Extrapyramidal motor side effects (EPMS)

Phenomenology
All currently available antipsychotics block dopamine D2 receptors in the nigrostriatal system to a certain extent; consequently, all of these drugs can induce movement disorders. The continuum of risk ranges from clozapine, with the lowest likelihood to induce such adverse events to traditional high potency antipsychotics such as fluphenazine or haloperidol having the highest risk for extrapyramidal motor side effects (EPMS). These side effects can occur either during acute treatment (even after the first dose of an antipsychotic) or after chronic exposure to an antipsychotic

Acute EPMS include acute dystonia, acute dyskinesia, acute akathisia and parkinsonism. All of these usually develop within the first days or weeks of treatment. Tardive syndromes include tardive dyskinesia, tardive dystonia and possibly tardive akathisia. Per definition, these adverse events commence after 3 months or later from the onset of treatment.

Dystonia is characterized by sustained abnormal posture. Common phenotypes include oculorgyric crisis, torticollis, or if the trunk is also involved, the Pisa-syndrome.
The phenomenology of parkinsonism includes tremor, rigidity and bradykinesia. Rigidity is characterized by cogwheel resistance during passive motion of the limbs. Motor activity even of facial muscles is reduced in bradykinesia. Parkinsonised patients are usually also *hypomimic*.

Dyskinesias include repetitive, involuntary hyperkinetic movements, often found in the face and mouth region. Writhing, choreoathetoid movements can also be found in limbs and trunk. Wormlike tongue movements, lip smacking and eye blinking are common features of both acute and tardive dyskinesia.
Akathisia generally consists of a strong subjective feeling of inner unrest and related motor symptoms including pacing, rocking and shifting the weight from foot to foot while standing.

Prevention and management of EPMS
One of the most prominent characteristics of the second generation antipsychotics is their lower risk to induce EPMS. Therefore, starting patients on such drugs or switching them from traditional neuroleptics to these agents will be the first step to decrease the incidence of drug induced movement disorders. The prophylactic use of anticholinergics is discouraged with the exception of patients with a high risk to develop EPMS: young male patients treated with first generation antipsychotics and patients with a history of strong EPMS during previous treatment episodes). Since severe acute dystonia is a very fearful event, patients and their significant others need to be informed about the potential risk for EPMS.

The acute syndromes of dystonia, dyskinesia and parkinsonism respond well to anti-cholinergics such as biperiden or benztropine. In the case of acute dystonia these drugs can also be administered intravenously for rapid effects. Betablockers are generally recommended for the management of akathisia, although other drugs such as anticholinergics or benzo-diazepines have also been found helpful.

There is, as yet, no established treatment for tardive EPMS. Since these disorders are also potentially irreversible, prophylaxis is key. In the case of emergent or persistent tardive syndromes, a switch to clozapine is the treatment option with the best documented remediative effect. Whether other second generation antipsychotics with low D2 occupancy, such as quetiapine, are similarly helpful is unknown.

(Fleischerhacker)

References

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