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α-adrenoceptor blocking drugs and female urinary incontinence: prevalence and reversibility

H. J. MARSHALL & D. G. BEEVERS
University Department of Medicine, City Hospital, Birmingham, UK

There have been occasional reports of female stress incontinence related to prazosin therapy for hypertension. This drug is now rarely used but recently longer acting α-adrenoceptor blocking drugs have been introduced. We have, therefore, investigated the prevalence of urinary incontinence in all our female patients who were receiving α-adrenoceptor blockers in comparison with women, matched for age and parity who were receiving other drugs. We identified a total of 49 women taking α-adrenoceptor blocking drugs (prazosin 4, terazosin 5, doxazosin 40) among current patients who were attending our hypertension clinic. Twenty of these (40.8%) reported some urinary incontinence whereas in the control patients, only 8 (16.3%) had this symptom ($P = < 0.02$, relative risk 2.5, 95% CI 1.22–5.13). α-Adrenoceptor blockers were withdrawn in 18 of the 20 patients with incontinence and in 13, their symptoms abated. Our results suggest that there is a significantly higher prevalence of urinary incontinence in women taking α-adrenoceptor antagonists with reversibility on withdrawal of these drugs. As both female urinary incontinence, hypertension and the use of α-adrenoceptor blocking drugs are common, this distressing side effect should be borne in mind so that gynaecological or urological treatment may be avoided in some women.

Keywords α-adrenoceptor blocking drugs hypertension urinary incontinence

Introduction

α_1-adrenoceptor receptor blockers have been widely used in the treatment of systemic hypertension. Initially, prazosin and more recently the newer once daily preparations, (doxazosin and terazosin) have been marketed as being safe, relatively free of side effects and possibly conferring beneficial effects on glucose and lipid metabolism. There have been some sporadic case reports of stress incontinence in women taking prazosin [1–7] but this has not been investigated systematically or reported with the newer long acting α-adrenoceptor blockers.

The neurophysiology of bladder control in women depends in part on the presence of α-receptors in the smooth muscle of the bladder neck and the urethra. α-receptor stimulation causes smooth muscle contraction and this may explain how α-receptor blockers may induce urinary stress incontinence. This mechanism is supported by experimental evidence with measurements of urethral pressures before and after the intravenous administration of the non-selective α-adrenoceptor blocker, phentolamine [8–9]. Partial or complete α-adrenergic receptor blockade with 10–20 mg of intravenous phenotolamine caused marked and rapid reductions in urethral pressure particularly in the middle portion. Furthermore, the use of prazosin has been shown to reduce urethral closure pressure and functional urethral length [9]. After encountering a patient with stress incontinence which completely resolved after stopping terazosin, we conducted a case controlled study in our hospital based hypertension clinic to establish the prevalence of urinary incontinence in all our hypertensive women receiving α-adrenergic receptor antagonists compared with women, matched for age and parity who were taking other forms of antihyper tensive medication. We also investigated the reversibility of any stress incontinence after the withdrawal of α-adrenoceptor blockers in these patients.

Methods

We conducted a questionnaire of all women who were receiving α-adrenergic receptor blockers attending the

Correspondence: Professor D. G. Beevers, University Department of Medicine, City Hospital, Birmingham, B18 7QH

hypertension clinic. Each patient was compared with a control matched for age (±2 years) and parity. All women were specifically asked if they had experienced urinary incontinence, enough to cause inconvenience, on more than one occasion during normal daily activities within the previous 6 weeks. No distinction was made between the types of urinary incontinence as it was felt the distinction between genuine stress incontinence and urge incontinence on the basis of reported symptoms alone would be unreliable without urodynamic studies.

Patients were not included in this study if they had undergone hysterectomy or any form of pelvic floor surgery. Also excluded were all women with pain on micturition or any symptoms suggestive of urinary tract infection. Urine specimens were tested by dipsticks for protein and blood routinely at all clinic attendances and any new onset of proteinuria or haematuria was investigated by urine microscopy and culture. No women with cough due to angiotensin converting enzyme (ACE) inhibitors were included in this study. In all patients information was collected on possible confounding variables or factors which might cause or aggravate urinary incontinence including concurrent diuretic therapy, the use of dihydropyridine calcium channel blockers and the presence of chronic chest disease or obesity (body mass index wt (kg)/ht $(m)^2) > 30$. Patients with heart failure or previous stroke were not included in this study.

Where possible treatment with α-adrenergic receptor blockers was discontinued in those patients complaining of or reporting any incontinence and they were requestioned about their symptoms at subsequent clinic visits within 4 weeks. We did not obtain information on incontinence prior to starting α-adrenoceptor blockers as this would lead to recall bias.

Statistical analysis of the results of this survey was by chi squared tests with Yates' correction for small numbers. Probability of <0.05 were considered statistically significant.

Results

We were able to identify 49 women attending our clinic, who satisfied the criteria for the study and who were currently taking α-adrenergic receptor blocking drugs (doxazosin 40, terazosin 5 and prazosin 4). Their mean age was 58.2 years (range 34 to 81) and their mean parity was 2.9 (range 0 to 8). The mean age of the control patients was 58.9 years (range 32 to 79) and their mean parity was 2.7 (range 0 to 10).

Of the women receiving α-adrenoceptor blocker therapy, 20 (40.8%), when specifically asked, reported stress or urge incontinence whereas only 8 (16.3%) of the age and parity matched controls complained of this symptom ($P=0.02$, relative risk = 2.5, 95% CI 1.22 to 5.13).

Of the patients complaining of incontinence whilst taking α-adrenoceptor blockers, 18 had them discontinued to assess the effect on their urinary symptoms. We were unable to stop these drugs in two women; one had entered her first pregnancy but had reported incontinence prior to conception and the other patient had severe resistant hypertension and we felt that withdrawing α-adrenoceptor blockers would be unsafe. Thirteen of the 18 women who could stop α-adrenoceptor blockers reported total or almost complete resolution of their stress incontinence.

One patient in whom urinary incontinence had completely disappeared after stopping doxazosin, was later inadvertently re-challenged at a reduced dose. She reported that her symptoms recurred within a few days and resolved when doxazosin was stopped again.

We assessed all the subjects for the presence of possible confounding variables, particularly the use of thiazide or loop diuretics, calcium channel blockers, obesity and chronic chest disease.

Only two of these (the use of loop diuretics and concomitant chest disease) had any association with either urinary incontinence or the use of α-adrenoceptor blockers. When we excluded patients taking loop diuretics from our analysis, the prevalence of incontinence in those receiving α-adrenoceptor blockers was 11/32 (34.4%) *vs* 7/40 (17.5%) in control patients. With these figures, the relative risk fell to 1.96 (95% C I (0.86–4.49). Concomitant chronic chest disease was slightly but not significantly commoner in patients receiving α-adrenoceptor blockers (25.5% *vs* 19.6%) and although incontinence was significantly commoner in patients with chest disease (40.7% *vs* 15.0%), this did not influence the association between α-adrenoceptor blockers and incontinence. Obesity, and the use of calcium channel blockers did not alter the association between α-adrenoceptor blockers and incontinence.

Discussion

Urinary incontinence is a common but neglected symptom in women. A recent MORI poll published after we had started our study reported that 14% of women had experienced either stress or urge incontinence at some time and that 6% had experienced incontinence within the week prior to questioning [10]. Hypertension is also a common problem particularly in older women and it is now often treated with α-adrenoceptor blocking drugs. Our study shows that there is a significantly higher prevalence of urinary incontinence in hypertensive women taking α-adrenoceptor blockers compared with those on other drugs. We noticed a tendency for patients receiving α-adrenoceptor blockers also to be taking loop (but not thiazide) diuretics and there was a modest excess of chronic chest disease. This probably reflects our tendency to use α-adrenoceptor blockers in patients with resistant hypertension who were also receiving other antihypertensive drugs including frusemide. The excess of chronic chest disease reflects the reluctance to prescribe β-adrenoceptor blockers in such patients. Even allowing for the use of loop diuretics in our patients, the relative risk of urinary incontinence on α-adrenoceptor blockade remained at almost two although as our numbers are

small, this trend did not reach statistical significance. The dihydropyrine group of calcium channel blockers (particularly short acting nifedpine preparations) have been reported to have some mild diuretic properties. These drugs may cause nocturia and may also reduce the frequency and size of bladder contractions [11]. These properties might either aggravate or reduce any tendency to stress incontinence. However, the use of nifedipine was similar in both α-adrenoceptor blocker patients and controls so this confounding variable along with the prevalence of obesity did not explain the association of α-adrenoceptor blockers and incontinence. Furthermore, the reversibility of the incontinence could not be explained by any of the possible confounding variables we examined.

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