Diffuse muscle pain with quetiapine

We report the case of a 28-year-old female out-patient with bipolar disorder, whose symptomatology was well-controlled with lithium carbonate 1200 mg (orally) (0.9 mEq/l plasma levels) and risperidone 1–2 mg (orally) daily. The patient had been treated for several years in our department and the course of her illness was well-known; it showed that only lithium was both effective and well-tolerated (topiramate was not effective and carbamazepine caused a rash) and only in coadministration with low doses of risperidone.

However, the use of risperidone caused a large increase in prolactin levels (above 2000 µU/l, with normal values below 500 µU/l) and amenorrhoea (the rest of the hormonal investigation and brain magnetic resonance imaging were normal). The patient was put on 5 mg olanzapine (orally), but she did not tolerate this agent because it made her feel 'confused' and 'tired'. She was then put on 200 mg quetiapine (orally). Within 24 h the patient manifested diffuse muscle pains and headache. She reported that her legs were stiff and she had pain in her knee joints. Neurological examination was normal, as were blood and biochemical tests including creatine phosphokinase. Vital signs were normal. No extrapyramidal signs or symptoms (especially akathisia) were present. The pain persisted for 5 more days and the patient demanded that quetiapine be discontinued. The pain disappeared within the first 48 h of shifting back to risperidone, which was according to the wishes of the patient. Six months passed and the patient is still free from symptoms.

To our knowledge, this is the first report of this kind of adverse effect related to quetiapine. Various other antipsychotics, including haloperidol and olanzapine, are reported to cause muscle pain and rigidity because of rhabdomyolysis, but the current case had no laboratory or clinical findings related to rhabdomyolysis.

Declaration of interest

K.N.F. has participated in field trials sponsored by Eli Lilley & Co. and by Astra-Zeneca.

K. N. Fountoulakis, A. Iacovides, St. G. Kaprinis, G. St. Kaprinis 53 Chrysostomou Smyrnis Street, 55132 Aretsou Thessaloniki, Greece

Adjunctive fluvoxamine with clozapine

We read with interest the article by Williams *et al* (2002). The authors summarise treatment options for patients resistant to clozapine monotherapy. However, in the section on combining antidepressants with clozapine, several issues deserve more attention. The authors disagree with utilisation of adjunctive antidepressants to reduce the cost of clozapine treatment. In our recent study (Lu *et al*, 2000), addition of 50 mg/day fluvoxamine to low-dose (100 mg/day) clozapine could raise the mean plasma clozapine level to over 400 ng/ml to achieve suitable therapeutic ranges. Therefore, concomitant fluvoxamine can reduce clozapine doses and, consequently, costs (Armstrong & Cozza, 2001).

Interestingly, this pharmacokinetic interaction is more pronounced in patients with high cytochrome P450 1A2 activity and at low clozapine plasma concentrations (Olesen & Linnet, 2000). This phenomenon could therefore be used to narrow down the wide interindividual variation in blood clozapine concentrations. Several open trials also demonstrated that coadministration of fluvoxamine could augment clozapine efficacy and curtail plasma norclozapine:clozapine ratios (Wetzel *et al*, 1998; Lu *et al*, 2000). Norclozapine has been suggested to be more toxic than its parent compound. Although addition of fluvoxamine to low-dose clozapine was well-tolerated in our pilot study (Lu *et al*, 2000), further studies are warranted to substantiate its safety and efficacy.

Armstrong, S. C. & Cozza, K. L. (2001) Consultation–liaison psychiatry drug–drug interactions update. *Psychosomatics*, **42**, 157–159.

Lu, M. L., Lane, H. Y., Chen, K. P., *et al* (2000) Fluvoxamine reduces the clozapine dosage needed in refractory schizophrenic patients. *Journal of Clinical Psychiatry*, **61**, 594–599.

Olesen, O. V. & Linnet, K. (2000) Fluvoxamine–clozapine drug interaction: inhibition *in vitro* of five cytochrome P450 isoforms involved in clozapine metabolism. *Journal of Clinical Psychopharmacology*, **20**, 35–42.

Wetzel, H., Anghclescu, I., Szegedi, A., *et al* (1998) Pharmacokinetic interactions of clozapine with selective serotonin reuptake inhibitors: differential effects of fluvoxamine and paroxetine in a prospective study. *Journal of Clinical Psychopharmacology*, **18**, 2–9.

Williams, L., Newton, G., Roberts, K., *et al* (2002) Clozapine-resistant schizophrenia: a positive approach. *British Journal of Psychiatry*, **181**, 184–187.

Declaration of interest

None. Funding was received from the National Science Council and the National Health Research Institutes, Taiwan.

M. L. Lu Department of Psychiatry, Taipei Medical University–Wan Fang Hospital, Taipei, Taiwan

H. Y. Lane Department of Psychiatry, China Medical College Hospital, No. 2, Yuh-Der Road, Taichung 404, Taiwan

Olanzepine-induced tardive dyskinesia

Tardive dyskinesia is a serious and common motor side-effect of treatment with traditional neuroleptics, with an unknown pathophysiological basis. It affects 20–30% of patients on long-term neuroleptic therapy, with elderly patients being at higher risk (American Psychiatric Association, 1994).

Olanzapine is an atypical antipsychotic agent with a reported lack of propensity to cause tardive dyskinesia (Beasley *et al*, 1999). Recently, it has been suggested that olanzapine can improve tardive dyskinesia in some patients (Littrell *et al*, 1998; Jaffe & Simpson, 1999). Other authors, however, have shown that the prolonged use of olanzapine can instead be associated with tardive dyskinesia/dystonia (Ananth & Kenan, 1999; Dunayevich & Strakowski, 1999). Here we report the case of a patient who experienced tardive dyskinesia after only few months of treatment with olanzapine.

A 62-year-old housewife with an unremarkable past medical history, sought out-patient treatment in June 2000 for anxiety, insomnia, difficulty thinking and concentrating, and frequent episodes of aggressive behaviour. She was evaluated by neurologists, and was submitted to routine biochemical investigations (unremarkable), a computerised tomography scan (normal), and the Mini-Mental State Examination (24/30). Olanzapine (10 mg/day) was started and this was the sole medication continued thereafter. The patient soon experienced a subjective improvement. Three to four months later she noticed slight involuntary movements of the tongue and jaw. Despite these symptoms, she continued taking olanzapine until it was eventually stopped 1.5 years later (December 2001).

She was admitted to our hospital in March 2002. On examination, she displayed marked and distressing involuntary

https://doi.org/10.1192/bjp.182.1.81-b Published online by Cambridge University Press

movements of the tongue and jaw, grimacing, and mild choreic movements in the upper limbs. Extensive biochemical, neuropsychological and imaging work-up was negative. A diagnosis of drug-induced tardive dyskinesia was thus made, other causes of dyskinesia excluded and therapy with vitamin E, lorazepam and tiapride initiated.

In this case, the tardive dyskinesia was most likely a result of olanzapine administration. The age of the patient may have favoured the early appearance of involuntary movements after initiation of the therapy, even though olanzapine has been claimed to carry a low risk for tardive dyskinesia and other extrapyramidal symptoms (Beasley *et al*, 1999).

As olanzapine is increasingly being used in elderly subjects for behavioural disturbances and/or insomnia in the absence of psychosis, our report underlines the need for a careful assessment for tardive dyskinesia and other movement disorders in patients (and in particular elderly patients) taking this atypical neuroleptic.

American Psychiatric Association (1994) *Diagnostic and Statistical Manual of Mental Disorders* (4th edn) (DSM–IV). Washington, DC: APA.

Ananth, J. & Kenan, J. (1999) Tardive dyskinesia associated with olanzapine monotherapy (letter). *Journal of Clinical Psychiatry*, **60**, 870.

Beasley, C. M., Dellva, M. A., Tamura, R. N., *et al* (1999) Randomised double-blind comparison of the incidence of tardive dyskinesia in patients with schizophrenia during long-term treatment with olanzapine or haloperidol. *British Journal of Psychiatry*, **174**, 23–30.

Dunayevich, E. & Strakowski, S. M. (1999) Olanzapine-induced tardive dystonia (letter). *American Journal of Psychiatry*, **156**, 1662.

Jaffe, M. E. & Simpson, G. M. (1999) Reduction of tardive dyskinesia with olanzapine (letter). *American Journal of Psychiatry*, **156**, 2016.

Littrell, K. H., Johnson, C. G., Littrell, S., *et al* (1998) Marked reduction of tardive dyskinesia with olanzapine. *Archives of General Psychiatry*, **55**, 279–280.

V. L. Bella, F. Piccoli Institute of Neuropsychiatry, University of Palermo, via G. La Loggia, 1 – 90129 Palermo, Italy

One hundred years ago

The unconscious mind.
To the Editors of The Lancet

SIRS,—In a short account of Sir F. Treves's address at Liverpool I observe that the two principal points mentioned both refer to a subject that is coming more to the front every day. I allude to the power of the mind over the body. He speaks with the greatest appreciation of the value of symptoms, pointing out that in diseases generally (specially naming appendicitis) they are nature's effort to cure the disease. In short, he fully recognises the value of the *vis medicatrix naturae*, or as "nature" in this connexion is a pure fiction, we may say the unconscious purposive action of the organism or more briefly, and more accurately, "the unconscious mind." The second point alluded to is that in a hospital patients should not know where the operating theatre is or when they are to be operated on. This is because of the depressing effect the conscious mind, dwelling on these points, has on the body, influencing, indeed, to some extent the operation itself. This address therefore gives two capital illustrations of the effect of the unconscious mind and conscious mind on the body in disease—a subject I am most anxious to see developed scientifically by the profession and no longer left to be exploited by quacks.

I am, Sirs, yours faithfully,
A. T. SCHOFIELD, M.D. Brux.
Harley-street, W., Oct 13th, 1902

REFERENCE

Lancet, 18 October 1902, p. 1078.

Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Epsom, Surrey

https://doi.org/10.1192/bjp.182.1.81-b Published online by Cambridge University Press