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Oxybutynin: is it Safe?

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Summary—Oxybutynin has been widely prescribed in the United Kingdom for more than 5 years on a named patient basis. Complete knowledge of its side effects is therefore particularly important. The literature contains remarkably little data on this topic. We therefore reviewed 192 consecutive patients for whom the drug had been prescribed in a district general hospital; 57% derived benefit while 76% noted side effects, none of which was dangerous or irreversible. Oxybutynin obtained from the two principal suppliers did not appear to differ either in efficacy or side effects. We discuss the uncertain medicolegal implications of named patient prescriptions.

Oxybutynin has been widely used in the UK in the treatment of detrusor instability for more than 5 years. In this country, however, unlike Europe and the United States of America, it has never been granted a full product licence and is available only on a named patient basis. The legal liability of a doctor using this method of prescription is not clear. It is therefore particularly important that the prescribing doctor is fully aware of any possible side effects. A comprehensive review of the literature revealed remarkably little information on Oxybutynin in general and its side effects in particular. We have therefore reviewed our own series of 192 consecutive patients who have received Oxybutynin over the last 5 years and report on both its efficacy and side effects.

Review of the Literature

Three independent computer searches of international journals produced 17 references to Oxybutynin (see References). Only 4 studies contained 20 or more patients to whom the drug was administered for 2 or more weeks (Moisey *et al.*, 1980; Riva and Casolati, 1984; Gajewski and Awad, 1986; Milani *et al.*, 1986).

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The indications, dosage and duration of treatment varied widely. Indications included spasm after transurethral surgery, enuresis, detrusor instability, neuropathic bladder, ureteric colic and bacterial cystitis. Many patients received only a single dose of Oxybutynin and in others the drug was administered for only a few days.

Almost all of the authors concluded that Oxybutynin was effective, the one exception being a study of bladder spasm after transurethral surgery (Wein *et al.*, 1978).

Only 5 of the 17 studies reported significant side effects, which were predominately anticholinergic (Brooks and Braf, 1980; Moisey *et al.*, 1980; Riva and Casolati, 1984; Bouwmeister *et al.*, 1986; Gajewski and Awad, 1986). Although these were a minority of the papers, in each the incidence of side effects was high (65–75%) and they were sufficiently unpleasant to justify discontinuation (intolerance) in 20 to 38% of patients.

Patients and Methods

Since Oxybutynin is available only on a named patient basis, our hospital pharmacy has been obliged to keep a record of each prescription: 192 new patients received the drug after it was first prescribed in 1982. We have inadequate data on 12 of these, leaving 180 patients whose records have been reviewed.

Results

Age and Sex

Figure 1 shows that the majority of our patients were female, between 40 and 70 years of age. The one patient under the age of 10 had a myelomeningocele. Most of the patients under the age of 30 were given the drug for either primary enuresis or a neurological disorder.

Indications for Treatment

Detrusor instability is the most widely accepted indication for Oxybutynin and this was the diagnosis in 151 (84%) of our patients. In 103 (57%) it was urodynamically proven. It was idiopathic in 117 (65%), associated with primary enuresis in 18 (10%) and with overt neurological lesions in 16 (9%). Of the 29 patients (16%) who appeared to have stable bladders, the majority suffered unexplained urgency (Fig. 2).

Dosage

The initial dose for detrusor instability was usually

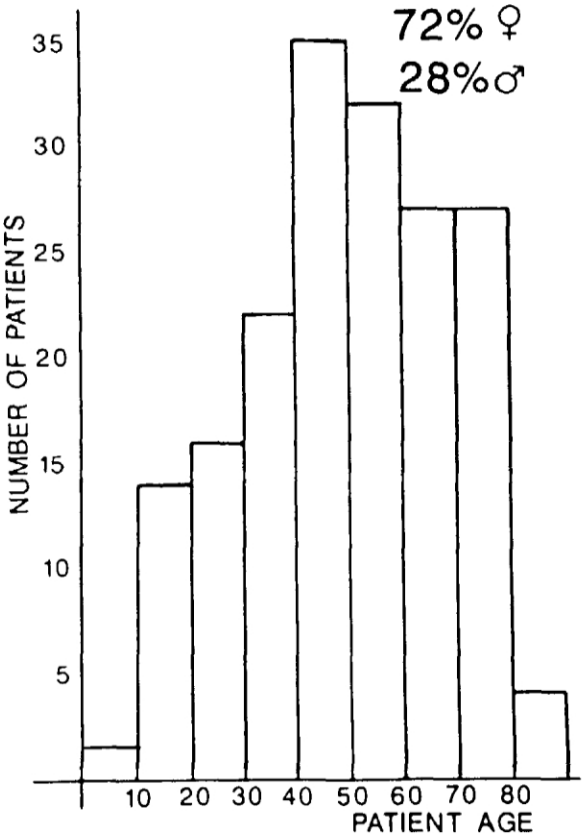

Fig. 1 Number and age of patients.

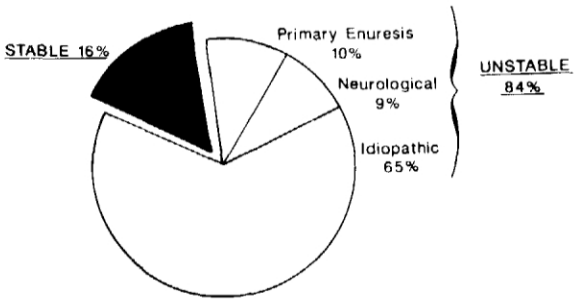

Fig. 2 Indications for Oxybutynin.

5 mg *tds*, and for enuresis 5 mg *nocte*. However, in elderly patients and those of small stature the dose was frequently reduced. Patients were initially prescribed 100 tablets and treatment was continued if the drug proved helpful and was well tolerated; 35 patients took the drug for more than 1 year and 13 of these took the drug for more than 3 years.

Efficacy

Figure 3 illustrates the number of patients who benefited from Oxybutynin. Those described as cured had a complete remission of symptoms which was maintained after the drug was stopped. The improved category includes all of those who derived any benefit from the drug; however, they relapsed when treatment was stopped.

Side Effects

Side effects were noted in 137 patients (76%) (Fig. 4). Forty-one patients (23%) had side effects so unpleasant that they stopped taking the drug (intolerance). The Table lists the various side effects which occurred, by far the commonest being dry mouth. However, a wide variety of side effects was reported, many related to the anticholinergic properties of Oxybutynin.

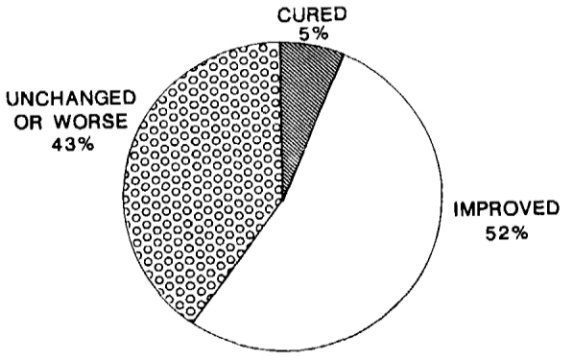

Fig. 3 Efficacy of Oxybutynin.

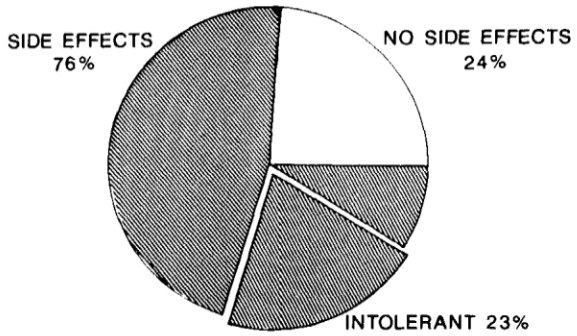

Fig. 4 Side effects and intolerance.

Scrutiny of the many haematological and biochemical screening tests did not reveal any worrying trends or changes.

Discussion

This is the first retrospective adult study of Oxybutynin reported in the literature. The number of patients and duration of treatment and study are far greater than in previous reports.

Only 57% of our patients derived benefit from the drug and in many cases this was only a modest improvement. This compares poorly with the results reported in the literature, where efficacy was never below 69% (Moisey *et al.*, 1980). However, the long duration of this study revealed a number of patients initially helped by Oxybutynin who subsequently abandoned it because worthwhile benefit was no longer obtained. It is probable that these patients were not detected in many of the short prospective trials previously reported.

Seventy-six per cent of our patients reported side effects which were usually anticholinergic and 23% were intolerant of the drug. The presence of side effects was the most important cause of non-compliance and the major limitation to Oxybutynin being more widely prescribed. However, none of the side effects was dangerous and all reversed when the medication was stopped. We were unable to find any pre-treatment factors reliably associated with either a good or a bad response to the drug.

Table Side Effects

Oral (144 patients)	Dry mouth Dysphagia Stomal ulcers
Visual (10 patients)	Dry eyes Blurred vision
Gastrointestinal tract (23 patients)	Diarrhoea Constipation Distension Nausea
Central nervous system (19 patients)	Headache Dizziness Drowsiness
Other (5 patients)	

It has been suggested that Oxybutynin obtained from the two principal suppliers (Tillots, Smith and Nephew) may differ in its side effects. Our series included 19 patients who changed from one supplier to the other during their treatment and were subsequently followed prospectively. Although the number was small, we found no evidence of any significant differences in side effects or efficacy between the two preparations.

The legal liability of a doctor prescribing a drug on a named patient basis is not clear. In the Pharmaceutical Journal (1986), one of the companies supplying Oxybutynin stated that until the drug was licensed, the prescriber had to take full responsibility for its use. However, one of the medical defence organisations stated in correspondence with the authors, "We do not believe that you will be placing yourselves in a vulnerable position if you continue to prescribe this drug on a named patient basis." They went on to state, "If any claim for damages were to be made against a doctor, the doctor will be covered by his indemnity insurance with a medical defence organisation in the same way as any other aspect of his professional work would be covered."

This study has highlighted the importance of side effects as a limitation to the use of Oxybutynin. Nevertheless, it has revealed no good reason why this drug should not be available under the normal method of prescription in this country. In view of this and the uncertain liability of the prescribing doctor, every effort should be made to encourage the suppliers of this drug to submit the necessary data to satisfy the Committee of Safety of Medicine's criteria for full registration.

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