Prescription of nonsteroidal anti-inflammatory drugs for elderly people in Alberta

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Objective: To examine the extent prescribed nonsteroidal anti-inflammatory drugs (NSAIDs) are used by elderly people in Alberta as well as the degree of concurrent use of multiple NSAIDs, of peptic ulcer medications and of certain medications known to have clinically significant adverse interactions with NSAIDs.

Design: Retrospective analysis of the Alberta Blue Cross database.

Setting: Alberta.

Patients: All people 65 years of age and older using the subsidized drug benefit plan for whom prescription claims were submitted for reimbursement between Jan. 1 and June 30, 1991.

Outcome measures: Number of people who received one or more prescriptions for NSAIDs, rates of prescribing peptic ulcer medications and drugs with the potential for clinically significant interactions with NSAIDs among NSAID users and non-NSAID users, and rate of prescribing more than one NSAID concurrently.

Results: Of the Albertan population 65 years of age and over 61 601 (26.7%) received at least one prescription for an NSAID during the study period. In decreasing order, the five most commonly prescribed NSAIDs were acetylsalicylic acid, diclofenac, naproxen, indomethacin and ibuprofen. The total cost of NSAID therapy was \$5 415 974. Of the people prescribed an NSAID 25.8% were also prescribed a peptic ulcer medication, as compared with 10.5% of the non-NSAID users. There was a significant relation between the increasing number of NSAID prescriptions and the likelihood of receiving a peptic ulcer medication. Those who received a prescription for an NSAID were more likely than non-NSAID users to have been prescribed coumarin anticoagulants, diuretics, angiotensin-converting-enzyme inhibitors, β-blockers, oral corticosteroids, methotrexate and lithium, all of which are known to have possible adverse interactions with NSAIDs. A total of 2631 people had two or more prescriptions for NSAIDs filled on the same day.

Conclusions: NSAIDs are prescribed frequently for elderly people and are associated with an increased likelihood of concurrent prescription of peptic ulcer medication and medications that could have adverse drug interactions with NSAIDs. Additional study is required to evaluate the appropriateness of NSAID use in elderly patients, to determine the degree of actual patient consumption of these medications, to document the true prevalence of clinically significant drug interactions and to formulate educational strategies to reach physicians with this information.

Objectif: Examiner dans quelle mesure les personnes âgées de l'Alberta utilisent des médicaments anti-inflammatoires non stéroïdiens (MAINS), ainsi que l'importance de l'utilisation simultanée de MAINS multiples, de médicaments contre les ulcères gastro-duodénaux et de certains médicaments qui ont, avec les MAINS, des interactions défavorables importantes et reconnues sur le plan clinique.

Conception : Analyse rétrospective de la base de données de la Croix bleue de l'Alberta.

Contexte : Alberta.

Patients: Tous les 65 ans et plus bénéficiant du régime de médicaments subventionnés et qui ont présenté une demande de remboursement d'une ordonnance entre le 1^{er} janvier et le 30 juin 1991.

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Mesures de résultats: Nombre de personnes qui ont reçu une ou plusieurs ordonnances de MAINS, taux d'ordonnance de médicaments contre les ulcères gastro-duodénaux et de médicaments qui peuvent provoquer, avec les MAINS, des réactions importantes sur le plan clinique chez les utilisateurs et les non-utilisateurs de MAINS, et taux d'ordonnance de plus d'un MAINS en même temps.

Résultats : Parmi les Albertains de 65 ans et plus, 61 601 (26,7 %) ont reçu au moins une ordonnance de MAINS au cours de la période d'étude. Par ordre décroissant, les cinq MAINS prescrits le plus souvent étaient l'acide acétylsalicylique, le diclofénac, le naproxen, l'indométhacine et l'ibuprofène. Le traitement aux MAINS a coûté au total 5 415 974 \$. Parmi les personnes à qui l'on a prescrit un MAINS, 25,8 % ont obtenu aussi une ordonnance pour un médicament contre les ulcères gastro-duodénaux, comparativement à 10,5 % chez les sujets n'utilisant pas de MAINS. Il y avait un lien important entre le nombre croissant d'ordonnances pour des MAINS et la probabilité de recevoir un médicament contre les ulcères gastro-duodénaux. Ceux qui ont reçu une ordonnance pour un MAINS avaient plus de chance que les sujets ne prenant pas de MAINS qu'on leur prescrive des anticoagulants coumariniques, des diurétiques, des inhibiteurs de l'enzyme de conversion de l'angiotensine, des β bloquants, des corticostéroïdes oraux, du méthotrexate et du lithium, médicaments qui peuvent tous réagir défavorablement avec les MAINS. Au total, 2 631 personnes ont fait remplir le même jour deux ordonnances ou plus pour des MAINS.

Conclusions: On prescrit souvent aux personnes âgées des MAINS qui sont liés à une probabilité accrue d'ordonnance simultanée de médicaments contre les ulcères gastro-duodénaux et de médicaments qui pourraient avoir des interactions médicamenteuses défavorables avec les MAINS. D'autres études s'imposent si l'on veut évaluer dans quelle mesure l'utilisation des MAINS convient chez les patients âgés, déterminer l'importance de la consommation réelle de ces médicaments chez les patients, documenter la prévalence véritable d'interactions médicamenteuses importantes sur le plan clinique et élaborer des stratégies d'éducation afin de communiquer ces renseignements aux médecins.

ppropriate use of medications remains an elusive goal.^{1,2} Adverse side effects are common and accompanied by a significant risk of morbidity and death and high costs.² This is particularly true for people 65 years of age and over, who consume 40% of all prescribed medications yet represent only 10% to 15% of the population.² The typical North American elderly person consumes four to five different medications per day.² Researchers claim that 10% to 30% of hospital admissions of elderly people are due in part to problems with medications.^{2,3}

Nonsteroidal anti-inflammatory drugs (NSAIDs) are some of the most commonly prescribed drugs and are also available over the counter.2 Approximately 40% to 60% of the people who use NSAIDs are 60 years of age and over.4 In the United States, there are an estimated 700 prescriptions for NSAIDs per 1000 people 65 and over every year. Studies suggest that the commonest indication for analgesic or anti-inflammatory doses of NSAIDs in elderly people is degenerative arthritis.5 Although NSAIDs are extensively used in the management of degenerative arthritis, there is little if any evidence supporting the assertion that they are more effective than simple analgesics.6 Recent studies have shown that acetaminophen, weight loss or exercise programs, or a combination, may be as effective as NSAIDs for the management of pain and functional limitations secondary to degenerative arthritis.7-9 A variety of other interventions are also available. 10-12 Most elderly patients taking an NSAID when admitted to hospital apparently

can have the drug successfully discontinued.¹³

The most serious side effect, gastric and duodenal ulceration, occurs in approximately 20% of those treated with NSAIDs.^{2,14} Elderly people are clearly at increased risk for serious NSAID-associated bleeding in the upper gastrointestinal tract. 4.15-19 Ranitidine, cimetidine, misoprostol and omeprazole appear to be effective in preventing NSAID-induced duodenal ulcerations.²⁰⁻²³ All of the agents approved for treating peptic ulcers are effective in healing gastric and duodenal injury if NSAID therapy is stopped. Only misoprostol has been reported to be effective in treating NSAID-induced gastropathy in patients continuing NSAID therapy.²³ Currently there is no evidence to suggest that the frequency of serious bleeding in the upper gastrointestinal tract is reduced by any agent, including misoprostol, in people taking an NSAID.24 The proportion of patients with NSAIDinduced peptic ulcers necessitating admission to hospital has been estimated to be 29%.25 In Alberta this would translate into approximately 300 admissions per year.²⁶ Edema, renal insufficiency, electrolyte abnormalities (e.g., hyperkalemia), liver function abnormalities, rash and various abnormalities of the central nervous system are other side effects of NSAID use. 2.14,27-29

NSAIDs have a number of clinically significant adverse drug interactions, some of which are outlined in Table 1.^{5,10,27–36} The whole area of drug interactions in elderly people remains unsettled.³⁷ Published reports suggest that 8% to 51% of such people are at risk.^{38–43}

The concurrent administration of two or more

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NSAIDs may lead to an increased risk of side effects, with little or no increase in efficacy.³⁰ There appears to be interpatient variability in clinical response to different NSAIDs; therefore, there may be some rationale for changing from one NSAID to another.²⁸

Another concern about these medications is their cost. In a report of the cost of NSAID therapy for arthritis 69% was for drug costs and the remaining 31% for the treatment of NSAID-induced adverse gastrointestinal reactions. Sustained-release preparations are more expensive than regular forms but are claimed to improve patient compliance. Patients have shown better compliance with NSAIDs if given once daily than if given frequent dosages during the day. It would be important to confirm that improved compliance leads to greater benefit without unacceptable adverse effects in the elderly population, particularly since sustained-release preparations are more expensive.

Leufkens and associates,⁴⁷ in a utilization study involving half a million people in the Netherlands, identified 8.6% of the people as having used one or more NSAIDs (excluding salicylates) during the preceding year. More than half of the "heavy" users showed concomitant use of H₂ blockers, antacids or diuretics, or a combination.

We wished to expand on this and other work by looking at NSAID use and the use of other drugs of interest in a large elderly population. In this paper we report on the extent and type of prescribed NSAID use by elderly people in Alberta as well as the degree of concurrent use of NSAIDs, of medications approved for the treatment of peptic ulcers and of select medications known to have clinically significant adverse drug interactions with NSAIDs.

Methods

We obtained from Alberta Blue Cross records of claims for reimbursement submitted to it between Jan. 1 and June 30, 1991, for prescriptions of interest dispensed to people 65 years and over. The Alberta Health Care Insurance Plan provides premium-free Alberta Blue Cross benefits for elderly residents. In 1991, there were 230 545 Albertans 65 years and over, the figure used to calculate our rates. Up to July 1, 1991, the cost of any medication prescribed by a licensed physician would be reimbursed. This benefit did not include medications prescribed while individuals were inpatients in general or acute care hospitals (approved bed complement of 12 277 in the province), auxiliary hospitals (approved bed complement of 5013), or mental health hospitals (approved bed complement of 1072). In addition, we were unable to include NSAIDs purchased over the counter (e.g., acetylsalicylic acid [ASA]), prescriptions covered by other drug benefit plans and not submitted to the Alberta Blue Cross and covered prescriptions dispensed between Dec. 1, 1990, and June 30, 1991, that were not submitted, for whatever reason, to the Alberta Blue Cross for reimbursement.

Using the American Hospital Formulary System we requested all prescription records for drugs in the following classes: antihistamines, antineoplastics, iron preparations, anticoagulants, cardiovascular drugs, analgesics and antipyretics, opiate antagonists, diuretics and uricosuric drugs, gastrointestinal drugs, sulfonylureas and unclassified agents. Data will not be provided on all of these drug classes in this report. This listing includes all prescriptions for NSAIDs, drugs for the treatment of peptic ulcer disease, coumarin anticoagulants,

Drugs	Type of interaction	Description	Significance		
Lithium	Pharmacokinetic	Impaired renal excretion	Increased risk of lithium toxic effects		
Methotrexate	Pharmacokinetic	Decreased renal clearance	Increased risk of methotrexate toxic effects		
ACE inhibitor,* B-blocker, diuretic	Pharmacodynamic	Attenuated anti- hypertensive or diuretic effects	May lead to ineffective therapy or adjustment of dosages		
Coumarin anticoagulant	Combined or uncertain	Prolonged prothrombin time; increased risk of hemorrhagic peptic ulcer disease	Increased risk of major hemorrhage		
Oral cortico- steroid	Combined or uncertain	Increased risk of peptic ulcer disease	Increased risk of symptomatic ulcera- tion of the upper gastrointestinal tract		

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diuretics, angiotensin-converting-enzyme (ACE) inhibitors, \(\beta\)-blockers, corticosteroids, methotrexate and lithium. The same NSAID formulation made by different manufacturers or different strengths of the same NSAID were counted as one type of NSAID.

We examined the use of 16 NSAIDs: ASA, diclofenac, diflunisal, fenoprofen, floctafenine, flurbiprofen, ibuprofen, indomethacin, ketoprofen, mefenamic acid, naproxen, phenylbutazone, piroxicam, sulindac, tiaprofenac acid and tolmetin. ASA was categorized as either plain ASA (including enteric-coated formulations) or ASA combinations (ASA combined with one or more active drug in the same preparation, such as ASA-codeine).

For this study low-dose ASA consumption was defined as 210 tablets or less during the study period. This would indicate the use of approximately one tablet or less per day (212 days from Dec. 1, 1990, to June 30, 1991). Previous studies have indicated a relation between the dose of ASA used and the likelihood of adverse effects.⁴⁸ However, results from more recent reports suggest that even low-dose ASA use carries measurable risks for gastrointestinal side effects.⁴⁹

We evaluated the extent of concurrent prescriptions of agents approved for the treatment of peptic ulcer disease (antacids, H₂-receptor anatagonists, misoprostol, omeprazole and sucralfate).⁵⁰ We also evaluated the extent of concurrent prescriptions of drugs for which there is a risk of clinically important adverse drug interactions (Table 1). For both the antiulcer medications and those with the potential for adverse drug interactions we defined concurrent use as the reimbursement for prescriptions of an NSAID and these medications any time during the study period. We felt that the strongest evidence of concurrent use of two or more NSAIDs would be the dispensing of multiple NSAIDs on the same day.

The Alberta Blue Cross provided all the pertinent prescription records as well as the drug-cost data. All invalid prescription records (e.g., those with missing data) and records of prescriptions dispensed before Dec. 1, 1990 (a prescription may have been dispensed earlier in 1990 but not submitted for reimbursement until January 1991 or later) were removed from the database before analysis. Each patient, physician and pharmacy was assigned a unique scrambled identifier, which was then used consistently in all prescription records.

Data analysis was performed with SPSS and Statistix software (version 4.0; Analytical Software, St. Paul, Minn.). Descriptive statistics, χ^2 analyses and relative risk ratios (with confidence intervals) were calculated with standard methods.⁵¹

Results

A total of 61 601 patients (26.7% of the total Albertan population 65 years and over) received at least one prescription for an NSAID between Dec. 1 and June 30,

1991. The total number of NSAID prescriptions reimbursed were 160 231 (2.60 prescriptions per NSAID claimant). Table 2 shows an overview of NSAID use by specific agent. Most (81.3%) of the patients received one type of NSAID, 15.8% two, 2.5% three and 0.5% four or more. The total cost of the NSAIDs was \$5 415 974.

ASA prescriptions

A total of 22 550 patients (9.8% of the elderly population in Alberta and 36.6% of those prescribed NSAIDs) received an ASA prescription. Most (97.2%) were reimbursed for a plain ASA preparation; of these people 97.3% received only one dose strength: 325 mg (prescribed for 63.1%) and 650 mg (prescribed for 36.0%) were the most common doses. The mean number of ASA tablets per individual was 194 (standard deviation [SD] 143). Of the people prescribed ASA 16 929 (77.2% of those who received plain ASA) received low-dose therapy.

Prescriptions for peptic ulcer medications

Table 3 shows the relative proportions of patients receiving peptic ulcer medications among those with and without an NSAID prescription. A total of 33 687 patients (14.6% of the elderly population) submitted a claim for one or more prescriptions of peptic ulcer medications. The relative proportion of these prescriptions among patients receiving an NSAID ranged from 40.0% (for omeprazole) to 87.1% (for misoprostol). Of the patients prescribed an antiulcer medication 47.2% had also been prescribed an NSAID. Fig. 1 shows the relation between the number of NSAID claims and the proportion of people prescribed a variety of medications, including those for peptic ulcers. There was a significant relation between the increasing number of NSAID prescriptions and the likelihood of receiving a peptic ulcer medication (p < 0.001).

If one assumes that the rate of prescribing peptic ulcer medications in the NSAID group would be the same as the rate in the non-NSAID group (10.5%) except for the concurrent prescription of NSAIDs, one can attribute 28% of all the prescriptions for peptic ulcer medications to the use of NSAIDs. The proportions attributable for the individual agents are as follows: misoprostol 82.1%, sucralfate 55.5%, nizatidine 31.9%, antacids 27.6%, ranitidine 26.1%, famotidine 25.7%, cimetidine 19.9% and omeprazole 19.0%. The total cost for peptic ulcer medications during the study period was \$5 079 529; therefore, the 28% of the total usage attributed to NSAIDs translates to an estimated \$1 422 268 as an indirect cost of NSAID use.

Adverse drug interactions

Table 4 shows the relative proportions of patients re-

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ceiving drugs for which there is a risk of clinically significant adverse drug interactions with NSAIDs among those with and without an NSAID prescription claim. The proportion of people who received a particular drug listed in Table 4 and who received an NSAID ranged from 28.2% (for coumarin anticoagulants) to 67.6% (for methotrexate). Fig. 1 shows the relation between the number of NSAID prescriptions and the likelihood of

‡In 1991 Canadian dollars.

of NSAID.

prescriptions for cardiac medications (i.e., ACE inhibitors, β -blockers, calcium-channel blockers, loop diuretics, spironolactone, thiazide diuretics and triamterene), oral corticosteroids and coumarin anticoagulants. There was a significant relation between the increasing number of NSAID prescriptions and the likelihood of a prescription for a cardiac medication (p < 0.001) and an oral corticosteroid (p < 0.001).

IST OFFICE OF FURNISHED AND		No.			
NSAID	No. of prescriptions	All		Received SR preparations	Cost, \$‡
ASA	populación l'asedante	remi.			
Plain	49 094	21 929	(9.5)	234 (1.1)	528 199
Combination	1 546	737	(0.3)	entrant	28 02
Total	50 640	22 550§	(9.8)	234 (1.0)	556 220
Diclofenac	30 534	13 864	(6.0)	9 640 (69.5)	1 660 25
Naproxen	15 051	7 956	(3.5)	1 434 (18.0)	575 759
Indomethacin	14 695	6 876	(3.0)	2 144 (31.2)	589 209
Ibuprofen	12 141	6 328	(2.7)		214 374
Ketoprofen	8 924	4 250	(1.8)	1 978 (46.5)	455 050
Tiaprofenac acid	6 974	3 187	(1.4)	100 (3.1)	336 82
Sulindac	6 339	2 907	(1.3)		304 36
Piroxicam	6 270	2 976	(1.3)		356 42
Flurbiprofen	3 421	1 789	(0.8)	77 (4.3)	146 17
Diflunisal	1 855	855	(0.4)	_	87 08
Floctafenine	1 283	704	(0.3)	_	44 67
Tolmetin	848	396	(0.2)	-	47 65
Phenylbutazone	500	364	(0.2)	_	9 14:
Mefenamic acid	450	235	(0.1)	_	17 91
Fenoprofen	306	136	(0.1)	-	14 85
Total	160 231	61 601§	(26.7)	15 607 (25.3)	5 415 97

Table 3: Relative frequency of use of drugs for peptic ulcer disease in elderly people prescribe an NSAID and those not prescribed an NSAID					
	No. (and %) of people				

\$The total number is lower than the sum of the numbers because some of the people received more than one type

	No. (and %) of people						
Drug	Prescribed an NSAID (n = 61 601)		Not prescribed an NSAID (n = 168 944)		R (ar	p value	
Ranitidine	6 293	(10.2)	8 192	(4.8)	2.08	(2.02, 2.14)	< 0.001
Antacid	3 901	(6.3)	4 438	(2.6)	2.42	(2.32, 2.52)	< 0.001
Cimetidine	2 502	(4.1)	3 572	(2.1)	1.95	(1.90, 2.00)	< 0.001
Sucralfate	2 453	(4.0)	1 186	(0.7)	5.71	(5.37, 6.07)	< 0.001
Omeprazole	1 276	(2.1)	1 879	(1.1)	1.91	(1.78, 2.05)	< 0.001
Famotidine	1 405	(2.3)	1 660	(1.0)	2.30	(2.15, 2.46)	< 0.001
Misoprostol	2 138	(3.5)	317	(0.2)	17.50	(17.05, 17.96)	< 0.001
Nizatidine	365	(0.6)	393	(0.2)	3.00	(2.55, 3.52)	< 0.001
One or more of the above	15 885	(25.8)	17 802	(10.5)	2.45	(2.40, 2.50)	< 0.001
*CL = confidence limits.	9,19,764.3	(60.0	1 08	TE OF			aliulini).

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Concurrent use of multiple NSAIDs

Prescriptions for two or more NSAIDs were dispensed on the same day for 2631 patients (1.1% of the elderly population, 4.3% of those receiving an NSAID). There were 4046 combinations (3959 combinations of two NSAIDs, 83 of three, 3 of four and 1 of five). Relatively few (494 [12.2%]) of the combinations included ASA. The prescriptions for multiple NSAIDs were usually prescribed by a single physician and dispensed by a single pharmacy — this was the case for the four people who received combinations of four or five NSAIDs.

Discussion

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NSAIDs are heavily used by elderly people in Alberta. Although ASA was found to be the commonest one prescribed, the most expensive agent used was diclofenac, which was predominantly provided in the sustained-release form and accounted for 30.7% of the total

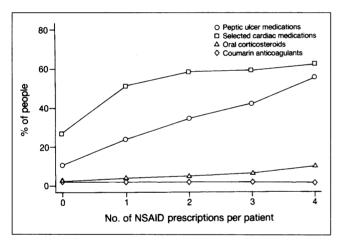


Fig. 1: Proportion of elderly people in Alberta prescribed select drugs that could have clinically significant adverse interactions with nonsteroidal anti-inflammatory drugs (NSAIDs), by number of NSAID prescriptions per patient, from Dec. 1, 1990, to June 30, 1991.

cost of NSAIDs. Further study of whether the use of sustained-release preparations leads to better clinical outcomes in older patients with degenerative arthritis is needed before the widespread use of such preparations can be supported in this clinical setting. Agents for the treatment of peptic ulcer disease were commonly prescribed for patients receiving NSAIDs. It is unclear how useful this intervention was in preventing NSAID-induced upper gastrointestinal ulceration. The agent that is arguably the most effective (misoprostol⁵²) was prescribed for only 3.5% of the peoole given an NSAID. Of those given misoprostol 87.1% were also receiving an NSAID.

NSAIDs are associated with many potentially significant adverse drug interactions. Our study was the first population-based one of the frequency of concurrent administration of NSAIDs and drugs with this potential. We have no way of knowing how many adverse interactions actually occurred and were detrimental to the patient. Linkages to hospital and physician databases might have provided information on this issue, but these data sets are likely inadequate as currently constructed. A finding of concern was that the NSAID users were more likely than non-NSAID users to be prescribed the interacting medications. This may reflect the underlying disease state of NSAID users rather than any direct causal relation. Another explanation is that any prescription is a marker of additional prescriptions, presumably because it means that the patient is seeing a physician. We feel that this area requires additional study.

We see little if any rationale for prescribing two or more NSAIDs concurrently other than possibly ASA as an antithrombotic given with another NSAID as an analgesic or anti-inflammatory drug; however, there is some evidence that NSAIDs as a class may offer a cardioprotective effect.⁵³ Measures should be taken to prevent this type of high-risk prescribing. Our method for estimating concurrent therapy was conservative and probably underestimated the true extent of the problem. This and alternative methods for determining concurrent use of NSAIDs should be validated

	No. (and %) of people						
Drug	Prescr an NS (n = 61	AID		scribed SAID 88 944)	Relative risk (and 95% CL)		p value
Coumarin							
anticoagulant	1 006	(1.6)	2 564	(1.5)	1.08	(1.00, 1.17)	< 0.05
Diuretic	19 702	(32.0)	26 271	(15.6)	2.07	(2.04, 2.10)	< 0.001
ACE inhibitor	8 753	(14.2)	10 403	(6.2)	2.29	(2.23, 2.35)	< 0.001
B-blocker	8 067	(13.1)	11 459	(6.8)	1.93	(1.91, 1.98)	< 0.001
Oral corticosteroid	2 008	(3.3)	3 540	(2.1)	1.57	(1.49, 1.66)	< 0.001
Methotrexate	69	(0.1)	33	(0.02)	5.74	,	< 0.001
Lithium	47	(0.1)	90	(0.05)		(1.01, 2.03)	< 0.05

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through a comparison of estimates and actual consumption.

Our study had a number of limitations. We did not attempt to evaluate the appropriateness of the daily doses prescribed, because this information was unavailable. If this information is felt to be important the "assumed" average daily dose could be calculated and then compared with maximum recommended doses established for each NSAID.⁵⁴ This estimation of consumption should be validated in empirical studies. Also, we grouped all NSAIDs together, when in fact patients' responses and side effects vary between different agents.²⁸ For example, enteric-coated ASA appears to cause less gastric and duodenal irritation than plain ASA and buffered ASA.⁵⁵

Severe restrictions are imposed by the Alberta Blue Cross database. It does not provide the sex and other relevant characteristics of drug users. Information relating to indications for therapy, directions given to patients, compliance and outcomes of therapy are lacking. Finally, because NSAIDs are available over the counter and consumption within health care facilities is not included in the database, this is an incomplete data set for total NSAID use. These qualifications would lead to an underestimate of actual use.

On the basis of our results we feel that NSAID use could be moderated by increased knowledge and use of alternative treatments for musculoskeletal disorders, particularly degenerative arthritis. Cost savings could arise from more selective use of sustained-release preparations in patients with known or suspected compliance problems. Research is required to clarify the issue of prescribing ASA for cardiovascular protection in patients using another NSAID. Finally, there appears to be a need for increased awareness on the part of physicians about drug interactions.

One of the main challenges will be to link prescription data with clinical information.⁵⁶ This, coupled with greater clarity on the indications for NSAIDs and guidelines for their appropriate use, would permit more definitive conclusions on the relative benefits and burdens of NSAID therapy.

We thank the Alberta Blue Cross for allowing us access to its database. This study was done in conjunction with the McGill-Calgary Drug Research Team, which is a collaborative group of researchers at these two institutions with an interest in rational drug use, particularly in elderly people.

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References

- Mahon WA, Godden JO: Control of therapy. Can Med Assoc J 1973; 109: 89-90
- 2. Hobson M: Medications in older patients. West J Med 1992; 157: 539-543

- Col N, Fanale JE, Kronholm P: The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Arch Intern Med* 1990; 150: 841-845
- Gurwitz JH, Avorn J: The ambiguous relation between aging and adverse drug reactions. Ann Intern Med 1991; 114: 956–966
- 5. Murray MD, Brater DC: NSAIDs. Clin Geriatr Med 1990; 6: 365-441
- Dieppe PA, Frankel SJ, Toth B: Is research into the treatment of osteoarthritis with NSAID misdirected? *Lancet* 1993; 341: 353-354
- Bradley JD, Brandt KD, Katz BP et al: Comparison of an antiinflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and acetaminophen in the treatment of patients with osteoarthritis of the knee. N Engl J Med 1991; 325: 87-91
- Kovar PA, Allegrante JP, MacKenzie CR et al: Supervised fitness walking in patients with osteoarthritis of the knee. Ann Intern Med 1992; 116: 529-534
- Felson DT, Zhang Y, Anthony JM et al: Weight loss reduces the risk for symptomatic knee arthritis in women. Ann Intern Med 1992; 116: 535-539
- Johnson AG, Day RO: The problems and pitfalls of NSAID therapy (part II). Drugs Aging 1991; 1: 212-227
- 11. Maxanec DJ: Conservative treatment of rheumatic disorders in the elderly. *Geriatrics* 1991; 46 (5): 41–45
- 12. Liang MH, Fortin P: Management of osteoarthritis of the hip and knee. N Engl J Med 1991; 325: 125–127
- Jones AC, Berman P, Doherty M: NSAID usage and requirement in elderly acute hospital admissions. Br J Rheumatol 1992; 31: 45-48
- Buechler JR, Malloy W: Drug therapy in the elderly. Postgrad Med 1989; 85 (6): 87-89
- 15. Guess HA, West R, Strand LM et al: Fatal UGI hemorrhage or perforation among users and nonusers of NSAIDs in Saskatchewan, Canada, 1983. *J Clin Epidemiol* 1988; 41: 35-45
- 16. Armstrong CP, Blower AL: NSAIDs and life threatening complications of peptic ulceration. *Gut* 1987; 28: 527–532
- 17. Clinch D, Banerjee AK, Levy DW et al: NSAIDs and peptic ulceration. J R Coll Physicians Lond 1987; 21 (3): 183-187
- Griffin MR, Piper JM, Daugherty JR et al: NSAID use and increased risk for peptic ulcer disease in elderly persons. *Ann Intern Med* 1991; 114: 257-263
- Gabriel SE, Jaakkimainen L, Bombardier C: Risk for serious gastrointestinal complications related to use of nonsteroidal antiinflammatory drugs. Ann Intern Med 1991; 115: 787-796
- Levy RA, Smith DL: Clinical differences among NSAIDs. Drug Intell Clin Pharm 1989; 23: 76–85
- Stalnikowicz R, Pollak D, Eliakim A et al: Cimetidine decreases indomethacin induced duodenal mucosal damage in patients with acute musculoskeletal disorders. Gut 1988; 29: 1578–1582
- Oddsson E, Gudjonsson H, Thjodleifsson B: Protective effect of omeprazole or ranitidine against naproxen induced damage to human gastroduodenal mucosa. [abstract] Scand J Gastroenterol 1990; 176 (suppl): 25
- Agrawal NM: Making sense of NSAID gastropathy and considering therapeutic options. Scand J Rheumatol 1992; 92 (suppl): 13-19
- Walt RP: Misoprostol for the treatment of peptic ulcer and antiinflammatory-drug-induced gastroduodenal ulceration. N Engl J Med 1992; 327: 1575-1580
- Griffin MR, Piper JM, Daugherty JR et al: NSAID use and increased risk for peptic ulcer disease in elderly persons. Ann Intern Med 1991; 114: 257-263
- 26. Hospital morbidity, 1989–90. *Health Rep* 1992; 4 (1, suppl): 32–35
- Johnson AG, Day RO: The problems and pitfalls of NSAID therapy in the elderly (part 1). Drugs Aging 1991; 1: 130-143
- Day RO, Graham GG, Williams KM et al: Clinical pharmacology of NSAIDs. In Orme MCLE (ed): Anti-Rheumatic Drugs, Pergamon Press, New York, 1990: 137–187
- Tatro DS (ed): Drug Interaction Facts, Facts and Comparisons, St Louis, 1992

321

- Verbeeck RK: Pharmacokinetic drug interactions with NSAIDs. Clin Pharmacokinet 1990; 19: 44–46
- 31. Knodel LC: NSAID adverse effects and interactions Who is at risk? *Am Pharm* 1992; 32 (Mar): 39–47
- 32. Houston MC: NSAIDs and antihypertensives. *Am J Med* 1991; 90 (suppl 5A): 429–479
- Piper JM, Ray WA, Daugherty JR et al: Corticosteroid use and peptic ulcer disease: role of NSAIDs. Ann Intern Med 1991; 114: 735-740
- Shinn AF (ed): Evaluations of Drug Interactions, Macmillan Publishing, Toronto, 1988
- Speight TM (ed): Avery's Drug Treatment, 3rd ed, Williams & Wilkins, Baltimore, 1987
- Shorr RI, Ray WA, Daugherty JR et al: Concurrent use of NSAIDs and oral anticoagulants places elderly persons at high risk for hemorrhagic peptic ulcer disease. Arch Intern Med 1993; 153: 1665-1670
- 37. Lamy PP: The elderly and drug interactions. *J Am Geriatr Soc* 1986; 34: 586–592
- 38. Adams KRH, Al-Homouz S, Edmond E et al: Inappropriate prescribing in the elderly. *J R Coll Physicians Lond* 1987; 21 (7): 39-41
- Gosney M, Tallis R: Prescription of contraindicated and interacting drugs in elderly patients admitted to hospital. *Lancet* 1984; 2: 564–567
- 40. Lindley CM, Tully MP, Paramsothy V et al: Inappropriate medication is a major cause of adverse drug reactions in elderly patients. *Age Ageing* 1992; 21: 294–300
- 41. Cartwright A: Medicine taking by people aged 65 or more. *Br Med Bull* 1990; 46: 63–76
- 42. Beers MH, Storrie M, Lee G: Potential adverse drug interactions in the emergency room. *Ann Intern Med* 1990; 112: 61–64
- 43. Tonks RS, Carruthers SG, Fox RA: Reviewing the medicines of elderly patients for potential drug interactions. [abstract] Clin Pharmacol Ther 1993; 53: 190
- 44. Bloom BS: Direct medical costs of disease and gastrointestinal side effects during treatment for arthritis. *Am J Med* 1988; 84 (suppl 2A): 20-24
- A double blind comparison of piroxicam and enteric coated ASA in rheumatoid arthritis. A Cooperative Multicenter Canadian trial. *J Rheumatol* 1985; 12: 68–77
- 46. Jacobs J, Goldstein AG, Kelly ME et al: NSAID dosing schedule and compliance. [letter] Drug Intell Clin Pharm 1988; 22: 727-728
- 47. Leufkens HG, Ameling CB, Hekster YA et al: Utilization patterns of non-steroidal anti-inflammatory drugs in an open Dutch population. *Pharm Weekbl* 1990; 12 (3): 97–63
- UK-TIA Study Group: United Kingdom transient ischaemic attack (UK-TIA) aspirin trial: interim results. Br Med J 1988; 296: 316–320
- Silagy CA, McNeil JJ, Dornan GA et al: Adverse effects of lowdose aspirin in a healthy elderly population. *Clin Pharmacol Ther* 1993; 54: 84–89
- 50. Drugs for treatment of peptic ulcers. *Med Lett Drugs Ther* 1991; 33: 111-114
- 51. Kirkwood BR: Essentials of Medical Statistics, Blackwell Scientific Publications, Oxford, England, 1988
- Graham DY, White RH, Moreland LW et al: Duodenal and gastric ulcer prevention with misoprostol in arthritis patients taking NSAIDs. Ann Intern Med 1993; 119: 257-262
- Inman WH: NSAID assessment of risks. Eur J Rheumatol Inflamm 1987; 8: 71–85
- Baker MJ: Saskatchewan's Patient Profile Release Program. [report] Canadian Association on Gerontology Pre-Conference Workshop on Medications and the Elderly. Edmonton, Oct 22, 1992
- Lanza FL, Roger GL, Nelson RS: Endoscopic evaluation of the effects of aspirin, buffered aspirin and enteric-coated aspirin on gastric and duodenal mucosa. N Engl J Med 1980; 303: 136–138
- Bergman U: Pharmacoepidemiological perspectives. J Clin Epidemiol 1992; 45: 313–317

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Sept. 21–22, 1994: Rationalizing Health Care in Canada: the New Realities (presented by Insight Conferences and *The Globe and Mail*)

Calgary

Insight Information Inc., 1700–55 University Ave., Toronto, ON M5J 2V6; tel (416) 777-1242, fax (416) 777-1292

Sept. 23–24, 1994: 3rd Annual International Sports Medicine
 Symposium — Instabilities: a Global Approach (presented with the Sports Medicine Council of Alberta)
 Edmonton

Dr. Lisa Stevenson, Glen Sather Sports Medicine Clinic, E-05 Van Vliet Centre, University of Alberta, Edmonton, AB T6G 2H9; tel (403) 492-4752, fax (403) 492-1637

Sept. 24–30, 1994: 14th World Congress of Gynecology and Obstetrics (FIGO '94)

Montreal

Official languages: English, French and Spanish Study credits available.

FIGO '94 Congress Secretariat, 100–4260 Girouard Ave., Montreal, PQ H4A 3C9; tel (514) 485-0855, fax (514) 487-6725

Du 24 au 30 sept. 1994 : 14^e congrès mondial de gynécologie et d'obstétrique (FIGO '94)

Montréal

Langues officielles : l'anglais, le français et l'espagnol Crédits d'éducation médicale continue.

Secrétariat du congrès FIGO '94, 100–4260, ave. Girouard, Montréal, QC H4A 3C9; tél (514) 485-0855, fax (514) 487-6725

Sept. 29–Oct. 1, 1994: Addictions Conference for Northern Ontario: Celebrating Recovery

Elliot Lake, Ont.

Keynote speakers: Earnie Larsen, Dr. Richard Irons, Frank O'Dea and Father William Hultberg

Sister Mae Kierans, director, Camillus Centre, tel (705) 848-7181, ext. 222

Du 29 sept. au 1^{er} oct. 1994 : Conférence internationale sur les effets préventifs et thérapeutiques des suppléments nutritionnels dans le traitement des maladies chroniques Toronto

Secrétariat de la conférence sur les suppléments nutritionnels, a/s Association des hôpitaux du Canada, 100–17, rue York, Ottawa, ON K1N 9J6; tél (613) 241-8005, fax (613) 241-5055

Sept. 29-Oct. 1, 1994: International Conference on Adjuvant Nutrition and Chronic Disease: Preventive and Therapeutic Effects

Toronto

Adjuvant Nutrition Conference Secretariat, c/o Canadian Hospital Association, 100–17 York St., Ottawa, ON K1N 9J6; tel (613) 241-8005, fax (613) 241-5055

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