LETTER TO EDITORS

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MAY THE BEST FRIEND BE AN ENEMY IF NOT RECOGNIZED EARLY: POSSIBLE CARDIAC ABNORMALITIES DUE ATYPICAL ANTIPSYCHOTICS IN THE TREATMENT OF AUTISM?

Dear Editors,

We read with great interest the elegant article by Posey and colleagues, which provided to us news and views about the use of atypical antipsychotics in the treatment of autism (1).

Autism Spectrum Disorders (ASD) cause severe and pervasive impairment in thinking, feeling, language, and the ability to relate to others (2). These disorders are usually first diagnosed in early childhood and range from a severe form, called autistic disorder, through pervasive development disorder not otherwise specified, to a much milder form, Asperger syndrome (2). Furthermore, they also include two rare disorders, Rett syndrome and childhood disintegrative disorder (2). The ASD are more common in the pediatric population than are some better known disorders such as diabetes, spinal bifida, or Down syndrome (3). Prevalence studies have been done in several states and also in the United Kingdom, Europe, and Asia. A recent study of a U.S. metropolitan area estimated that 3.4 of every 1,000 children 3-10 years old had autism (4).

Although the availability of antipsychotic treatment in ASD has expanded, we will be very careful with side effects of these pharmacological agents. There is great concern over cardiovascular disease in the schizophrenic population owing to the high incidence of cardiovascular mortality (5). The excess of mortality is accounted for by a combination of increased risk factors, as patients' life style, suicide, premature development of cardiovascular disease, high prevalence of metabolic syndrome, carbohydrate and lipid metabolic disorders (6, 7). Quite interesting, one important factor that increases cardiovascular risk is the medications used to treat the core features of schizophrenia (5). In these lines, emerging data indicate that some atypical antipsychotics may be associated with cardiovascular adverse events (e.g., QT interval prolongation), suggesting that this could leads to torsade the points or sudden death (8, 9). In accordance to this reasoning, a pertinent question could be evaluated: should the physician pay more attention with possible cardiac abnormalities during antipsychotic treatment in ASD? Although the incidence of serious adverse cardiac events in response to atypical antipsychotic medications is relatively low, some considerations should be made. For example, Ravin an Levenson described a patient who developed fatal pulse less electrical activity following initiation of risperidone therapy, suggesting that prolongation of the QTc interval with severe adverse effects remains a possibility with the use of this atypical antipsychotic (10). Recently, Janion and colleagues (11) reported a case of a 53 year old female with olanzapine-induced QT interval prolongation and fatal ventricular fibrillation, suggesting that all antipsychotic drugs have the potential for serious adverse events. In 2004, Kurt and Maguire called our attention about the risk of QTc interval prolongation associated with quetiapine administration (12). They related a 14-year-old boy who ingested 1900 mg of quetiapine. One and one

half hours after ingestion, the QTc interval lengthened from 453 msec to 618 msec on the printout (manual calculation was 444 msec to 500 msec, respectively), suggesting a relationship between higher doses of quetiapine, higher serum levels and the propensity for QTc interval prolongation. Concerning ziprasidone, Posey and co-workers (1) related the potential for QTc interval prolongation with this drug on electrocardiography led to a warning in the full prescribing information. The authors suggested that ziprasidone should not be given to individuals with cardiac arrhythmias or long QT syndrome or who take other medications that can prolong the QTc interval.

Finally, we express our congratulations to Posey and colleagues for the stimulating review (1) and we are totally in agreement with their conclusion that the development of new purposes and therapeutic strategies should be evaluated with the aim to prevent and treat people with autism. In this way, new considerations and experimental, epidemiological and clinical studies should be developed to establish with precision the relationship between cardiac alterations, atypical antipsychotics and autism. In the meantime, strategies, such as taking a detailed cardiovascular history, looking for cardiovascular co-morbidity, cardiovascular risk factors and prior cardiac findings (electrocardiogram and echocardiogram), should be developed in an attempt to prevent possible cardiac abnormalities in ASD patients treated with atypical antipsychotics. We are sure that balancing these risks with the positive effects of treatment poses a challenge for psychiatry.

Yours Faithfully,

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