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CASE REPORT
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Post-injection delirium/sedation syndrome
Two case reports and brief literature review

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Post-injection delirium/sedation syndrome (PDSS) is a rare adverse effect of long-acting olanzapine injection. The danger of PDSS is not related to the duration of treatment. It may be manifested even after months or years of treatment, but usually presents within the first few minutes of injection, despite meticulous measures of preparation and drug administration. Here, we present two cases of PDSS from our outpatient clinic. The first case was mild and was treated in our clinic. The second case was severe and necessitated transfer of the patient to an emergency medical department. Both patients continue monitoring in our clinic, without manifesting adverse effects again.

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Περίληψη στο τέλος του άρθρου

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Long-acting injectable antipsychotics (LAIs) were introduced during the 1960s to treat patients who are non-adherent to medication prescription, and patients with a history of serious relapse after drug discontinuation.[1] Their use is currently considered among the first line forms of treatment for psychosis[2–4] since LAIs can improve treatment adherence and achieve better therapeutic management of patients with psychosis who lack insight or who do not comply with an oral drug regimen.[5,6]

Newer atypical LAIs, such as olanzapine, have been studied extensively in patients with schizophrenia and both safety and efficacy have been documented.[7,8] Olanzapine LAI (OLAI) has similar safety and efficacy with oral olanzapine, apart from occasional adverse effects related to its route of administration.[9–11] One of these adverse effects, post-injection delirium/sedation syndrome (PDSS), has an incidence rate of less than 0.1% of injections, and its presentation reflects the effects of olanzapine overdose, including sedation and delirium.[11–13]

We describe here two cases of PDSS from the LAIs outpatient clinic of our department, for educational purposes, to emphasize the need for continuous pharmacovigilance of patients under treatment with OLAI. The first case was mild, but the second was severe enough to warrant transfer of the patient to an emergency medical department.

CASE PRESENTATIONS

The first patient was a 36-year-old woman diagnosed with schizophrenia who was attending the LAIs clinic, under treatment with OLAI 405 mg q4 weeks. The patient was not receiving other medications, had no other medical history and denied alcohol or drug abuse. Approximately 10 minutes after the administration of the 17th injection, she complained of malaise, dizziness, weakness and mild sedation. Her vital signs were: BP 85/47 mmHg, pulse rate 117 bpm, and oxygen saturation 96%. The electrocardiogram (ECG) showed only sinus tachycardia. She was placed under continuous observation for about two hours without any intervention. Her condition improved, and she asked to return home when her

symptoms had fully subsided later that afternoon. Since that event, she has continued attendance in our clinic for the last 3.5 years, and is currently receiving OLAI 210 mg q4 weeks, due to improvement in her clinical condition, without manifesting another PDSS event.

The second patient was a 33-year-old male with schizophrenia under treatment with OLAI (405 mg q4 weeks), oral olanzapine 20 mg (gradually discontinued during the first 3 months after hospitalization), risperidone (12 mg daily) and biperiden (6 mg daily). He had no other medical history and denied alcohol or drug abuse. Approximately 5 minutes after the 7th injection, the patient complained of malaise, but insisted on signing against the recommended stay in the hospital for 3 hours, and returned home with his relative. After 4 hours, his family reported that his situation had worsened and they were asked to bring him to the hospital. Clinically, the patient manifested somnolence, dysarthria, difficulty in walking and disorientation to time. His family described behavioral disorganization at home. His vital signs were: BP 142/87 mmHg, pulse rate 122 bpm and oxygen saturation 96%. Because of his clinical picture, the patient was transferred to an emergency medical department, where he was kept for about 18 hours under observation, receiving supportive care. The results of examinations were non-significant, and his situation gradually improved, with full resolution of symptoms after 48 hours. Since then, after approximately one year, he has continued attending our clinic without manifesting PDSS again.

DISCUSSION

PDSS is a serious adverse effect of OLAI administration, described for the first time in 2008.[14] Its symptoms may mimic those of three other, potentially lethal, acute conditions in psychopharmacology: Neuroleptic malignant syndrome, serotonergic, and central anticholinergic syndrome.[15] Its diagnosis is based on clinical criteria[12] and the syndrome appears to be a unique characteristic of OLAI: Studies have shown no such adverse effect with risperidone or paliperidone LAIs.[16,17] The risk of presenting PDSS is the same with every injection, and is thus additive for each patient.[18]

In a clinical study of OLAI, from August 2000 to October 2008, 30 cases of PDSS were reported in 29 patients. The symptoms included sedation, confusion, disorientation, slurred speech, ataxia and malaise. The mean time between injection and symptom manifestation was 25 minutes.[12] This time period is explained based on the chemical characteristics of the injection, which must first be dissociated to the base (olanzapine) and the acid (pamoic acid). Although dissociation is faster in blood than in muscle tissue, it does not take place immediately and symptoms continue to evolve over hours, during which the levels of olanzapine rise.[18] The majority of the patients were transferred to hospitals for further investigation, but only needed observation or supportive care, with symptoms resolving within 72 hours.[12] Similar findings were described in a report of another 338 cases published in 2015.[19]

Pathophysiologically, PDSS may be manifested after accidental contact of the salt with a large quantity of blood or serum, as is the case with intravascular injection or injection in an area with a rich capillary network. This results in the entry of large dose of the drug into blood circulation, leading to a high drug concentration.[20]

After administration of the injection, patients should remain under observation by appropriately trained personnel for at least 3 hours, and they should avoid driving or handling machinery that day.[13] Correct injection technique is important; aspiration must always precede injection administration to check for vascular trauma. If this has happened, the injection should be disposed of, and a new syringe and dose used instead, preferably in another area, such as the opposite gluteal muscle.[12] Additional measures include using the "Z" technique, carefully preparing the injection site, taking measures for infection control, using the correct volume of drug solution liquid, alternating the injection sites, using local anesthetics for pain control, observing the patient for a sufficient time period, and administering the drug at adequate time intervals.[17]

Even correct injection technique cannot exclude the possibility of intravascular injection, which can occur in the absence of blood during aspiration. Consequently, even the best education about injection technique will not completely prevent PDSS.[20]

We described here the two cases of PDSS in patients attending the LAI outpatient clinic that were the only cases observed among over 1,000 OLAIs administered during the 7 years that the clinic has been in operation. Both patients were suffering from schizophrenia, and both manifested the symptoms within the first 15 minutes of drug administration. Neither had any other medical history and both denied alcohol or drug abuse. The symptoms in the first case were mild but those in the second case were severe enough for the patient to be transferred to an emergency medical department.

According to the relevant literature, PDSS appears to be a rare side effect of OLAI, but not of other LAIs, and in our clinic we have not observed a similar syndrome in patients under treatment with LAIs other than olanzapine. The symptoms usually appear quickly and resolve in 2–3 days with only observation and supportive care.

Despite the careful preparation during drug administra-

tion, patient observation, both clinically and by monitoring vital signs, and instructions to stay at the hospital for approximately 3 hours after the injection, PDSS cannot be prevented. For this reason, continuous pharmacovigilance is necessary, in order to intervene as quickly as possible to help symptom resolution, ensure the safety of the patients and build a therapeutic alliance with them and their families.

ΠΕΡΙΛΗΨΗ

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Το σύνδρομο μετά από ενέσιμη ολανζαπίνη μακράς δράσης είναι μια σπάνια ανεπιθύμητη ενέργεια. Ο κίνδυνος εκδήλωσής του δεν σχετίζεται με τη διάρκεια θεραπείας. Μπορεί να εκδηλωθεί ακόμη και μετά από μήνες ή έτη αλλά, συνήθως, εντός των πρώτων λίγων λεπτών μετά την ένεση παρά τα πολύ προσεκτικά μέτρα προετοιμασίας και χορήγησης του φαρμάκου. Στο παρόν άρθρο περιγράφουμε δύο περιπτώσεις ασθενών με σύνδρομο μετά από ενέσιμη ολανζαπίνη μακράς δράσης από το εξωτερικό ιατρείο της κλινικής μας. Η πρώτη ήταν ήπια και αντιμετωπίστηκε στο ιατρείο μας. Η δεύτερη ήταν σοβαρή και απαιτήθηκε η διακομιδή του ασθενούς σε τμήμα επειγόντων περιστατικών. Αμφότεροι οι ασθενείς συνεχίζουν να παρακολουθούνται στο ιατρείο μας χωρίς να έχουν παρουσιάσει ξανά παρόμοια ανεπιθύμητη ενέργεια μέχρι σήμερα.

Λέξεις ευρετηρίου: Αναφορά περίπτωσης, Ανεπιθύμητες ενέργειες, Ενέσιμα αντιψυχωσικά μακράς δράσης, Ολανζαπίνη μακράς δράσης, Σύνδρομο μετά από ενέσιμη ολανζαπίνη μακράς δράσης

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