Journal of Pharmaceutical and Scientific Innovation

www.jpsionline.com

Research Article

IS MG^{++}-DEFICIENCY ASSOCIATED WITH AN ANTIPSYCHOTICS-INDUCED QTC-PROLONGATION?

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DOI: 10.7897/2277-4572.02690
Published by Moksha Publishing House. Website www.mokshaph.com

Received on: 15/10/13 Revised on: 20/11/13 Accepted on: 05/12/13

ABSTRACT
Atypical antipsychotics have been reported to prolong the QTc interval. Mg^{++} deficiency may also be a cause for QTc prolongation. For that reason it can be assumed that atypical antipsychotics may cause Mg^{++} deficiency and that Mg^{++} supplementation might compensate the QTc prolongation, caused by atypical antipsychotics. We compared Mg^{++} levels of 40 patients, 20 of which received atypical antipsychotics and 20 of which didn`t. Furthermore, we checked the effect of Mg^{++} supplementation on the prolonged QTc interval in patients, who received atypical antipsychotics. The data of this study show, that atypical antipsychotics decrease serum Mg^{++} level ($p = 0.001$) and are also associated with a QTc prolongation ($p = 0.069$) and that Mg^{++} supplementation abbreviates an atypical AP-induced QTc prolongation. In patients who show a QTc prolongation while receiving atypical antipsychotics, Mg^{++} serum levels should be checked and, if lowered, Mg^{++} should be supplemented before ceasing antipsychotic medication.
Keywords: Antipsychotics, Mg^{++}, QT_C.

INTRODUCTION

It is well known that a variety of drugs may prolong the QTc interval[1,2]. Especially (atypical) antipsychotics are prone to cause this adverse side effect[3,4]. This adverse side effect is often the reason for ceasing the antipsychotic medication or switching to another drug. Some drugs may also lead to a magnesium deficiency[2]. Hypomagnesaemia itself may lead to various cardiovascular adverse events, including a QTc prolongation, especially in alcoholic[5] and schizophrenic patients treated with neuroleptics[6]. As shown in case reports, magnesium supplementation improved the QTc interval in hemodialysis patients[7] and in a fetus[8]. For that reason we assumed that hypomagnesaemia may be associated selectively with a QTc prolongation in schizophrenic patients treated with atypical antipsychotics. If this hypothesis is proved, ceasing medication with atypical antipsychotics could be avoided in many cases.

Methods

We investigated Magnesium levels (blood samples were drawn in the morning hours) and QTc intervals (12-lead ECG, registered in the morning hours) of 40 in-patients in our clinic, recruited in 2012, aged 15-30 years, IQ 80-110. This sample was subdivided into two parts, i.e. that 20 patients, suffering from schizophrenia according DSM-IV, received atypical antipsychotics (quetiapine, ziprasidone, risperidone, olanzapine, amisulpride) and 20 patients, suffering from personality disorders according DSM-IV, without any former or actual neuroleptic medication. Both subsamples were well matched with respect to age (17-34 years, mean = 24 years) and sex (13 males, 7 females). Cardiac diseases were defined as exclusion criteria. Patients did not receive co-medications. The patients of the antipsychotics subsample received atypical antipsychotics for >2 months. Statistics (ANOVA) have been performed by means of SPSS 12.0. The local ethical committee approved the study.

RESULTS

Mean serum Mg^{++} level of the patients without any antipsychotic medication was 0.82 mmol/l (SD = 0.09) (reference value 0.75-1.10 mmol/l), that of the patients who received atypical antipsychotics was 0.69 mmol/l (SD = 0.11). Mean QTc interval of the patients without any antipsychotic medication was 399 ms (SD = 19), that of the patients who received atypical antipsychotics was 402 ms (SD = 22) (reference value: <500 ms). ANOVA showed that the difference between both subsamples regarding serum magnesium levels was significant ($F = 18.41$, $p = 0.001$) and not significant regarding QTc intervals ($F = 0.13$, $p = 0.715$). We could also observe a correlation of Mg^{++} and the QTc interval in the group of the patients who received atypical antipsychotics ($r = -0.62$, $p = 0.069$), but not in the group of the patients without any antipsychotic medication ($r = 0.28$, $p = 0.908$) (Figure 1). Sodium and potassium levels did not differ significantly between the subsamples.

DISCUSSION

These results suggest that hypomagnesaemia may be associated with prolongation of the QTc interval in patients who receive atypical antipsychotics: low magnesium serum levels seem to prolong the QTc interval. In the control group, i.e. in the patients without medication, we could not observe any significant correlation between serum magnesium levels and the QTc interval. This fact suggests that hypomagnesaemia is associated with QTc prolongation especially in patients with antipsychotic medication. Furthermore we could observe that serum magnesium levels are significantly lower in patients who receive atypical neuroleptics. Interestingly, QTc intervals did not differ significantly. This observation supports the hypothesis that atypical antipsychotics may drop the serum magnesium level, also in patients without a prolonged QTc interval.

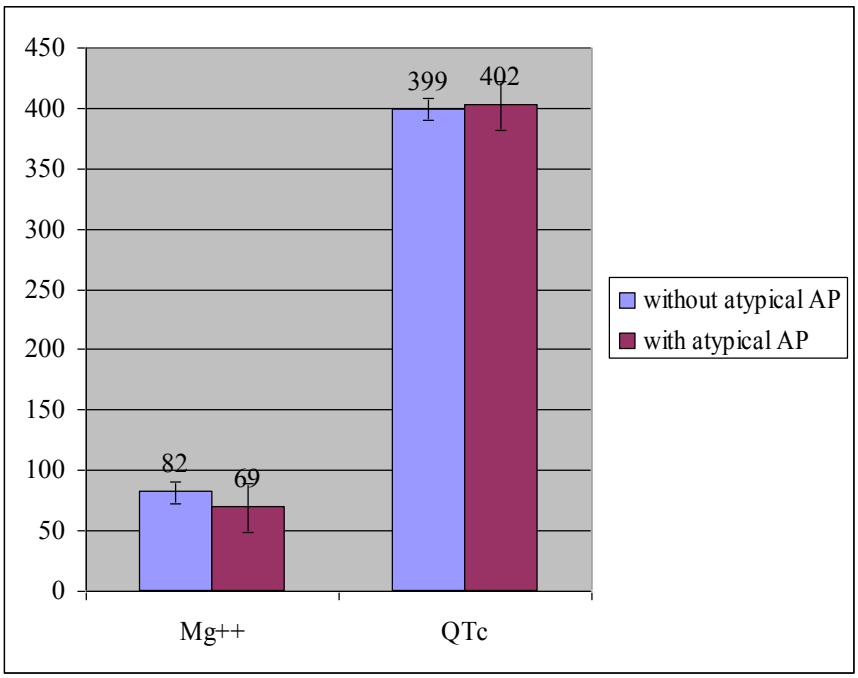

Figure 1: Mg^{++} Serum levels and QTc intervals in patients with and without atypical antipsychotics

Our hypothesis is additionally supported by the fact, that in two patients, who were medicated with atypical antipsychotics (ziprasidone), the low serum magnesium level (initially 0.64 mmol/l) rose to a level within the normal range (finally 0.80 mmol/l) and contemporarily the QTc interval also improved remarkably from initially 406 ms to finally 381 ms. The small sample size limitates the reliability of our results. Furthermore, we did not include patients with QTc interval >450 ms. Perhaps in that case a significant difference between patients with and without medication with atypical medication regarding the QTc interval could be observed, as well as higher correlation between Mg^{++} and the QTc interval in the group of patients who received atypical antipsychotics. However, our results suggest that hypomagnesaemia could be a reason for QTc prolongation in patients who receive atypical neuroleptics. Although it is much too early not to cease neuroleptic medication in case of QTc prologation, the serum magnesium level should be checked and Mg^{++} supplemented, if necessary, before another attempt with the same or another atypical antipsychotic can be considered.

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Source of support: Nil, Conflict of interest: None Declared

QUICK RESPONSE CODE	ISSN (Online) : 2277 –4572
	Website http://www.jpsionline.com

How to cite this article:
Dipl.-Psych. Dr. phil. Dr. med. Helmut Niederhofer. Is Mg++-deficiency associated with an antipsychotics-induced QTC-prolongation?. *J Pharm Sci Innov*. 2013; 2(6): 34-35.