinical correlation with the EKG findings although we should have considered in diabetics. We may conclude that after we put a sublingual nifedipine dose, it mixes with saliva and goes through the esophagus to be absorbed in the gastric mucosa. The higher the heart rate the higher the possibility of myocardial ischemia. After 30 minutes of one dose, the symptoms improved and the BP was lowered, but not to a normal range, and all the patients were discharged and recommended for a follow up visit with their primary care provider. Nifedipine does cause changes in the EKG. Using nifedipine in the treatment of a hypertensive crisis is not safe neither reliable, and we should not use it in the treatment of hypertensive crisis.

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