EXPERIENCE OF THE ADVERSE EFFECTS OF HALOPERIDOL: TORSADE DE POINTES

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[Esperienza sugli effetti avversi dell’aloperidolo: torsione di punta]

SUMMARY
Having analyzed the cardio-toxic effects of haloperidol, the authors consider the molecular mechanisms responsible for the cardiac toxicity and they describe a clinical case of torsade de pointes that they have observed. They also analyze the inherent problems of the case and they consider the therapeutic treatment adopted.

They conclude asserting the validity of this treatment, the objective of which is to bring the QT interval back within physiological range.

Key words: Schizofrenia, haloperidol, cardiotoxic effects, extension of the Q-T, torsion of point

Introduction

The tolerance profile of the haloperidol has recently been re-evaluated, to European levels, in the light of evidence of serious cardiac toxicity; in fact, it causes an extension of the Q-T line and torsades de pointes and it is responsible for cases of sudden death.

In particular, the extension of the Q-T line is an indication of heterogeneity of the ventricular re-polarization phase, a risk factor for the triggering of ventricular heart trouble (torsade de pointes and ventricular fibrillation) from a precocious ventricular systole.

The precise relationship between the genetic alteration of the re-polarization, the lengthening of the Q-T and torsade de pointes is still not clear.

One of the molecular mechanisms put forward to explain the cardiac toxicity is the blockage of the channels to the K. These channels are responsible of the re-polarizing IKR current of the potential for cardiac action.

Among first generation anti-psychotics, haloperidol is one of the medicines most used for the management of psychiatric emergencies and for the maintenance therapy of schizophrenia.

Its mechanism of action is connected to its ability to influence the activity of the neuronal dopamine, noradrene and serotonin transmission system through a mechanism of prolonged transfer of the active molecule, guaranteeing a prolonged action of the active principle.

The adverse effects of haloperidol are caused by the activity of the medicine in the limbic system of the cerebral bark which causes behavioural effects and in the ganglions of the base, inducing extra-pyramidal motor effects.

Clinical case

The patient A.G., a male aged 52, who had been suffering from schizophrenia for 5 years, according to the DSM IV criteria and was taking haloperidol 5mg 1 tablet three times/die, arrived at the hospital after a syncopic episode.

He complained about darkening of the vision and dizziness.

From the anamnesis it emerged that another syncopic episode had occurred the previous day.

We then made an ECG recording that allowed to highlight the presence of torsade de pointes: an unusual form of ventricular-tachycardia characteri-
zed by: modification of the width of the QRS in every cycle with a sinusoidal appearance, broadened ventriculograms, paroxysms, with irregular R-R and ventricular frequency: 200-250/min (Fig. 1).

In the haematic examinations, levels of potassium of 2,8 mEq/l wew shown. Given the gravity of the situation a therapeutic treatment was immediately choosen to avoid a progression towards ventricular fibrillation.

We then carried out an intravenous infusion of magnesium sulphate 1gr in 100 ml of physiological solution, in about 10-20 minutes, verifyng the haematic levels of magnesium during the course of the infusion.

To correct the low levels of potassium, potassium chloride 10 mEq/l diluted in 500 ml of physiological solution was administered in a continuous infusion.

The sudden suspension of the treatment with haloperidol, which was responsible for the torsade de pointes, is of fundamental importance.

After a period of observation, the patient was discharged following the recovery of the physiological concentrations of electrolytes and the stabilization of the ECG picture.

Discussion

Haloperidol is one of the medicines most used for the management of psychiatric emergencies and for the maintenance therapy of schizophrenia: its use is not, however, without side effects, particularly on the heart.

At this level it can cause the appearance of torsade de pointes, which often lead to sudden death.

Torsade de pointes is an unusual form of ventricular tachycardia, characterized by modifications of the width of the QRS, broadened ventriculograms and paroxysms, with irregular R-R intervals and ventricular frequency oscillating between 200 and 250 bpm; it occurs in a sinusal rhythm in people that have a notably lengthened Q-T interval.

In almost all cases this extension is secondary to hydro-electrolytic imbalances, in particular, low levels of potassium caused by the blockage of the K channels that are responsible for the re-polarizing IKR of the potential for cardiac action; it is now a known fact that haloperidol acts as a powerful blocker of these channels. It has been suggested that the risk of cardiac toxicity posed by haloperidol should be classified in relation to the basal values of the QT interval, and that other risk factors that may be present in the pathogenesis of torsade de pointes should also be analysed. A careful monitoring of the QT line using the ECG is therefore fundamental to keep the cardiac toxicity of haloperidol under control and to schedule a suspension of the medicine if alterations of the cardiac rhythm are observed.

Despite the large amount of data available on the cardiac toxicity of haloperidol, this medicine continues to be used in clinical practice, even outside hospitals where it is not possible to monitor its effects on the QT interval and the possible onset of arrhythmias associated with the extension of this interval.

Conclusion

On the basis of our experience with the patient which is described in the case report, we can state that the correction of the electrolytic imbalances (responsible for the extension of the Q-T) through the administration of magnesium sulphate and potassium chloride is the therapeutic treatment of choice.

In fact, it results in the complete clinical recovery of patients with torsade de pointes; this occurs because the magnesium sulphate is able to perform an important anti-arrhythmic action as a result of the ability of this compound to activate the pumps of Na and Ca present at the level of the plasmatic membrane, thus allowing them to be expelled from the cell against the gradient and re-establishing the physiological electrolytic equilibrium of the organism.

The advantage of this medicine derives from its extreme manageability which is associated with the ability of the kidneys to eliminate the excess amount: for this reason Mg poisoning is rare, but can occur if large quantities of it are taken.

The therapeutic purpose of the potassium chloride, on the other hand, is to replace the losses of K in order to prevent cardiac complications (particularly the paralysis of the cardiac muscle because of a hyper-polarizing block) and to stabilize the ECG picture ECG bringing the Q-T interval within the range of physiological values.
References


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