Lesson of the Week

Anticholinergic drug abuse: a common problem?

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Anticholinergic drugs are widely used to counteract the extrapyramidal effects of neuroleptic medication; a recent survey showed that half of those receiving neuroleptic drugs were also prescribed anticholinergic agents.[1] The *British National Formulary* (1984) states: "The most commonly used drugs are orphenadrine and benzhexol. They may have a mood elevating effect which is useful in the management of phenothiazine induced Parkinsonism." What the *BNF* does not mention is that anticholinergics may be deliberately abused for their stimulating and euphoriant effects.

The first recorded case in 1960[2] has been followed by reports from Britain, North America, Australia, India, Israel, and Poland. Benzhexol (trihexyphenidyl, Artane) is by far the most frequently abused drug of this class, but abuse of biperiden (Akineton), benztropine (Cogentin), orphenadrine (Disipal), and procyclidine[5] (Kemadrin) has also been reported. Some of the published reports have been reviewed by Smith.[3]

Patients who are treated with neuroleptics for schizophrenia may abuse anticholinergic drugs prescribed to counteract the extrapyramidal effects. Benzhexol is the drug most frequently abused but others include orphenadrine and biperiden

Case reports

Clinical and informal contacts lead us to believe that anticholinergic abuse is important among longstanding patients with psychiatric illness attending Oxford hospitals.[4] Table I lists 28 abusers seen by us between 1980 and 1982. Their ages ranged from 22 to 56 (average 34·7); 25 were men, 21 had been diagnosed as suffering from schizophrenia (average length of illness 15 years), and all but one (case 24) had been prescribed neuroleptics at some time. The four cases described below illustrate further aspects of the problem.

Case 1—This 24 year old man of superior intelligence had a family history of schizophrenia. Shortly after his father's death, when the patient was aged 15, he first saw a psychiatrist. Two years later he was diagnosed as having an anxiety neurosis and was prescribed trifluoperazine together with orphenadrine. Over the next few years his behaviour became increasingly bizarre and on his first admission to hospital in 1980 he complained of paranoid delusions and auditory hallucinations and was diagnosed as suffering from a schizophrenic illness. In July 1981, when he was transferred to the care of one of us (GPP), he was receiving an intramuscular dose of fluphenazine decanoate (Modecate), 75 mg every three weeks, giving reasonable control of his positive symptoms, though he experienced appreciable parkinsonian side effects, for which he was receiving benzhexol. A reduction in his dose of fluphenazine decanoate to 25 mg every three weeks led to some decrease in side effects, but it was also observed that his tremor was variable and seemed to have a psychogenic component. At one time he complained of visual hallucinations, and it was then discovered that he was stealing orphenadrine and benzhexol from a fellow resident at his group home.

Biperiden was substituted for benzhexol for both this resident and the patient, but he quickly learned that four or more 1 mg tablets also had a stimulating effect and he increasingly abused this medication. Procyclidine (Kemadrin) was then prescribed as we could find no previous record of abuse for this drug at that time (but see Coid and Strang, 1982).[5] The patient soon discovered that he could get a "high" from it (see also case 10), however, and he was readmitted to hospital after swallowing fourteen 2·5 mg tablets. On examination he was anxious and restless with a tachycardia, raised blood pressure, and gross tremor. His speech was rapid but coherent and no abnormality of thought was elicited. His physical and mental condition returned to its previous state after 24 hours without further medication.

Case 17—This man spent much of the past eight years as an inpatient receiving treatment for paranoid schizophrenia. Like the first patient he stole benzhexol, but he was also one of several of our group who would purchase tablets from fellow patients. In addition, he could feign oculogyric crises to induce doctors who did not know him to prescribe anticholinergic drugs.

Case 4—After an extremely disturbed childhood, this man first presented to the psychiatric services at the age of 17 with an acute psychotic episode. This was diagnosed as schizophrenia, although the symptoms were atypical and proved extremely resistant to treatment with neuroleptic drugs. He abused a wide variety of drugs, including benzhexol. He had several short admissions to hospital, the most recent being for an amphetamine induced psychosis. We now consider his major psychiatric problem to be his polydrug abuse.

Case 24—This patient suffered from Klinefelter's syndrome and had a number of personality problems which led to psychiatric contact. He received neither phenothiazine nor anticholinergic medication and was not known to have any contact with patients with psychiatric illness. He drank excessively and abused a number of drugs, including benzhexol, which he purchased "on the street."

Informal contacts lead us to believe that anticholinergics are abused by other people in the Oxfordshire district who have never had contact with the psychiatric services.

Discussion

Anticholinergic drug abuse is quite common if judged by our unselected series of 40 known local abusers collected over two years.[4] Abuse was not necessarily confined to those with previous or present exposure to neuroleptic drugs, and indeed only 28 subjects from our series are presented here as the other 12 were not current psychiatric patients. There are, however, no better estimates available for the real prevalence of anticholinergic drug abuse and, as the risks of true dependence are still unknown, a systematic study is needed to develop further knowledge about its best management and prevention. A

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Details of 28 patients who abused anticholinergic drugs

Case No	Sex	Age	Psychiatric diagnosis	Duration of illness (years)	Anticholinergic abused	Other drugs abused
1	M	24	Schizophrenia	9	Procyclidine, biperiden, benzhexol, orphenadrine	Cannabis, lysergide
2	M	33	Schizophrenia	13	Benzhexol	Multiple
3	M	38	Schizophrenia	19	Orphenadrine, benzhexol	
4	M	23	Schizophrenia	9	Benzhexol	Multiple
5	F	38	Schizophrenia	13	Benzhexol	
6	F	41	Borderline personality disorder	22	Benzhexol	
7	M	32	Schizophrenia	18	Orphenadrine, benzhexol	
8	F	36	Schizophrenia	16	Benzhexol	Benzodiazepines
9	M	32	Schizophrenia	14	Benzhexol	Cannabis, lysergide
10	M	56	Schizo-affective disorder	20	Procyclidine, benzhexol	
11	M	32	Manic depressive illness	9	Benzhexol	Multiple
12	M	31	Schizophrenia	15	Benzhexol	Multiple
13	M	33	Schizophrenia	11	Benzhexol	Multiple
14	M	35	Personality disorder	6	Benzhexol	Multiple
15	M	33	Schizophrenia	16	Biperiden, benzhexol	Multiple
16	M	36	Schizophrenia	10	Biperiden	Multiple
17	M	31	Schizophrenia	8	Orphenadrine, benzhexol	
18	M	34	Schizophrenia	16	Benzhexol	
19	M	46	Schizophrenia	21	Benzhexol	
20	M	34	Schizophrenia	13	Benzhexol	
21	M	22	Schizo-affective illness	4	Biperiden	Multiple
22	M	32	Schizophrenia	8	Benzhexol	
23	M	36	Schizophrenia	18	Benzhexol	
24	M	22	Klinefelter's syndrome; personality disorder	9	Benzhexol	Alcohol, cannabis
25	M	42	Schizophrenia	24	Biperiden	
26	M	56	Schizoprenia	26	Orphenadrine	
27	M	32	Schizophrenia	18	Benzhexol	Multiple
28	M	31	Manic depressive illness	16	Orphenadrine	Multiple

history of abuse of other drugs was obtained in 15 subjects but it is difficult to be sure if this abuse preceded exposure to anticholinergics or developed concomitantly with it. Those who do abuse anticholinergic agents find the euphoriant and stimulant effects pleasurable, and this liability for abuse must detract from the usefulness of the mood elevating effect as described in the *BNF*. Twenty one subjects with schizophrenia predominated in this group, and work by one of us (NB) suggests that they may abuse these drugs in an attempt to counter the restricting effects of their blunted affect and social withdrawal.

No anticholinergic drug appears to be free from the potential for abuse. In both our series and in published reports benzhexol is the most favoured, with orphenadrine and biperiden also popular and procyclidine and benztropine seeming to be the least abused. These preferences may reflect either a real difference in their mood elevating properties or current prescribing patterns and therefore availability.

Abuse should be suspected in outpatients who ask for additional supplies of anticholinergic drugs claiming that they are running out quickly or that they have lost their prescription. With those patients having stable maintenance neuroleptic treatment who claim worsening extrapyramidal symptoms, it is advisable to examine and check their complaints as these side effects should reduce over time and some patients may feign parkinsonian symptoms (see case 17). The possibility of anticholinergic abuse should also be considered in patients who develop new and unusual symptoms, such as excitability, dizziness, tachycardia, or visual hallucinations, since they may be manifesting features of a toxic confusional state (see case 1).[2 5]

Nevertheless it is important to be cautious in changing these medication schedules, since abrupt withdrawal of anticholinergics may precipitate worsening of parkinsonian side effects in an appreciable number of patients having prolonged neuroleptic treatment, and it may also lead to an apparent recurrence of psychotic symptoms.

Anticholinergic drugs should be restricted to those patients with parkinsonian side effects that cannot be controlled by lowering their dose of neuroleptic. In patients already having anticholinergic drugs reduction in the dosage may be attempted while watching for increasing extrapyramidal or psychotic signs, and with patients having depot neuroleptics anticholinergic drugs can often be limited to the seven to ten days after the injection. With fluphenazine decanoate injections it may be possible to give intramuscular biperiden or procyclidine at the same time, and for this to be sufficient to counter the parkinsonian side effects that accompany the initial release of neuroleptic. For those patients who continue to require medication for extrapyramidal side effects, the lowest possible dose of anticholinergic drugs should be used, with prescriptions for short periods only, and a repeated attempt to reduce the dosage may be worth while after three to six months.[6-8]

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How rare is it for carcinoma of the prostate to be diagnosed from the presence of a secondary deposit in the lung visible in an x ray film of the chest?

Carcinoma of the prostate is the most frequent malignant tumour of men aged over 65. It is rare before the age of 40 and does not occur, interestingly enough, in eunuchs. Most patients present with local symptoms of prostatic obstruction. The next commonest group of symptoms is the development of backache or sciatica due to bony metastases and indeed these features occur in about half of cases. Pulmonary metastases are unusual, occurring in about 1% of patients, and usually take the form of multiple small deposits throughout both lung fields. A solitary metastasis in the lung would be a rare finding indeed. A more likely primary focus in a man would be from a carcinoma of the kidney, suprarenal, thyroid, or from the gastrointestinal tract.—HAROLD ELLIS, professor of surgery, London.

Correction

Empty epididymal syndrome

We regret that there was an error in the last sentence of the answer to this Any Question (18 August, p 425). It should read "The much less common condition of intratesticular obstruction with an associated empty epididymis cannot be treated surgically."