Clinical Differences Between Metoclopramide- and Antipsychotic-Induced Tardive Dyskinesias

Anthony E. Lang

ABSTRACT: A patient with tardive dyskinesia dominated by pelvic thrusting movements is described. A retrospective review of the clinical features documented in patients with metoclopramide- and antipsychotic-induced tardive dyskinesias seen over a six year period demonstrated that the occurrence of pronounced pelvic thrusting and respiratory dyskinesias were significantly more common in the metoclopramide treated group. The occurrence of bucco-linguo-masticatory movements, limb stereotypies or chorea, and mild truncal or abdominal rocking were not significantly different between the two groups. None of the tardive dystonia patients had metoclopramide as the causative agent. These findings will require confirmation in larger, better matched patient populations. Whether the differences relate to different pharmacologic profiles of drug action, patient populations exposed, or other factors, remains to be elucidated.


All of the so-called “extrapyramidal” side effects of neuroleptic drugs have now been reported with metoclopramide. To date, there is little to suggest that the characteristics of these side effects differ from those seen with more typical neuroleptics. One exception may be the reported higher incidence of acute dystonic reactions in females treated with metoclopramide in contrast to the well-recognized predisposition of young males to this complication with antipsychotic drugs. The first case of tardive dyskinesia due to metoclopramide was reported in 1978. Since then, a number of cases have been mentioned in the literature. There has been no evidence presented to date suggesting that the clinical manifestations of tardive dyskinesia due to metoclopramide differ in any way from those due to neuroleptic drugs. The recent review of a patient with metoclopramide-induced tardive dyskinesia dominated by pelvic thrusting movements (“copulatory dyskinesias” a term adopted from reference 4) prompted a retrospective analysis of the clinical features of tardive syndromes seen over the last six years. The results of this survey suggest that some clinical differences do exist between the tardive syndromes caused by metoclopramide and antipsychotics.

CASE REPORT

This 74-year-old woman had been treated with metoclopramide 10 mg tid for a one year period for symptoms of a hiatus hernia. Her past history included diabetes controlled by diet, distant cervical spine injury, mastectomy for carcinoma of the breast, and herpes zoster involving the left leg. Eight months prior to her first assessment, she had the subacute development of pelvic rocking movements which interfered with her ability to lie, sit or stand still. She also noted some general slowing of activity and softening of her voice. She denied any other neurological symptoms.

On examination, she had a masked facies, mild limb and axial rigidity, marked bradykinesia and poor postural stability. There were repetitive, at times rhythmic, movements occurring approximately once per second involving bilateral quadriceps and tensor fasciae latae synchronously with paraspinal muscles. Contractions of adductor magnus and biceps femoris alternated with those in quadriceps. These move-
PATIENTS, METHODS AND RESULTS

The charts of all patients with a diagnosis of a tardive syndrome seen at the Toronto Western Hospital Movement Disorders Clinic from its opening in mid-1982 until June 1988 were reviewed. All patients had been seen and documented by the author. The dominant movement disorder had been characterized as “classical” (choreatic) tardive dyskinesia or tardive dystonia as defined by Burke et al. In all cases, extensive descriptions of the movement disorders were available, outlining the distribution and nature of the abnormal movements seen.

Table 1 outlines the patient data. A total of 42 patients with “classical” tardive dyskinesia had been seen, nine induced by metoclopramide and 33 caused by a variety of antipsychotic drugs. There were no differences in sex or age between these two groups (Table). Twenty patients had tardive dystonia and in all of these cases, the causative agent was an antipsychotic drug. The tardive dystonia group was younger (mean age 36.1 years, range 22-50) and contained more males than females (13:7) (in contrast to the other tardive dystonia groups). Because of the differences between the tardive dystonia and tardive dyskinesia populations, the former cases were excluded from further analysis.

The Table outlines a comparison of the clinical features in the two groups with tardive dyskinesia. Pelvic thrusting and respiratory dyskinesias were significantly more common in the metoclopramide group. The frequency of dystonia as a minor component of the movement disorder was no different in the two classical tardive dyskinesia subgroups (i.e. antipsychotics vs metoclopramide). However, in none of the metoclopramide cases did dystonia predominate (i.e. tardive dystonia). There were no other significant differences in the frequencies of various types of abnormal movements accompanying the tardive dyskinesia syndromes.

DISCUSSION

There are a number of reports of tardive dyskinesia due to metoclopramide in the literature. However, it is extremely difficult to provide an accurate number of the cases reported since some authors have published more than once on the topic and several cases have come from country-wide surveys which probably include previously reported patients. Most cases have been poorly described clinically. As expected, and confirmed by the present study, bucco-linguo-masticatory movements predominated. Only rarely are other abnormal movements commonly seen in tardive dyskinesia syndromes mentioned. Interestingly in the second report of tardive dyskinesia due to metoclopramide, one of the three patients demonstrated prominent "repetitive 'copulatory' rocking movements of the pelvis and the lumbar spine" and another patient had involuntary contraction of anal and vaginal muscles. In a report by Grimes and his colleagues in 1982, the only one of seven patients who was described in detail had respiratory dyskinesia and grunting in addition to orofacial dyskinesias. Board reported a woman developing transient pelvic rocking movements after several courses of high-dose parenteral metoclopramide. The only case of metoclopramide-induced tardive dyskinesia mentioned in a report by Pall and Williams also suffered from pelvic dyskinesias. Finally, the case report of Samie et al demonstrated respiratory and pelvic dyskinesias as part of a severe metoclopramide-induced movement disorder. This limited experience may support the finding of a higher incidence of pelvic and respiratory dyskinesias in this group. The second finding of the current survey was the lack of cases of metoclopramide-induced tardive dystonia. Review of the literature reveals that there have been no examples of well documented tardive dystonia due to metoclopramide reported to date.

The causes for the clinical differences between tardive syndromes induced by metoclopramide and antipsychotic drugs remain to be elucidated. One possible explanation is the difference in the pharmacological profile of metoclopramide compared to classical antipsychotic drugs. For example, although both block central dopamine receptors, in contrast to most neuroleptics, metoclopramide is a pure D2 receptor antagonist with rather weak binding properties as demonstrated by an IC50 for spiperone binding which is 10-100 times greater than that of classical neuroleptics. Another explanation might relate to differences in patient populations exposed to the drugs, as has been proposed for antipsychotic-induced tardive dyskinesia. Certain undefined patient characteristics may have predisposed the metoclopramide patients to the greater likelihood of “copulatory” and respiratory dyskinesias while predisposing
those exposed to antipsychotics to dystonia. However, it must be emphasized that the retrospective nature of this survey is a source of several potential confounding variables. Differences in referral patterns, for example between gastroenterologists and psychiatrists, could have been important but unlikely in view of the broad referral base of our clinic and the easy accessibility of health care through government supported health insurance. The predominance of elderly women in the metoclopramide group is of some concern even if there were no significant differences in age and sex between the two tardive dyskinesia populations. The age of the population exposed to the causative drug may also account for the lack of cases with predominant dystonia (i.e. tardive dystonia) in the metoclopramide group. It is still possible that the dominant symptom has as much to do with the age of the patient exposed as it does with the agent. Further assessment of larger numbers of more closely matched patients, ideally in prospective fashion, is required to confirm the findings reported here. The increasing awareness of the potential complications of long-term metoclopramide therapy and the availability of domperidone in Europe and Canada may make the completion of such a study problematic.

REFERENCES