Prolactin, a protein hormone synthesised and released by the anterior pituitary, promotes mammary tissue development and lactation and suppresses gonadotrophin secretion. Dopamine is the natural inhibitor of prolactin release and so standard antipsychotics, which block dopamine receptors, will cause prolactin levels to rise. This hyperprolactinaemia can lead to gynaecomastia, galactorrhoea, menstrual disturbances, a reduction in sperm count, erectile dysfunction, failure of ejaculation and reduced libido. Prolactin-related adverse effects are frequently encountered in patients on antipsychotics and are a cause of substantial morbidity.

All antipsychotics except clozapine are associated with hyperprolactinaemia. In the majority of cases the rise in prolactin levels causes few problems. If, however, troublesome adverse effects occur, prolactin serum levels may be reduced by decreasing the dose of antipsychotic or discontinuing treatment. If this is not practicable, limited trial work has supported the use of amantadine or bromocriptine. This is reviewed below.

Amantadine’s mechanism of action remains unclear but it is thought to enhance dopaminergic activity by causing a release of dopamine or by direct agonist activity. Because amantadine had been used successfully to treat...
Parkinson's disease while engendering few adverse psychiatric phenomena, it was suggested that it may be successful in decreasing prolactin levels without worsening psychosis. In one study (Siever, 1981), a group of eleven patients (ten women, one man), of whom five had galactorrhoea, were given amantadine at a dose of 100 mg three times a day for two weeks. Prolactin levels were measured in eight of the eleven patients before and after amantadine treatment. Six of these patients showed a reduction although levels still remained above normal. Importantly, all five of the women who had experienced galactorrhoea showed some improvement in their symptoms.

A second study by Correa et al (1987) evaluated amantadine's effect on prolactin-mediated side effects in ten patients (six males, four females). Amantadine was given in doses of 200-300 mg/day for three weeks. At the end of this time, prolactin levels had decreased by an average of 21% (P<0.0005). Weight loss was observed in all ten patients and a decrease in breast tenderness, gynaecomastia, galactorrhoea and sexual dysfunction occurred in all patients who had presented with these adverse effects. Menstruation also returned in the women who had been amenorrhoeic before the study. According to an extrapyramidal rating scale, scores improved for seven out of nine patients. There was a significant but small fall in the overall Brief Psychiatric Rating Scale score indicating that amantadine did not worsen psychosis.

There are also two published studies evaluating the use of bromocriptine, a direct dopamine agonist. In the first (Beumont et al, 1975), bromocriptine was given in a dose of 2.5 mg twice daily to nine female patients to investigate its effects on prolactin levels, galactorrhoea and menstrual disturbances. In all but one of the patients prolactin levels fell but menses returned in only one of the eight patients. Five patients who had pronounced galactorrhoea before the study all experienced a reduction in symptoms. No discernible adverse effects were noted.

A trial published in Japan in which bromocriptine was given in a dose of 5-7.5 mg twice daily was reported in a review by Marken et al (1992). Treatment was generally successful with seven of ten subjects experiencing a return of menses, and several showing an improvement in galactorrhoea. Psychotic symptoms appeared not to be worsened by bromocriptine. A case report (Ramakrishnan et al, 1983) has also described the successful use of bromocriptine, up to 10 mg/day, in reducing prolactin levels and improving symptoms of galactorrhoea and amenorrhoea.

These open, small-scale trials indicate that both amantadine and bromocriptine may lower prolactin levels and improve prolactin-related adverse effects. Both drugs seem not to worsen psychotic symptoms. Nevertheless, bromocriptine is well known to cause psychosis in patients with Parkinson's disease and amantadine has been reported to cause hallucinations in an elderly patient with moderate renal failure (Borison, 1979). Amantadine may also precipitate mania (Regó et al, 1989).

In conclusion, if adverse effects associated with hyperprolactinaemia present as a serious problem and a reduction in the antipsychotic dose does not help, amantadine or bromocriptine may be helpful. Prolactin levels are usually lowered in a few days but prolactin-related adverse effects may take weeks to improve. Amantadine should be prescribed at a dose of 100 mg/day for the first week. This can be increased by 100 mg weekly until a dose of 200-300 mg/day is reached. Adverse effects include livedo reticularis and postural hypotension as well as nervousness, insomnia, dizziness, convulsions and hallucinations. If bromocriptine is prescribed it should be started at a dose of 1.25 mg at night. This can then be increased by 1.25 mg every two to three days until a daily dose of between 5 mg and 15 mg is achieved. Common adverse effects include nausea, postural hypotension, dizziness and headache; hallucinations occur rarely. Either drug should be withdrawn if any worsening of psychosis is suspected. Amantadine is not officially licensed for use in hyperprolactinaemia but is perhaps the drug of first choice because bromocriptine is generally held to be contra-indicated in any psychotic illness.

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Denise Duncan, Drug Information Pharmacist; and David Taylor, Principal Pharmacist, The Maudsley Hospital, Denmark Hill, London SE5 8AZ

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