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# ACUTE DYSTONIA ASSOCIATED WITH INITIATING PALIPERIDONE TREATMENT: REPORT OF TWO CASES

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**Abstract**

Paliperidone is a second- generation antipsychotic which is used in the treatment of schizophrenia . It is an active metabolite of risperidone and shows almost the same high affinity for dopamine D2 receptor and serotonin 5-HT2 receptor .The data about the association between acute dystonia and paliperidone treatment is restricted in literature. In this paper, we reported two cases who devoloped acute dystonia after initiating of paliperidone treatment. We suggest that paliperidone might acts a potential dopamine D2 receptor blocking agent in some vulnerable patients and acute dystonia should kept in mind as an early side effect of paliperidone even initating with low doses.

**Key Words:** Acute dystonia, Paliperidone

# PALİPERİDON TEDAVİSİ BAŞLANMASI İLE İLİŞKİLİ AKUT DİSTONİ: İKİ VAKA BİLDİRİMİ

**Özet**

Paliperidon şizofreni tedavisinde kullanılan ikinci kuşak bir antipsikotiktir. Risperidonun aktif metabolitidir ve neredeyse dopamin D2 reseptörü ve serotonin 5-HT2 reseptörü için risperidon ile aynı yüksek afiniteyi gösterir. Literatürde paliperidon tedavisi ve akut distoni arasındaki ilişki ile ilgili bilgiler kısıtlıdır. Bu yazıda, paliperidon tedavisine başlangıç sonrasında akut distoni görülen iki hastayı bildirdik. Paliperidonun bazı hassas hastalarda güçlü bir D2 reseptör blokeri gibi etki edebileceği ve akut distoninin paliperidonun düşük dozla başlangıç tedavisinde dahi erken bir yan etki olarak akılda tutulması gerektiğini düşünmekteyiz.

**Anahtar Kelimeler:** Akut distoni, Paliperidon

**Introduction:**

Antipsychotic medications are used to treat a wide range of psychiatric disorders including schizophrenia, schizoaffective disorder and bipolar disorder. Since the first antipsychotic chlorpromazine was investigated and used in the treatment, it has been recognised that antipsychotic agents are associated with numerous neurological side effects, one of which is dystonia (1). Atypical antipsychotics also called as new generation antipsychotics (2) consist of clozapine, olanzapine, quetiapine, ziprasidone, aripiprazole, risperidone and paliperidone (3-5). These are commonly considered safer than conventional antipsychotics in terms of extrapyramidal symptoms such as impaired involuntary movements (e.g. acute dystonia and tardive dyskinesia), akathisia and parkinsonian symptoms (e.g. tremor, bradykinesia and muscle rigidity ) (5). However, recent data and experience has demonstrated that many of the atypical antipsychotic drugs, in fact are not safe in terms of EPS, could provoke acute dystonia (1).

Paliperidone is a second - generation antipsychotic and is throughly used as drug treatment for schizophrenia (6). It is an active metabolite of risperidone (9-OH risperidone) and shows almost the same pharmacological effect with high affinity for dopamine D2 receptor and serotonin 5-HT2 receptor (7). In literature there have been numerous reports which described that risperidone is associated with dystonia (1). However, our knowledge about the association between acute dystonia and paliperidone is restricted.

Here, we are reporting two psychotic cases who devoloped acute dystonia after initiating paliperidone treatment.

**Case 1:** Mr. E.Y. 46- year- old man admitted to our outpatient clinic with the symptoms of torticollis and tongue dystonia. In patient's history, having been diagnosed as schizophrenia ten years ago, he was started to be treated with quetiapine 600 mg/day, risperidone 4 mg/day at different hours. In the last two years of illness, he was treated with olanzapine 10 mg/day, however, olanzapine 10 mg/day treatment was switched to paliperidone 6 mg/day treatment because of some metabolic side effects of olanzapine. Two days after paliperidone 6 mg/day treatment, Mr. E. demonstrated torticollis and tounge dystonia. His vital signs and serum chemistries and blood counts were within normal limits. Biperiden 5 mg administered intramusculary. After 45 minutes, torticollis and tongue dystonia were resolved and paliperidone 6 mg/day treatment was switched to aripipirazole 10 mg/day. On outpatient clinic control, there was no EPS and psychotic symptom.

**Case 2:** Miss A. L. 19-year-old woman was assessed in our outpatient clinic. She had symptoms of audotory hallucinations, delusions of persecution, disorganised speech and

behaviour. She had no psychiatric history. Physical examination, vital signs, serum chemistries, blood counts and brain MR imaging were within normal limits. She was diagnosed as acute psychotic attack according to DSM-IV-TR. Paliperidon 6 mg/day was initiated for treatment. However, after 10 hours of a single dose, torticollis devoloped. Biperiden 5 mg administered intramusculary and after 30 minutes, torticollis was resolved. Paliperidone 6 mg/day treatment was switched to olanzapine 10 mg/day. 15 days later, there was no dystonic symptoms and psychotic symptoms which remitted partially.

**Discussion:**

Exact mechanism of neuroleptic-induced acute dystonia still remains unclear and possibly attributable to a higher ratio of dopamine-acetylcholine antagonism or postsynaptic dopamine hypersensitivity in the basal ganglia (1, 7,8). The most important cause of drug associted acute dystonia is antipsychotic medication. The propensity of any antipsychotic agent to induce akathisia correlates significantly with its pharmacological affinty to D2 receptors on the striatal pathway (9). There have been several risk factors for devoloping acute dystonia. Younger age, cociane addiction, previous dystonic reaction, high potency antipsychotic use and concurrent AIDS infection are well established risk factors for acute dystonic reaction (1). In our second case, we suggest that she is vulnerable to antipsychotic induced acute dsytonic reaction because of her young age. However, we can not explain why our first case devoloped acute dystonic reaction even though he was given a low dose of paliperidone.

Premarketing data for paliperidone have described the occurrence of dystonia with this drug and the percentage is 1% on 6 mg/day dosage which has been reported to be insignificant compared with placebo group (10). However, a PubMed research done through June 2007 using the key words ‘acute dystonia’ and ‘paliperidone’ in English literature only revealed one case report which described acute dystonia after paliperidone overdose (11). To the best of our knowledge, there is just one study which described tardive dsykinesia during paliperidone treatment in Turkey (12). Our case reports differ from Lapid et al.’s report (11) because of the fact that our cases devoloped acute dystonia in theurapatic doses of paliperidone. The relationship between drug dose and risk for acute dsytonia is not as straightforward as it is supposed (1) . There are evidences that suggest middle range doses are more likely to produce dystonia than very low or very high doses of antipsychotics (13). While comparing our cases with the cases that devoloped acute dystonia during risperidone treatment, it is obviously seen that most of the patients devoloped acute dystonic reaction

during the first week of treatment and in a wide range of doses as 1 mg/day-8 mg/day (1). We suggest that there is a similarity on devoloping acute dystonic reaction between risperidone and paliperidone in terms of the time period during which dsytonic reaction develops, and doses of drugs. We can say that paliperidone has a structure with extended relaease. The study which investigated the effect of paliperidone on striatal and extrastriatal dopamine D2 receptor occupancy suggested that paliperidone at 6-9 mg provides an estimated level of D2 occupancy between 70-80%( 14). As it is known, occupancy greater than 80% significantly increases the risk of EPS. Thus, we argue that paliperidone might act as a potential dopamine D2 receptor blocking agent in some vulnerable patients and, for this reason, acute dystonia should be kept in mind as an early side effect of paliperidone even initating with low doses.

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