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Ventricular Tachycardia due to Flumazenil Administration

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Abstract: Flumazenil is one of imidazo-benzodiazepine (Anexate) which has been generally used as benzodiazepine competitive antagonist for the treatment of benzodiazepine intoxication during recent decades. Some has recommended diagnostic usage in ICU as well, for suspected benzodiazepine intoxicated cases. In this study we present a patient intoxicated with lorazepam who developed a ventricular tachycardia after receiving flumazenil as therapeutic mean, though the attack was appropriately terminated by administration of a bolus dose of Amiodarone. We believe that the ventricular tachycardia onset in above mentioned case is secondary to Flumazenil administration in susceptible patient with previous history of ischemic heart disease. Ventricular tachycardia has rarely reported as flumazenil side effects.

Key words: Flumazenil, ventricular tachycardia, amiodarone, ischemic heart disease, benzodiazepine intoxication

INTRODUCTION

Flumazenil is an Imidazo-benzodiazepine derived medication, generally used as competitive benzodiazepine antagonist in benzodiazepine poisoning during previous years. Some has recommended using flumazenil just in benzodiazepine poisoning in ICU (Anonymous, 1992).

CASE

The patient discussed, was a 60 year old man brought in Emergency Department (ED) of Imam Reza hospital, Tabriz University of medical sciences, Iran in coma. According to the companion's claims, he had not been wakening up in the morning but they had just found him snoring and then they transported him to the hospital. Concerning deep comatose status, endotracheal intubation was carried out once patient entered the emergency department and in continue a plenty of milky secretion was extracted by suction. In physical examination, pupils were reactive and isochoric. A trivial rhonchi was heard on lungs auscultation and other examinations revealed no positive finding in head, neck, abdomen, pelvic and extremities. The only positive findings were decreased muscular tone and bilateral extensor plantar reflexes. Concerning medical history of ten years of diabetes mellitus and a five years history of hypertension and ischemic heart disease (2 vessle disease) and psychiatric positive background he was clearly receiving only glibenclamid, nitrocantine and atorvastatin including intermittent courses of lorazepam. Echocardiography had shown a mild left ventricular hypertrophy with left ventricular ejection fraction of 35% without any obvious valvular heart disease or pulmonary arterial hypertension. The coronary angiography showed 90% stenosis in the proximal of the left anterior descending coronary artery while the mid portion of the right coronary artery had 80 to 90% stenosis. The patient had the history of unstable angina, though never experienced MI or VT. When, presenting to emergency Department, vital sign were recorded as follows: BP: 100/50, HR: 71, RR: 26, PH = 7.23, PCO_2 = 55 mmHg, HCO_3 = 25.5 mmol L^{-1} and SPO_2: 75%, though then increased to 92%. Cardiac biomarkers were within normal range. The primary ECG was a normal sinus rhythm with T-wave inversion in the anterior precordial leads (IHD). Electrolyte studies in ED were normal. EMS had recorded the SPO_2 of 90% at home before falling to 75% during 7 min of transport to the hospital. BS was measured as 136 mg dL^{-1}. Concerning decreased level of consciousness, naloxan administration was firstly tried which didn't change the clinical status. Not having the advantage of urine drug screen tests in our ED setting, we tried to obtain the most reliable past drug and medical history as possible. Accordingly, family brought an empty sheet of 15 lorazepam pills found on his bedside; therefore, 0.2 mg of Flumazenil was primarily administered to approve the probable diagnosis of benzodiazepine

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intoxication. The administration process had completed a gap of about 20 min after the last 0.1 mg diluted boluse of naloxan. Since proper response with increased Loss of Consciousness (LOC) was acquired, titrated dosages of flumazenil were intermittently tried until complete awareness was achieved at a total dose of 3 mg. Regarding to the level of consciousness, patient was extubated after a bolus of lidocaine (100 mg IV). Seconds after extubation, patient developed a pulsative ventricular tachycardia detected on monitor screen. One hundred milligram of lidocaine was pushed intravenously which failed to control the arrhythmia. Therefore, a 150 mg of amiodarone was tried IV which terminated the arrhythmia in 90 sec. For documentation a second ECG was recorded then. It showed a tachycardia sinus rhythm (HR = 108). Before overall disposition a brain CT scan was prepared that revealed on pathologic finding.

DISCUSSION

Flumazenil, a specific benzodiazepine antagonist has been used in increasing frequency in recent years (Votey *et al*., 1991). Although, essentially quite safe, serious adverse events (cardiac dysrhythmia, bradycardia and death) related to its administration to patients with mixed overdose have been reported, particularly when tricyclic antidepressants have been ingested (Dart *et al*., 2004). These adverse reaction included seizure, ventricular tachycardia (Marchant *et al*., 1989; Salah, 2005) acute decrease in blood pressure (Hojer *et al*., 1990).

Two deaths have been reported after administration of flumazenil to patients intoxicated with a mixed of drugs (including benzodiazepines) even death (Burr *et al*., 1989; Lim *et al*., 1989).

Benzodiazepines are the most commonly used drugs in intentional self-poisoning; they have been reported to be involved in more than 50% of all intoxications in Europe (Hojer *et al*., 1989; Leykin *et al*., 1989).

Another study also showed that bolus administration of high doses of flumazenil in mixed intoxication implicating benzodiazepine and cyclic antidepressants has the potential risk of cardiac dysrhythmia in animals (Lheureux *et al*., 1992).

There are three triggers, can be mainly discussed as causing agents for developing ventricular tachycardia in above mentioned case.

First of all, Naloxan can start ventricular tachycardia as a profound noxious stimulus. However, in this case, such effects sound unlikely, because Ventricular Tachycardia occurred 20 min after last administered 0.1 mg of diluted Naloxan.

Extubation can play as a noxious stimulus as well. But in our case, as regarded, extubation pretreatment with 100 mg of lidocaine (IV) makes contribution of such cause very unlikely.

We believe that this patient developed ventricular tachycardia due to flumazenil administration as the last but the most likely proposed trigger (Short *et al*., 1988). This phenomenon has likely occurred in base of primary sympathetic release or secondary to benzodiazepine withdrawal (Marty *et al*., 1986; Smith and Wesson, 1985). Patients with history of ischemic heart disease are especially susceptible to develop such reactions (DiMicco, 1987). According to the literatures, developing ventricular tachycardia has been limitedly reported as a side effect of Flumazenil administration (Anonymous, 1992; Marchant *et al*., 1989).

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