Levosulpiride-induced Movement Disorders: A Compelling Case for Prudent Use!

Dear Sir,

We appreciate the article by Dr. Joe describing levosulpiride (LVS) induced neurological adverse effects.[1] More than half (56.67%) of the patients had extrapyramidal features in form of tremor ± rigidity while Radhakrishnan *et al*. had highlighted more dystonia in their series.[2] In the South Korean series, most common LVS induced movement disorder (LIM) was Parkinsonism (93.4%).[3] Levosulpiride induced parkinsonism (LIP) was asymmetric in 37.6% cases

and these patients had rest tremors more frequently than those with symmetric features.[3] The mean dosage of LVS (mg) that caused reversible and irreversible LIP in the South Korean study was 70.06 ± 15.8 and 84.46 ± 29.7, respectively. It is interesting to note that at one year of follow-up, 48.9% (25/52) had irreversible Parkinsonism requiring levodopa therapy.[3] However, LVS dosage, duration, asymmetry of symptoms or rest tremors were not predictive of the reversibility of LIP in their study. None of these patients had TRODAT Scan. Worsening of the subclinical nigrostriatal defect by LVS may be the explanation of clinical manifestations in patients with irreversible LIP.[4-6] LVS is also known to cause worsening of symptoms in patients with Parkinson's disease (PD).[7] One should remember that drug-induced Parkinsonism can be asymmetric and detailed drug history should be elicited in any new patients presenting with PD or PD plus syndromes.

Another interesting fact about LIM is that it occurs more frequently in elderly population. The mean age of patients in Dr. Joe's cohort was 65 ± 12 years, in Shin HW *et al.* series, 85.7% of patients were aged more than 60 years. Whereas in the study by Radhakrishnan *et al*., the mean age was 65.7 ± 9 years. Greater frequency of LIM seen in the elderly population might be due to the higher incidence of dyspepsia and more use of prokinetics than younger subjects.[8] Increased susceptibility of the elderly brain due to age-related changes in the striatal system might be another possible explanation.

It is assumed that a higher dose of LVS is associated with LIP and lower doses at dystonia. However, Choudhury *et al*. didn't observe any relation between LVS induced dyskinesia and drug dosage.[9] In the series by Radhakrishnan *et al*., LIP was seen only in one patient.[2] Their patient was a 75-year-old male who developed acute onset jaw opening dystonia and Parkinsonism within 3 days of LVS (25 mg) therapy. Genetic susceptibility and advanced age might be the reason for developing LIM at lower doses. Henceforth, physicians should be extra cautious in prescribing LVS to older patients.

Dr. Joe observed a significant positive correlation (r = 0.8295, P = 0.0154) between the duration of LVS treatment and the incidence of extrapyramidal features.[1] Shin HW *et al*. had recommended restricting the duration of LVS therapy to 8 weeks.[2] Unfortunately, many of the Indian brands of LVS or combination therapy with proton pump inhibitors are still not mentioning extrapyramidal side effects or maximum duration of therapy in their package insert. At least in half of the patients, LIP is irreversible. A drug prescribed for minor ailment causing disabling disease is not desirable. Treating physicians must be sensitized about the neurological adverse effect of LVS and drugs should be withdrawn at the slightest suspicion of side effects. A package insert warning about neurological side effects is highly recommended.

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Conflicts of interest

There are no conflicts of interest.

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