ORIGINAL RESEARCH PAPER

Psychiatry

SPECTRUM OF UNUSUAL PSYCHOTROPIC DRUG-RELATED ADVERSE EVENTS: A CASE SERIES FROM A TERTIARY CARE PSYCHIATRY CENTRE

KEY WORDS:

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ABSTRACT

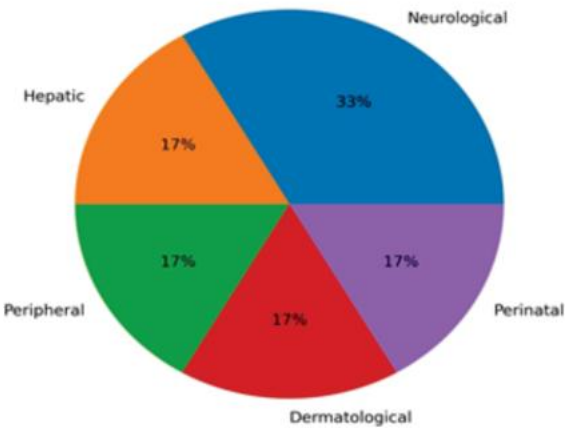
Background: Psychotropic medications are generally considered safe and effective when prescribed appropriately. However, rare adverse drug reactions (ADRs) continue to emerge and may remain under-recognized in routine clinical practice. Such reactions often mimic primary medical disorders, resulting in diagnostic uncertainty and delayed intervention. **Objectives:** To describe uncommon and clinically significant adverse events associated with psychotropic medications encountered in psychiatric practice and to evaluate their causality using standardized pharmacovigilance methods. **Methods:** A retrospective case series was conducted involving six patients who developed unusual adverse events temporally associated with psychotropic medications. Clinical records, laboratory investigations, imaging findings, treatment details, and outcomes were reviewed. Causality assessment was performed using the Naranjo Adverse Drug Reaction Probability Scale. **Results :** Six uncommon adverse events were identified:

1. Neuroexcitatory effects associated with acute Olanzapine toxicity
2. Reversible alkaline phosphatase elevation associated with Olanzapine
3. Bilateral lower limb edema temporally associated with Escitalopram
4. Cutaneous adverse reaction associated with Melatonin
5. An uncommon presentation of Sertraline-associated hiccups
6. Non-immune hydrops fetalis associated with maternal olanzapine exposure during pregnancy

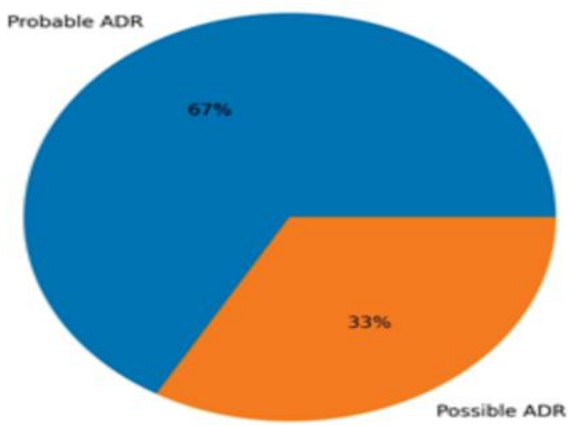
Four cases were categorized as probable ADRs and two as possible ADRs. Clinical improvement occurred following withdrawal or modification of the suspected offending medication in all cases.

Case	Drug	Adverse Effect	System Involved	Naranjo
1	Olanzapine	Agitation + Seizure	Neurological	Probable
2	Olanzapine	ALP Elevation	Hepatic	Probable
3	Escitalopram	Peripheral Edema	Peripheral	Probable
4	Melatonin	Rash	Dermatological	Possible
5	Sertraline	Intractable Hiccups	Neurological	Probable
6	Olanzapine	Non-Immune Hydrops Fetalis	Perinatal	Possible

Organ Systems Involved



Naranjo Causality Assessment



CASE PRESENTATIONS

Case 1

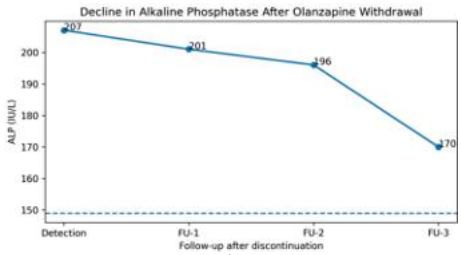
Neuroexcitatory effects associated with acute Olanzapine toxicity

A 27-year-old male consumed approximately 100 mg olanzapine and subsequently developed abnormal limb movements, unconsciousness, agitation, and aggressive behavior. EEG demonstrated generalized epileptiform activity. Symptoms improved after discontinuation of olanzapine and initiation of antiepileptic treatment.

Naranjo Score: Probable ADR

Case 2

Reversible alkaline phosphatase elevation associated with Olanzapine

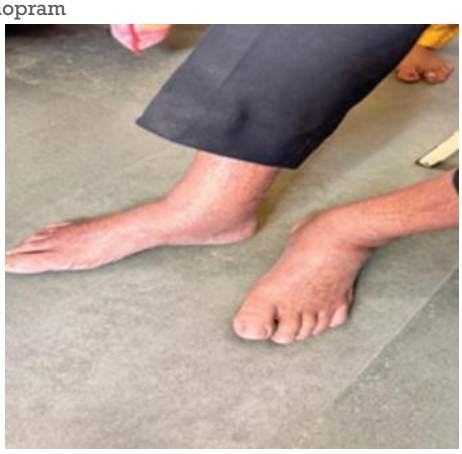


An adult patient developed nausea and vomiting shortly after initiation of olanzapine therapy. Liver function testing revealed isolated elevation of alkaline phosphatase (270 IU/L) while bilirubin, AST, and ALT remained within normal limits. Progressive normalization occurred after discontinuation of olanzapine.

Naranjo Score: Probable ADR

Case 3

Bilateral lower limb edema temporally associated with Escitalopram



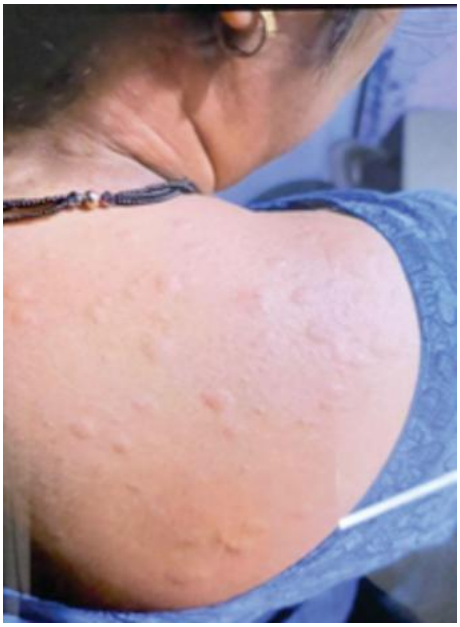
A 48-year-old male developed bilateral pedal edema within two weeks of initiation of escitalopram. Cardiac, hepatic, renal, and thyroid evaluations were unremarkable.

Symptoms resolved completely following withdrawal of escitalopram.

Naranjo Score: Probable ADR

Case 4

Cutaneous adverse reaction associated with Melatonin



A 44-year-old woman developed generalized erythematous pruritic skin lesions shortly after initiation of melatonin for sleep disturbance. No infectious or allergic cause was identified. Rash resolved after discontinuation of melatonin.

Naranjo Score: Possible ADR

Case 5

An uncommon presentation of Sertraline-associated hiccups

A 48-year-old woman developed persistent hiccups following escalation of sertraline dosage. Extensive medical evaluation failed to identify an alternative etiology. Symptoms resolved within 48 hours after discontinuation of sertraline.

Naranjo Score: Probable ADR

Case 6

Non-Immune Hydrops Fetalis Associated with Maternal Olanzapine Exposure

A 27-year-old multigravida woman with a history suggestive of bipolar spectrum illness had been maintained on olanzapine 5 mg/day with satisfactory symptom control. During pregnancy, prolonged fetal exposure to olanzapine occurred.

Ultrasonography at approximately 33 weeks demonstrated:

- Polyhydramnios
- Breech presentation
- Fetoplacental insufficiency
- Features consistent with non-immune hydrops fetalis

The neonate required NICU admission and exhibited generalized edema along with laboratory abnormalities including elevated inflammatory markers and hepatic dysfunction.

Although definitive causality could not be established, the temporal relationship between prolonged prenatal olanzapine exposure and fetal hydrops raised concern regarding a potential drug-related association.

Naranjo Classification: Possible ADR

Figure. Non-Immune Hydrops Fetalis Following In-Utero Olanzapine Exposure

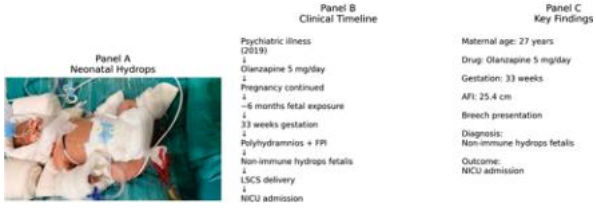


Table 1. Summary of Uncommon Psychotopic Medication -Related Adverse Events

Case	Drug	ADR	System	Outcome
1	Olanzapine	Agitation + Seizure	Neurological	Resolved
2	Olanzapine	ALP Elevation	Hepatic	Resolved
3	Escitalopram	Peripheral Edema	Peripheral	Resolved
4	Melatonin	Cutaneous Rash	Dermatological	Resolved
5	Sertraline	Intractable Hiccups	Neurological	Resolved
6	Olanzapine	Hydrops Fetalis	Perinatal/Fetal	Observed

DISCUSSION

This case series illustrates the broad spectrum of rare adverse reactions associated with psychotropic medications.

Olanzapine accounted for the highest number of ADRs and was implicated in neurological, hepatic, and possible fetal complications. While seizure induction and hepatic abnormalities have occasionally been reported, the occurrence of non-immune hydrops fetalis represents a highly unusual observation warranting further investigation.

Escitalopram-associated peripheral edema remains a rare but clinically relevant adverse effect that may lead to extensive medical evaluation if unrecognized.

Melatonin is widely perceived as a benign therapeutic agent; however, hypersensitivity reactions may occur and should be considered in patients presenting with unexplained dermatological manifestations.

Sertraline-induced hiccups are uncommon and likely result from serotonergic modulation of central hiccup pathways.

Collectively, these cases emphasize the importance of maintaining a high index of suspicion for medication-related causes when evaluating atypical clinical presentations.

Clinical Implications

- Rare ADRs can mimic medical illnesses.
- Temporal association remains critical for diagnosis.
- Early drug withdrawal often results in symptom resolution.
- Pharmacovigilance reporting improves recognition of uncommon reactions.
- Perinatal psychopharmacology requires careful monitoring and risk-benefit assessment.

Limitations

- Single-center retrospective design.
- Small sample size.
- Lack of rechallenge in most cases.
- Definitive causality cannot be established in all cases.

CONCLUSION

This case series highlights six uncommon adverse events associated with psychotropic medications involving neurological, hepatic, dermatological, vascular, gastrointestinal, and fetal systems. Most reactions improved following discontinuation of the suspected offending agent and demonstrated probable or possible causality according to the Naranjo algorithm. Continued vigilance, systematic monitoring, and reporting of unusual ADRs are essential to enhance psychotropic medication safety and expand current pharmacovigilance knowledge.