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Letter to the Editor (Case report)

Dose-dependent increase in the QTc interval in aripiprazole treatment after risperidone

Sir:

Aripiprazole (ARP) is a new atypical antipsychotic drug that has been shown to have fewer side effects in comparison to other atypical antipsychotic drugs. Antipsychotic drugs extend the QT interval (Glassman and Bigger, 2001), and are believed to cause ventricular fibrillation and sudden death. Whereas, ARP has been reported as having few actions for extending the QT interval (Stip and Tourjman, 2010), although the details remain unclear.

We treated a case in which risperidone (RIS), which has been reported as having greater actions for extending the QT interval in comparison to ARP, was switched to ARP. Then the QT interval was extended in a dose-dependent manner in relation to ARP, and we herein report the findings of this case. This study was approved by the Gene Ethics Committee of the Faculty of Medicine of Niigata University, and written consent was obtained from the patient after providing sufficient explanations.

The case was a 30-year-old male. He had no history of cardiac disease, or arrhythmia. He was undergoing single-agent therapy for schizophrenia with 4 mg of RIS per day on an outpatient basis at our department, and his psychotic symptoms were stable. However, because his psychotic symptoms worsened with no immediate cause, the dosage of RIS was increased to 6 mg per day. Because his psychotic symptoms thereafter did not improve by 29 days after increasing the dosage of RIS, we then started to switch the patient to ARP, and thereafter gradually reduced the RIS dosage until its administration was completely stopped. As a result of increasing the dosage of ARP from 18 mg to 24 mg, and then 30 mg per day, the patient's psychotic symptoms became stable. At 4 points after 6 mg of RIS, 18 mg of ARP, 24 mg of ARP, and 30 mg of ARP, each administered as single agents at a fixed dosage for 4 weeks or more, electrocardiography and biochemical examinations were performed. During the examinations, only benzodiazepines could be concomitantly used, and RIS and ARP were administered once before sleep, and electrocardiographic measurements were conducted between 9:00 and 10:00 a.m. The QT interval was corrected using Bazett's correction formula ($QTc = QT/RR1/2$).

When electrocardiography was conducted at each time point, biochemical examinations revealed no electrolyte abnormalities in the serum Na, K, Cl, or Mg levels, etc. (Table 1), and no cardiac diseases, such as arrhythmia or any other new physical disorders were observed. After switching from 6 mg of RIS to 18 mg of ARP, the QTc briefly contracted, but when the dosage was increased to 24 mg and 30 mg, the QTc was extended in a dose-dependent manner (Table 1), although torsades de pointes and other forms of arrhythmia were not observed. The switch from RIS to ARP resulted in normalization of the prolactin level in the blood, and there were no changes in body weight, or fasting blood sugar.

There have been previous reports indicating that ARP has almost no actions for extending the QT interval (Pigott et al., 2003; Stip and Tourjman, 2010), and there is also a report of a direct comparative trial with RIS in which the QTc-extending actions of ARP were comparable to those of RIS and a placebo group (Potkin et al., 2003). However, in this case, after switching from RIS to ARP, the QTc was extended in a dose-dependent manner in relation to ARP. The QTc was 406 ms, which is within the normal range, even when the dosage of ARP was increased to 30 mg, but because the QTc is affected by many other factors, such as drug interactions and age, if such other factors are present, the dose-dependent QTc-extending actions of ARP observed in this case may be a non-negligible finding.

Because the concentrations of RIS and ARP in the blood were not measured in this report, it is believed that it is necessary to conduct detailed studies including careful measurements of blood concentrations.

Supplementary materials related to this article can be found online at doi:10.1016/j.pnpbp.2010.10.024.

Competing interests

None declared.

Authorship

All authors fulfill the criteria of authorship based on their substantial contribution to conception and design, or analysis and interpretation of the data; drafting the article or revising it critically for important intellectual content; and final approval of the version to be published. No one else who fulfils these criteria has been excluded as an author. Dr. Toshiyuki Someya is the guarantor for the present manuscript; he accepts full responsibility for the finished article, has access to all data, and controls the decision to publish.

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