Haloperidol- Induced Cardiopulmonary Arrest: A Case Report

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ABSTRACT:
Haloperidol is an antipsychotic which is widely used in emergency and psychiatry units. Sometimes, it is encountered some serious complications associated with haloperidol use, particularly haloperidol induced cardiac ones. In literature, life-threatening arrhythmias have been reported as case reports. Here, we report a case who had haloperidol-induced cardiopulmonary arrest.

Keywords: haloperidol, cardiopulmonary arrest, side effect

Journal of Mood Disorders (JM000) 2016;6(1):28-31

INTRODUCTION

The average life expectancy of the patient with schizophrenia is approximately fifteen years less than that of the general population. Cardiovascular diseases are one of the most leading factors that cause death in schizophrenic patients; and there has recently been a 1/3 increase in the relative risk of death related to cardiovascular diseases (1,2). The effects of antipsychotic drugs on the cardiovascular system are prolonged QT interval and arrhythmia, conduction disorders, left ventricular conduction disorder, sinus node abnormalities, receptor blockage, myocarditis, cardiomyopathy and postural hypotension. Being one of the most important one of these effects, the delayed ventricular repolarization, and as its projection in electrocardiogram, the prolonged of QT interval may increase the risk of ventricular tachyarrhythmia and cardiac-dependent sudden death (3,4).

It has been reported that many typical antipsychotic drugs such as thioridazine, pimozide, haloperidol and chlorpromazine cause to prolong the QTc interval (5). It has, however, been shown that the risk is relatively higher with thioridazine, and its rate of cardiac complication (QRS and QT interval lengthening) is equal to or higher than those of tricyclic antidepressant drugs (6).

Haloperidol is a butyrophenone derivative, typical antipsychotic drug still used in the treatment of psychotic disorders, agitation and aggressive behaviors, delirium and mania. In addition to the D2 blockage, it also inhibits the α1 adrenergic receptors. It has far less effect on muscarinic, cholineric or histaminergic receptors (7). If enough care is not taken during the use of this medication,
severe complications may occur. Among these complications, hypotension, QT interval lengthening and sudden death are especially important (8). While sudden deaths related to Haloperidol are possible in case of overdose, they are also possible with normal intravenous and oral therapeutic doses (9,10).

Cardiopulmonary arrest related to the use of haloperidol is reported as case reports, though not very often, in the relevant literature (11,12). No such a case is reported in our country.

We aimed to report a case of cardiopulmonary arrest occurring with the use of haloperidol in this study.

CASE

Z.Ç. was a 31-year-old, divorced, illiterate, non-working female patient who had no history of any organic disease including any cardiac disease, hypertension, and diabetes mellitus, and of any cardiac risk factor. In her familial history, there were no relatives who had sudden death before 30 years old. She was also not on additional treatment. The patient was diagnosed as atypical psychosis and followed by out patient units. She had been admitted to another inpatient clinic because of agitation, disorganized speech, auditory hallucinations and paranoid delusions. This exacerbation in positive symptoms seemed to be associated with treatment non-compliance, as learned by her first degree relatives. She was started 20 mg per day of haloperidol and 4 mg per day of biperiden intramuscularly. She had a history of olanzapine, quetiapine and clozapine use. She did not use haloperidol before. At the day 4 of her admission, she developed a sudden shortness of breath and cyanosis following cardiopulmonary arrest. The patient was begun to receive a cardiopulmonary resuscitation, and was intubated. During the resuscitation, a ventricular fibrillation occurred, and a cardioversion was performed. When her pulse returned to normal, the patient was hospitalized to the internal medicine intensive care unit of Fırat University.

When the patient who was being followed in the intensive care was brought to hospital, her vital parameters were as follow: Blood pressure: 140/80, pulse: 88, sinus rhythm in electrocardiography (ECG), first degree atrioventricular block (AV) block, negative T wave in anterior and inferior derivations, and the QTc was 520 msec. Her laboratory tests were as: Blood urea nitrogen: 20(10-50 mg/dL), Creatinine: 0.5(0.6-1.2 mg/dL), potassium: 3(3.5-5.5 meq/L), sodium: 141(138-145 mmol/L), aspartate aminotransferaz: 62(5-40 U/L), alanine aminotransferaz: 56(5-40 U/L), magnesium: 4.4(1.7-2.7 mg/dL), calcium: 9(8.5-10.8 mg/dL), white blood cell: 13,410(4-10 10^3/mm^3). The patient who was monitored during the clinical care experienced ventricular tachycardia (VT) attacks, and thus was began to be medicated with amiodarone. The patient who was asked for a psychiatric consultation because of her agitations was given a 100 mg/day quetiapine. The patient whose VT attacks decreasingly continued in the intensive care was extubated when her general medical condition recovered in the 12th day of hospitalization. As a hemiplegia related to hypoxic-ischemic encephalopathy occurred in the patient, she was transferred to the neurology department in the 22nd day of her hospitalization, and she was taken to a physical therapy program.

DISCUSSION

In the first ECG after resuscitation of our patient without a history of any organic disease, there was T wave negativity in anterior and inferior derivations, and first degree Av block; and the QTc interval with the value of 520 msec. These findings point out the cardiac side effects, as the reason for the cardiopulmonary arrest occurred in the case, of haloperidol used in the treatment.

The QT interval stands for the time between the beginning of the QRS complex and the end of T wave, and the ventricular repolarization time in ECG (13). As the length of the QT interval decreases with the increasing heart rate, in the QT assessments, heart rate changes should necessarily be taken into account, and “the QT interval corrected according to heart rate (QTc)” should be specified (14). The QT interval may be affected by heart rate, autonomic tonus, catecholamine level, age, gender, serum electrolytes and some drugs (15).

Significant QTc prolongation is described as the QTc interval being longer than 450 msec. in males, and then 470 msec. in females. Although there is no consensus on the QTc value in which the arrhythmia risk is the least, some experts have suggested a 500 msec. QTc value as the lower limit in the actual risk for ventricular tachyarrhythmia (16,17). The QTc prolongation is a risk factor for the development of life-threatening cardiac arrhythmias, and may cause polymorphic ventricular tachycardia, ventricular fibrillation and sudden death (18).
Drugs constitute the biggest group among the acquired reasons inducing the QTc prolongation. Many of these drugs generally affect the potassium ion channels in heart muscle cells (in ventricular myocytes), and lead to the decrease of repolarization, the lengthening of action potential duration and QT interval. The drugs that prolong the cardiac repolarization may lead to potential fatal arrhythmias (19).

It has been reported that many typical antipsychotic drugs such as thioridazine, pimozide, haloperidol and chlorpromazine lead to the prolongation of QTc (5,20). It has been found in a study that the QTc interval is longer than 453 msec in 7% of 163 schizophrenia in-patients (5). Warner et al. report that the QTc interval is lengthened in 23% of 111 chronic schizophrenia patients and in 2% of 42 control subjects (21). In a study performed in Turkey, 44 patients using antipsychotic drugs were compared with a 32 non-users group, and it was reported that the QTc values were longer in the patients using haloperidol or thioridazine than in those using risperidone or zuclopenthixol, and the control group (22).

Except for sertindole and ziprasidone, the effect of other atypical antipsychotics on the QTc interval is very low (23). It is reported in a study done on 35 patients with psychotic disorder that the ziprasidone with a dose of 160 mg/day increased the QTc value averagely 17 msec. (24). In another study, the QTc interval’s getting over 500 msec with ziprasidone is reported to have been less than 1% (25). In a study conducted upon 37 schizophrenia patients, ziprasidone with a dose of 16 mg/day is reported to have increased the QTc value 19 msec on average (26).

In another study, in which 6,693 patients were performed a 24-hour ECG monitorization, it is identified that the QTc interval over 440 msec increased the risk of sudden death twice (27). In a case-control study done on the residents of aged care facilities in six American states, Liperoti et al. report that the risk of hospitalization due to cardiac arrest and ventricular arrhythmia in especially the patients having a heart disease beforehand and using typical antipsychotics nearly doubled (28). In the literature, there are few case reports of life-threatening and arrest due to the lengthening of QT upon use of haloperidol (11,12). The potential of Haloperidol for causing arrhythmia and sudden death bears less risk compared to thioridazine. In an autopsy study, it is reported that of the 46 sudden death cases occurring with antipsychotics 28 cases were those of using thioridazine, while only 6 cases were of those using haloperidol. It is further reported that in none of these 6 cases haloperidol medication was alone, whereas 15 of the 28 thioridazine cases used only thioridazine (29).

It is thought that by blocking the potassium ion channels in heart muscle cells (in ventricular myocytes), Haloperidol leads to the decrease of repolarization, the lengthening of action potential duration and QT interval, and arrhythmias (30).

If there are flat T waves in the ECG of the patients using Haloperidol, and if there are U waves, and the QTc interval is over 450 ms, or the QTc interval is lengthened by 15-20%, the medication should be stopped. Moreover, such electrolyte values of the patient as sodium, potassium, calcium should be followed, and any medication lengthening the QT interval should be avoided (31).

By the way, QTc prolongation of the patient might have been associated with ventricular fibrillation, atrioventricular block and hypokalemia apart from haloperidol use.

As to conclude, the risk of QT prolongation and cardiac arrest should be taken into account when using haloperidol, which is still used very often in the treatment of delirium and agitation. Periodical ECG tracings should be performed for the patients using haloperidol, and special precautions should be taken for the patients who have risk of QT lengthening. Further research that may involve wider patient groups and that can explain the mechanism of haloperidol’s lengthening QT interval needs to be carried out.

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