NMS With Concomitant Use of Oral Risperidone and Paliperidone Palmitate

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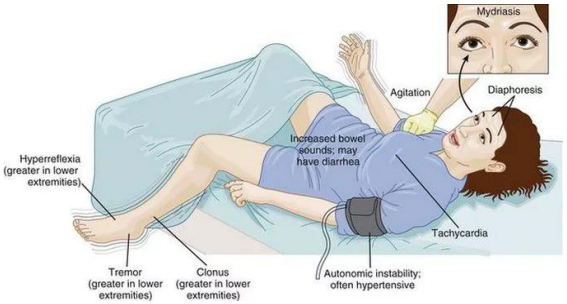
What is NMS?

Neuroleptic malignant syndrome (NMS) is a rare and potentially life-threatening adverse reaction to psychotropic medications (Chen & Chen, 2018). Hallmark features include muscle stiffness, fever, altered mental status and autonomic dysregulation. Incidence rates can range from 0.2 – 3 percent of people taking neuroleptics (Kane et al., 2019).



Case details

The patient was a 21-year-old African-American male who was diagnosed with Schizoaffective disorder. Upon admission, the patient presented with disorganized behavior, disorganized speech, auditory hallucinations, persecutory delusions, decreased need for sleep, increased goal-directed behavior, along with poor impulse control. He was on multiple neuroleptics in the past, including long acting injections (LAIs), and had no history of serious adverse events associated with these medications. He had a history of medication noncompliance, and was therefore an ideal candidate for a LAI. Treatment was initiated upon admission with oral risperidone, lithium and lorazepam. His clinical condition appeared to be improving incrementally. He was hemodynamically stable and afebrile throughout the early course of treatment. He was given an intramuscular injection of paliperidone palmitate 234mg on day 4 of his hospitalization. On day 5, the patient developed symptoms of NMS, including a fever, muscle rigidity and AMS. All oral medication were discontinued, and the patient was given IV fluids. He did not receive a second paliperidone palmitate injection. Despite this, the patient's CK continued to rise (648 U/L → 1064 U/L→1700 U/L). He was transferred to another facility, where he received supportive care and ICU monitoring. After approximately 1 week, the patient's medical condition improved, and he was readmitted to our facility for treatment of his underlying mental illness. Therapy was initiated with oral aripiprazole. The medication was well tolerated, and the dose was increased to 15mg daily. He achieved moderate improvement of his symptoms, and was discharged home with some residual symptoms of psychosis and mania.

Table 1 Risk factors of NMS[11-14]

Related with the drug	Related with somatic condition	Related with psychiatric conditions
- High doses	- Dehydration	- Catatonia
- Rapid increase of the does	- Electrolytic alterations	- Extreme agitation
- Parenteral administration	- Infection	- Alcoholism
- Combination of several neuroleptics	- Traumatism	- Mental retardation
- Association with lithium	- Surgery	- Affective disorders
	- Malnutrition	- Previous treatment with ECT
	- Iron deficiency	
	- Organic brain disorders	

Understanding the relationship between risperidone and paliperidone palmitate

Risperidone is a second-generation antipsychotic (SGA) used in the treatment of multiple psychiatric illnesses, including schizophrenia (Al-Mahrouqi et al., 2021). Paliperidone palmitate is a long acting injection (LAI) SGA that is administered intramuscularly. These two medications share significant chemical similarities, as paliperidone is an active metabolite of risperidone (Kaur et al., 2016). Commonly, tolerance will be assessed by administering oral risperidone for a few days, prior to administering paliperidone palmitate.

References

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Discussion

This patient was initially tolerating treatment with oral risperidone well, without any notable side effects. It was not until he received his first injection of paliperidone palmitate, that he started to show signs of NMS. FDA labeling, as well as labeling from Janssen Pharmaceuticals suggest that a patient being initiated on therapy with paliperidone palmitate should receive 2 IM injections approximately 7 days apart. After receiving the second IM dose, there is no need for further oral supplementation. They suggest studies are limited in assessing concomitant use of oral antipsychotics while receiving the LAI. It is commonplace for physicians to prescribe oral supplementation for patients who are taking LAI's. Prior studies have demonstrated patients are prescribed oral supplementation along with LAI injections, in a manner that is inconsistent with FDA labeling (Alastanos et al., 2019). There have been limited studies which demonstrate better clinical outcomes in patients who take oral supplementation after receiving LAIs, as opposed to patients who immediately discontinue oral supplementation (Hsia et al., 2017).

So What's Next?

Future studies looking at the use of short-term oral risperidone supplementation in combination with paliperidone palmitate intramuscular injection should be done to assess the possible increase in risk of developing serious, life-threatening adverse reactions such as NMS.

Further research, delving into clinical outcomes in those receiving oral supplementation plus LAI, versus LAI alone could be highly beneficial. Such studies can assess monitoring parameters such as readmittance rates.

Such information would be helpful to psychiatrists as well as patients. This would serve as a great tool when discussing possible risks and benefits of different treatment options. This is of particularly important because of the large shift in practicing principles, where more patients are receiving LAIs than ever before.