

Non-steroidal anti-inflammatory drugs and hypertension in the elderly: a community-based cross-sectional study

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- 1 Whether non-steroidal anti-inflammatory drug (NSAID) usage in the elderly elevates blood pressure or antagonises the blood pressure-lowering effect of antihypertensive medication is presently unknown. The primary aims of this study were to estimate the prevalence of NSAID usage, to evaluate the prescription of NSAIDs for arthritis and to determine whether NSAID usage was an independent predictor of hypertension in a large elderly community.
- 2 All non-institutionalised elderly (> 60 years) residents of Dubbo, NSW who attended for a baseline assessment were enrolled (1237 males, 1568 females). A questionnaire was administered and blood pressure was measured according to the Prineas protocol. The frequency of NSAID usage was determined, with stratification by age, sex, blood pressure group and history of arthritis.
- 3 NSAID usage was 26% overall (females 28%, males 23%), increased with age and was higher in females than males for every age group studied. Amongst patients with a past history of 'arthritis', 45% were using NSAIDs. Twelve percent were taking NSAIDs and antihypertensive medication concurrently, constituting the population at risk of an adverse drug–drug interaction. Employing a multiple logistic regression model which adjusted for several confounders in the cross-sectional analysis, NSAID usage significantly predicted the presence of hypertension (odds ratio: 1.4, 95% confidence interval: 1.1–1.7) with an attributable risk of 29%.
- 4 Amongst non-institutionalised elderly persons, NSAID usage may be an independent risk factor for hypertension. Considering the substantial consumption of NSAIDs by elderly patients, physicians should review their NSAID prescribing patterns for this community group.

Keywords anti-inflammatory agents non-steroidal hypertension elderly

Introduction

The prevalence of hypertension rises with age (Davidson *et al.*, 1989). Non-steroidal anti-inflammatory drugs (NSAIDs) have been reported to elevate blood pressure in previously normotensive subjects (Hardy *et al.*, 1988) and in patients with mild hypertension either untreated (Gerber *et al.*, 1990) or controlled by drug therapy (Chalmers *et al.*, 1984; Wong *et al.*, 1986). However, these effects are controversial (Pedrinelli *et al.*, 1982; Wright *et al.*, 1989) and have not been studied in the elderly. Any adverse influence of NSAIDs on

blood pressure control may potentially affect a substantial proportion of the elderly community.

The aims of the present study were to estimate the prevalence of NSAID usage and to evaluate antiarthritic drug prescribing patterns for the non-institutionalised elderly, to examine concurrent NSAID and antihypertensive drug usage and to determine whether NSAID usage was a significant, independent predictor of hypertension in a well-defined, elderly population.

Methods

The study population consisted of all non-institutionalised residents of Dubbo, NSW, who were born before January 1, 1930 (i.e. those > 60 years) and who attended for a baseline assessment, numbering 2805 subjects (1237 males and 1568 females). The study was approved by the Research Ethics Committee at St Vincent's Hospital and the Australian National University Ethics In Human Experimentation Committee. All participants gave written, informed consent. The methods and measures employed have been described in detail previously (Simons *et al.*, 1990, 1991).

Briefly, a review of the electoral roll and the records of all 21 general practitioners in Dubbo was coupled with written inquiry, telephone contact or home visitation and this identified 3860 eligible subjects (1693 males and 2167 females). Subjects were invited by mail to participate. Those who did not reply to the invitation were re-invited by mail, by telephone or by home visitation at a later date. Assessments took place over a 13 month period from August 1988. The attendance was 2805/3860 (73%), declining slightly with age from 77% in the age range 60–69 years to 61% in those > 80 years.

A questionnaire was administered by a trained volunteer interviewer, exploring a range of demographic and health-related issues including age, sex, self-prescribed medication, current tobacco and alcohol usage and past medical history. One of two registered nurses assessed the use of prescribed drugs and performed clinical investigations. An attempt to validate drug exposure data was made by inspection of actual drugs or a list of drugs brought to the assessment. Current NSAID use was defined as any NSAID usage (excluding aspirin prescribed for non-arthritic conditions) within 2 weeks preceding the assessment.

Medical assessment included anthropometry and blood pressure measurement. Blood pressure was measured with a mercury sphygmomanometer and standard cuff according to the Prineas protocol (Rose *et al.*, 1982); systolic and phase V diastolic were measured twice after 10 min seated rest and the mean values used in analyses. The nurses measuring blood pressure were unaware of the hypotheses under study in the present paper.

Blood pressure groupings

Subjects were allocated to one of three blood pressure groupings as defined in a previous report (Simons *et al.*, 1992); (i) normal blood pressure (systolic < 160 mm Hg and diastolic < 95 mm Hg, on no drugs for hypertension or cardiac disease); (ii) untreated high blood pressure (systolic \geq 160 and/or diastolic \geq 95 mm Hg, on no drugs for hypertension or cardiac disease); (iii) on drug treatment for hypertension. These criteria were selected in order to eliminate subjects using drugs for cardiac disease but not simultaneously for hypertension, since certain drugs (for example diuretics or β -adrenoceptor blockers) are employed for both cardiac disorders and hypertension. Consequently, 194 males and 274 females were eliminated from the original data set (approximately 17% of the sample).

Statistical methods

The equality of means across the three blood pressure groups was tested by one way analysis of variance, with the individual groups being contrasted by the Duncan procedure where appropriate. Frequencies were contrasted employing χ^2 analysis. The frequency of NSAID usage was tabulated in the study population according to age, sex, blood pressure group and history of arthritis.

Since the description of hypertension was arbitrary, two definitions were used in the analyses: (1) those in group (iii) only and (2) groups (ii) and (iii) combined. A multiple logistic regression model was employed to evaluate the prediction of hypertension (using either definition) by NSAID usage, adjusting for known confounders such as age, sex, body mass index (weight/height²), prevalent coronary heart disease, current smoking and any current alcohol. Age and body mass index were introduced as continuous variables, while all others were treated as categorical variables. Odds ratios were computed from the regression coefficients as an approximation of the relative risk of hypertension by NSAID usage. The risk of hypertension attributable to NSAID usage (i.e. attributable risk percent) was calculated from the equation: (odds ratio – 1/odds ratio).100 (Feinstein, 1985).

A separate multiple linear regression model was used to predict absolute blood pressure by NSAID usage after adjustment for the confounders listed above. In this model, analyses were restricted to the study population in groups (i) and (ii); blood pressure was studied as a continuous variable and all other variables were treated in the same manner as before. Statistical analyses were performed using SPSS, release 4.1 on a mainframe computer.

Results

NSAID and antihypertensive drug usage by age and sex is presented in Table 1. Twenty six percent of this elderly cohort were using NSAIDs (females 28%, males 23%); 38% were using antihypertensive medication for blood pressure reduction (females 41%, males 33%). The use of NSAIDs and antihypertensive drugs increased with age. More females than males were using either NSAIDs or antihypertensives in every age group studied. Amongst patients with a clinical history of 'arthritis', 91% (females 91%, males 92%) were on drug treatment for arthritis and 45% (females 44%, males 47%) were using NSAIDs. There were nine different NSAIDs prescribed, but the sample sizes were insufficient to analyse by individual NSAID type.

The prevalence of concomitant NSAID usage and hypertension in the entire cohort is presented in Table 2, stratified by sex. For definition 1 'hypertension', 12% (females 14%, males 9%) were using NSAIDs and antihypertensive drugs concurrently. Using definition 2 'hypertension', 15% (females 17%, males 13%) were using NSAIDs and were hypertensive concurrently. A summary of the clinical findings by sex and blood pressure grouping is presented in Table 3. Some of

Table 1 NSAID and antihypertensive drug usage by age (years) and sex

	Males				χ^2 , P	Females				χ^2 , P	
	60-69 n (%)	70-79 n (%)	≥ 80 n (%)	Age Adj* (/100)		60-69 n (%)	70-79 n (%)	≥ 80 n (%)	Age Adj* (/100)		
NSAIDs	146 (20)	118 (29)	22 (25)	24	12.2, < 0.005	211 (25)	167 (30)	57 (33)	28	7.5, < 0.025	
Anti-BP drugs	204 (31)	114 (36)	26 (39)	33	4.1, < 0.25	269 (36)	213 (49)	54 (50)	43	24.6, < 0.001	
<i>All males</i>						<i>All females</i>					
	n (%)					n (%)					
NSAIDs	286 (23)					435 (28)				7.7, < 0.01	
Anti-BP drugs	344 (33)					536 (41)				17.4, < 0.001	

Frequencies were contrasted using χ^2 analysis.

*Age-adjusted frequency of drug usage per 100 cohort subjects.

Table 2 Prevalence (%) of concomitant NSAID usage and hypertension in the study population

	Definition 1 hypertension	Definition 2 hypertension
Males	8.8	12.8
Females	13.9	16.5
Total	11.6	14.9

these relationships were discussed in our recent report (Simons *et al.*, 1992). The prevalence of hypertension by definition 2 was 52% (females 54%, males 50%) and current NSAID usage was significantly higher in both sexes amongst subjects on antihypertensive medication compared with subjects not taking antihypertensives.

In the multiple logistic regression model, after adjustment for age, sex, body mass index, prevalent coronary heart disease, current smoking and any current alcohol use, NSAID usage significantly predicted the presence of hypertension (regression coefficient, odds ratio estimate, 95% confidence interval)—definition 1 'hypertension': 0.30, 1.4, 1.1-1.7; definition 2 'hypertension': 0.21, 1.2, 1.0-1.5. Attributable risk percent estimates of NSAID use causing hypertension were 28.6% (definition 1 'hypertension') and 16.7% (definition 2 'hypertension').

A separate multiple linear regression model evaluated the prediction of absolute systolic and diastolic blood pressure by current NSAID usage. After adjustment for the above confounders, current NSAID usage did not significantly predict blood pressure in subjects not using antihypertensive medication (regression coefficient, 95% confidence interval, P , r^2 %)—systolic blood pressure: 1.03, -1.8 to 3.9, >0.40, 14.2; diastolic blood pressure: -0.16, -1.6 to 1.3 >0.80, 9.6.

Discussion

Between one quarter and one third of the non-institutionalised elderly population of Dubbo were current NSAID users in 1988-89. Such a high prevalence of NSAID usage may be generalised to the non-institutionalised elderly Australian population since the Dubbo population closely resembled the Australian elderly on numerous demographic, sociological and

health-related variables (Simons *et al.*, 1990, 1991). The prevalence of NSAID usage in elderly subjects in Newcastle, NSW has been reported to be more than 20% (Henry, 1988), which confirms the findings in this study.

Amongst the Dubbo elderly NSAID usage increased with age. Others (Armstrong & Blower, 1987; Walt *et al.*, 1986) have also reported a rising prevalence of NSAID usage with age which may reflect a higher incidence of musculoskeletal disorders and pain reporting (Baskin *et al.*, 1981). More females reported using NSAIDs than males for each age division studied. In two British group practices, more females were also found to be using one of six commonly prescribed NSAIDs than males (Steele *et al.*, 1987).

In the Dubbo cohort, 45% of those with a history of arthritis were using NSAIDs. Since the prevalence of osteoarthritis rises with increasing age such that it is almost universally found in individuals ≥ 75 years (Magaro *et al.*, 1989), it is likely that many elderly patients were taking NSAIDs for osteoarthritis. While NSAIDs are effective in reducing the symptoms associated with osteoarthritis (Bollet, 1981; Bradley *et al.*, 1991), the widespread usage of these agents in the elderly, who may be more at risk of certain gastrointestinal (Guess *et al.*, 1988; Langman, 1986), renal (Blackshear *et al.*, 1983), CNS (O'Brien & Bagby, 1985) and haematological (Inman, 1977) NSAID toxicity than relatively younger patients, raises the possibility that their prescription rates in the elderly may be excessive. Furthermore, in a randomized, double-blind, parallel study, Bradley *et al.* (1991) demonstrated that in patients with osteoarthritis, high (anti-inflammatory) doses of ibuprofen were not significantly different from low (analgesic) doses of ibuprofen or standard daily doses of paracetamol in pain relief or improvement of function, all three treatments being effective.

The prevalence of usage of antihypertensive medication increased with age and was higher in females than males for each age division studied, probably reflecting the prevalence of hypertension in this population. It is noteworthy that 12% of the cohort were at risk of a drug-drug interaction between NSAIDs and antihypertensives and that 15% were at risk of a drug-disease interaction between NSAIDs and hypertension (Table 2). Although the potential for such interactions does not define their actual incidence in the non-

References

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