Test the Antiarrhythmic Effect of Intravenous Nitroglycerine on Ischemic Quadrigeminy

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Abstract
Premature ventricular contractions are one of the most common cardiac arrhythmias. In the current case, there had happened dramatic response of premature ventricular contractions quadrigeminy after nitroglycerin infusion. Although of information rarity about the true incidence of quadrigeminy, they are common in clinical practice. Independent negative prognostic implications of premature ventricular contractions in the setting of advanced structural heart disease are established. Undoubtedly, they represent an increased risk of sudden death in structural heart disease. However, premature ventricular contractions are one of the manifestations of ischemic heart disease. Specifically, in coronary artery disease, the frequency and complexity of premature ventricular contractions are associated with mortality. Nitroglycerin is a standard anti-ischemic agent. So why don’t use it as antiarrhythmic in like the current case?

Keywords: Antiarrhythmic; Nitroglycerine; Ischemic; Quadrigeminy; Ischemic Heart Disease

Abbreviations: AMI: Acute Myocardial Infarction, ECG: Electrocardiogram, IHD: Ischemic Heart Disease, PVC: Premature Ventricular Complexes

Introduction
Nitroglycerin is the most commonly and oldest prescribed short-acting anti-anginal agent. Although the drug was introduced in clinical use since 1879, there remains an important need to educate both patients and health care providers on the various benefits of short-acting nitrates. Nitrates are vasodilators with predominant venous effects on large capacitance vessels. However, they increase coronary collateral circulation, increase aortic compliance and conductance and blood flow to ischemic areas of the myocardium. Nitrates alleviate anginal symptoms by directly influencing the coronary arteries, coronary collateral circulation, aortic compliance and conductance, and blood flow to ischemic areas of the myocardium [1]. Short-acting nitrates are beneficial in acute ischemic heart disease (IHD) [2]. Myocardial ischemia is the result of an imbalance between myocardial oxygen demand and myocardial oxygen supply. Despite of nitroglycerin clinically effective in the therapy of this condition, its exact mechanism of action is still uncertain [3]. Because of clinical observations suggesting that nitroglycerin may suppress premature ventricular contractions (PVCs) during acute ischemia, a study was undertaken to assess the effect of nitroglycerin on incidence of PVCs in patients with acute myocardial infarction (AMI) [4]. Nitroglycerin yield a significant more rapid reduction in ventricular arrhythmias: 6 hours after onset of recording, the number of PVCs had declined to 39% of the baseline value [5]. Nitroglycerin is one of the most useful anti-ischemic agents. IHD may manifest and presented with ventricular arrhythmias like PVCs. Despite of nitroglycerin is not known as antiarrhythmic drug but Suzanne B. and her fellows in reported that: the clinical observations suggesting that nitroglycerin may suppress PVCs during acute ischemia [6]. The corresponding author also reported case of bigeminy premature ventricular contractions with dramatic response of bigeminy to nitroglycerin infusion [7]. The data indicates that nitroglycerin may decrease the number of premature ventricular complexes for up to 3 hours in patients with AMI [8].

Quadrigeminy means a cardiac arrhythmia in which every fourth beat is a ventricular premature complex (extrasystole) or three sinus beats between extrasystoles [9]. PVCs are characterized by premature and bizarre shaped QRS complexes that are unusually long (typically >120 msec) and appear wide on the ECG. The QRS complexes are not preceded by a P wave, and the T wave is usually large and oriented in a direction opposite the major deflection of the QRS [10]. Patients are usually asymptomatic [10]. The clinical significance of PVCs depends on their frequency, complexity, and hemodynamic response [10]. The most suitable differential diagnoses for quadrigeminy is a concealed bigeminy. Concealed bigeminy is a recurrent unifocal extrasystoles separated from one another by an odd number of normally conducted sinus beats (S) [11,12]. Odd or even numbers of interectopic sinus beats (S) in long electrocardiographic strips are essential for both analysis and differentiation. The following equations are used to analyze the rhythm of concealed bigeminy: (S = 2n - 1) or quadrigeminy; (S = 4n - 1), where n is any positive integer, S is numbers of interectopic sinus beats [9,12]. PVCs are caused by an ectopic cardiac pacemaker located in the ventricle.
Suggested pathophysiological mechanisms for PVCs are reentry, triggered activity, and enhanced automaticity [10]. Factors that increase the risk of premature ventricular contractions include: male sex, advanced age, African American race, hypertension and underlying ischemic heart disease, a bundle-branch block on 12-lead ECG, hypomagnesaemia, and hypokalemia. The followings causes implicate in PVCs: Hypokalemia, hypomagnesaemia, acute myocardial infarction, ischemic heart disease, myocarditis, cardiomyopathy, myocardial contusion, mitral valve prolapse, hypoxia and/or hypercapnia, digoxin, sympathomimetics, tricyclic antidepressants, aminophylline, caffeine, cocaine, amphetamines, alcohol, tobacco, and hypercalcemia [10,12].

**Case Presentations**

A 70-year-old worker, heavy smoker, Egyptian married male patient presented to the emergency room with epigastric pain, dizziness, and palpitations. The gastroenterologist referred him to hospital for cardiac consultation. He had managed him as gastritis. Patient showing no reliving of epigastric pain after about 6 weeks of treatment with oral omeprazol (40 mg once daily) and ranitidine (150 mg twice daily). The Patient denied any history for cardiac disease. He is still heavy cigarette smoker (60 cigarettes daily) for about 40 years. The case was admitted in the critical care unit for symptomatic multiple PVCs. On examination, the patient was conscious. His vital signs were as follows: blood pressure: 150/90 mmHg, pulse rate: 70/minute, irregular pulse with dropped beats, and temperature: 37.1°C. Cannon waves were seen on Jugular venous pressure examination. He appeared a dizzy and dyspneic. Irregular heartbeats were noted on heart auscultation. No more relevant other clinical data. Sine wave of hyperkalemia was possible differential diagnosis for the case.

The initial ECG tracing showed quadrigeminy through all ECG leads with pathological Q wave in the inferior leads; II, III, aVF, ST wave depression in V4,5 ±6 leads, and intraventricular conduction defect (Figure 1). The physician had started to giving

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**Figure 1:** ECG tracing of presentation A: showing quadrigeminy through all ECG leads except technical artifact moved of lead V6 (Blue arrows) with pathological Q wave in the inferior leads; II, III, aVF (Red arrows), ST wave depression in V4,5 ±6 leads (Green arrows) and intraventricular conduction defect. B: ECG strip showing quadrigeminy (Blue arrows)

**Figure 2:** ECG tracing was taken within 2 hours after nitroglycerin IV Infusion. A: showing complete electrocardiographic disappearance for quadrigeminy with normalization of ST segment in V4,5 ±6 leads (Green arrows) and persistent pathological Q wave in the inferior leads; II, III, aVF (Red arrows). B: ECG strip showing pathological Q wave in the inferior leads; II, III, aVF (Red arrows)
of nitroglycerin IVI in very low dose (2.5mg/50 ml solvent, 7.5 ug/min, with 3 drops/min) relatively for 30 minutes only as a therapeutic and diagnostic test [7]. No more added any medications with nitroglycerin at this time. Complete clinical improvement and electrocardiographic disappearance for quadrigeminy had happened within 20 minutes. His vital signs within 20 minutes post nitroglycerin IV infusion were as follows: blood pressure:130/70 mmHg, pulse rate:84/minute, completely regular pulse with disappeared the above-dropped beats, and temperature: 37.1°C. ECG tracing was taken within 2 hours of nitroglycerin Infusion (Figure 2). Standard anti-ischemic drugs (Aspirin 75 mg tablet; OD, nitroglycerin retard (2.5 capsule; BID); bisoprolol (5 mg tablet; OD) and atorvastatin (40 mg tablet; OD) were given to the case for about 8 hours then discharged with no problem. The requested workup was: Electrolytes profile show: Na+:137 mmol/L, K+:4.6 mmol/L, ICa++:1.11 mmol/L, Hb: 14.4 gm/dl, Random blood glucose: 123 mg/dl. Unfortunately, no any problem. The requested workup was: Electrolytes profile show: Na+:137 mmol/L, K+:4.6 mmol/L, ICa++:1.11 mmol/L, Hb: 14.4 gm/dl, Random blood glucose: 123 mg/dl. Thyroid function tests were normal. The echocardiographic report showed evidence of IHD with inferior regional wall motion abnormality with systolic dysfunction and low ejection fraction (51%, that was measured with 2-D). Troponin T test was negative. Unfortunately, coronary angiography was not done.

Discussion

Overview

• The current case was a quadrigeminy related to the ECG evidence for ischemic heart disease like a pathological Q wave in the inferior leads; II, III, aVF and ST wave depression in V4,5 ± 6 leads rather than the later ischemic echocardiographic evidence.

• Presence of pathological Q wave in the inferior leads; II, III, aVF without past history of IHD or AMI indicating silent coronary heart disease.

• Quadrigeminy was identified in both clinical and electrocardiographic data. Regards of the clinical status; there was one skipped beat every three normal beats on fixed continuous pulse assessment for one minute. But on electrocardiograph examination; there were: fixed continuous PVCs with the fourth beat ventricular premature complexes every three sinus beats between extrasystoles rather than unusually long compensatory pauses.

• Quadrigeminy in ECG tracing is multiform in morphology that is an indication for the presence of multiple cardiac foci. PVCs that all have the multiple different appearances, they are labeled "multifocal"; this is a possible sign of higher a risk of complications [13].

• Q wave in the current case are considered pathological due to: Q wave was; > 40 ms (1 mm) in width, > 2 mm in depth, and > 25% of the depth of QRS complex.

Study method was observational case study

• I can't compare the current case with similar conditions. There are no similar or known cases with the same management for near comparison.

Study question here; How did quadrigeminy yield dramatic response to nitroglycerin?

• The primary objective for my case study was clearing the impact of ischemic heart disease in inducing quadrigeminy.

• Secondary objective was clearing the dramatic response for ischemic quadrigeminy to nitroglycerin.

Limitations of the study

• There are no known limitations for the study.

• Despite of the used dose was suboptimal, but hypotension is possible contraindication for nitroglycerin.

Recommendations

• It is a recommended to widening the research in ischemic quadrigeminy-nitroglycerin relationship.

• Using for the other nitroglycerin and nitrates formulations like sublingual spraying tablet are suggested for possible success in future broad spectrum studying.

Conclusions

• Testing the dramatic response of quadrigeminy with nitroglycerin IVI to differentiate the ischemic cause from the others.

• As regards to the dramatic response of quadrigeminy PVCs to nitroglycerin, it may be used therapeutically as a new antiarrhythmic agent in like quadrigeminy case. Nitroglycerin may have indirect effect through increasing myocardial perfusion not due to documented clear antiarrhythmic effect.

• This test may decreases the overload uses of antiarrythmic drugs and their adverse effects.

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References


