LETTERS TO THE EDITOR

Table I Patient details

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<td>Months off treatment</td>
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4. Gottleib, M.S. & Young, L.S. Adverse reactions to pyrimethamine-sulfadoxine in context of AIDS. Lancet 1985; i: 1389

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Clomiphene citrate in Tourette’s syndrome

Sir,

We have recently successfully treated a 39 year old man with Tourette’s syndrome using the anti-estrogenic agent, clomiphene citrate (Clomid®). The patient exhibited motor and phonic tics associated with obsessive-compulsive behaviour, deviant sexual behaviour and sleep disturbances since the age of 7 years. Over the past few years he had experienced frequent unpleasant, sexually-oriented dreams. The patient’s symptoms were unresponsive to administration of haloperidol (dose range: 2–20 mg/day), diazepam (10–40 mg/day), clonidine (0.1–0.3 mg/day), clonazepam (1–4 mg/day) and chlorpromazine (25–75 mg/day). A recent neurological evaluation disclosed severe motor tics that involved the neck and shoulder muscles and, to a lesser extent, the extremities. In addition, he was frequently grunting and sniffing. Vocalizations were only noted during extreme mental excitement.

Based on recent evidence implicating deranged gonadotrophic functions in Tourette’s syndrome,1 we measured plasma luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels pre- and post-luteinizing hormone releasing hormone (LHRH) stimulation (100 μg s.c.). While baseline plasma LH levels were low (2.2 IU/l/ml), FSH levels were in the normal range (6.7 IU/l/ml). Following LHRH stimulation (after an overnight fast), LH levels rose to a peak of 108.6 IU/l/ml within 60 minutes, while FSH levels rose only moderately to 12.7 IU/l/ml at the same time. Baseline plasma testosterone levels were in the normal range (7.1 ng/ml). These findings suggested hypothalamic-mediated LHRH deficiency. After receiving informed consent from the patient and approval to proceed by the Human Subjects Committee, the patient was placed on clomiphene citrate (25 mg twice daily). Following one week of therapy, there was a dramatic reduction in the severity and, to a lesser extent, in the frequency of the motor and phonic tics. This was supported by a blinded videotape evaluation by two independent neurologists. In addition, the patient appeared relaxed, less depressed and also reported experiencing more pleasant, sexually-oriented dreams and an improvement in his sleep onset and duration. Paradoxically, plasma LH levels were undetectable, while FSH levels rose to 16.8 IU/l/ml. Testosterone levels rose slightly to 8.9 ng/ml within one week of therapy.

Clomiphene citrate, a non-steroidal oestrogen, has been shown to inhibit competitively oestradiol binding to oestrogen receptors in the rat pituitary and hypothalamus, suggesting that it acts as an anti-oestrogen.2 Other workers have suggested that clomiphene, like oestradiol, acts by increasing the responsiveness of gonadotrophs to LHRH.3 More recently, Kerin et al.4 provided evidence to suggest that clomiphene acts at a hypothalamic site by inducing an increase in the frequency of LHRH release. Whatever the mechanism of action of clomiphene in our patient may be, improvement of symptoms was accompanied by a depression of LH, elevation of FSH and testosterone levels, suggesting that his baseline abnormal gonadotrophin functions were somehow linked to the clinical expression of his disorder. Moreover, the supramaximal response of LH to administration of LHRH in our patient suggests the presence of supersensitive LHRH receptors in the hypothalamic-pituitary axis and further supports the clinical evidence for deranged hypothalamic functions in Tourette’s syndrome.5

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References


Stroke after heavy cannabis smoking

Sir,

We would like to report two cases of acute central nervous system dysfunction in previously fit young men with no risk factors for stroke, that followed severe cannabis intoxication. Stroke is known to be associated with acute alcohol intoxication in similar circumstances.1,2

Case 1

A 27 year old West Indian man with no previous medical history was admitted following a period of heavy cannabis smoking. Examination was unremarkable except that the patient was euphoric. The next morning he had developed a pseudo-bulbar palsy. All investigations were normal, including the sickle solubility test, haemoglobin, ESR, serum cholesterol and triglycerides, blood urea and electrolytes, liver function tests, glucose tolerance, chest and skull X-rays and the cerebrospinal fluid (CSF). Blood and CSF VDRL were negative. Intravenous thiamine made no impact. A year later he was still dysarthric and emotionally labile with a residual right-sided weakness.

Case 2

A 28 year old West Indian man with no past medical history was admitted to the psychiatric unit acutely confused and euphoric following a prolonged bout of cannabis smoking. On admission a conjugate deviation of the eyes to the left was noted though physical examination was otherwise normal. All investigations as for case 1 were normal. Intravenous vitamin B complex daily was examined. The conjugate deviation settled over 2 days. He was discharged with no permanent sequelae.

In a small, under-developed, independent island-state resources are limited and it is not possible to measure urine or plasma cannabinoids nor to perform computed tomographic scans, but it is clear that both these previously fit young men developed acute brain lesions, perhaps vascular in origin, following severe cannabis intoxication.

Similar cases have been described. Garrett et al.3 reported a young man who presented unconscious with bilateral pyramidal signs following a large dose of tetrahydro-cannabino. Mohan & Sood4 described a case of conjugate deviation of the eyes following cannabis intoxication very similar to case 2.

All this suggests that, similarly to alcohol, severe cannabis intoxication may be a factor in the cause of stroke, especially if the patient is initially euphoric. The mechanism is unknown as in stroke associated with alcohol. Dehydration or hypotension may play a role or perhaps the phenomenon of intoxication itself may lead to areas of neuronal death.

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References

Clomiphene citrate in Tourette's syndrome.

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