Effect of Nonsteroidal Anti-Inflammatory Drug Use on the Incidence of Erectile Dysfunction

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Purpose: We estimated the effect of nonsteroidal anti-inflammatory drug use on the incidence of erectile dysfunction.
Materials and Methods: The target population consisted of men 50, 60 or 70 years old residing in the study area in Finland in 1994. Questionnaires were mailed to 3,143 men in 1994 and to 2,864 men 5 years later. The followup sample consisted of 1,683 men who responded to baseline and followup questionnaires. We estimated the effect of NSAIDs on the incidence of ED in men free from moderate or complete ED at baseline (in 1,126). ED was assessed by 2 questions on subject ability to achieve or maintain an erection sufficient for intercourse. Confounding was assessed by stratification and by adjustment in multivariate Poisson regression model.
Results: The incidence of ED was 93 cases per 1,000 person-years in men who used and 35 in those who did not use NSAIDs. Among men with arthritis, the most common indication for NSAID use, ED incidence was 97 cases per 1,000 in those using and 52 in men who did not use NSAIDs. Compared with men who did not use NSAIDs and were free from arthritis, the relative risk of ED after controlling for the effects of age, smoking, and other medical conditions and medications was higher in men who used NSAIDs but were free of arthritis (IDR 2.0, 95% CI 1.2-3.5) and in those who used NSAIDs and had arthritis (IDR 1.9, 95% CI 1.2-3.1). The relative risk was only somewhat higher in men who had arthritis but did not use NSAIDs (IDR 1.3, 95% CI 0.9-1.8).
Conclusions: The use of nonsteroidal anti-inflammatory drugs increases the risk of ED and the effect is independent of indication.

Key Words: analgesics, arthritis, impotence

ED is a common medical problem affecting a substantial proportion of middle-aged and elderly men worldwide.[1–3] It is important to elucidate the effect of medications on erectile function because ED causes the impairment of the quality of life and ED as a side effect of drug therapy leads to noncompliance.

Several common drugs may increase the risk of ED.[4] The association between medications and ED is necessarily confounded by underlying medical conditions. This bias is called confounding by indication. A drug related effect on ED is difficult to distinguish from the effect of the disease, and from concomitant exposure to other diseases and drugs.

In previous cross-sectional studies arthritis has been associated with ED,[1,3,5–7] while the relationship between nonsteroidal anti-inflammatory drugs and ED remains unclear. To our knowledge there are no previous studies on the incidence of ED in relation to NSAID use, ie studies on the use of NSAIDs recorded before the occurrence of ED. We conducted a population based followup study among Finnish men 50 to 70 years old at baseline to assess the effect of NSAIDs on the incidence of ED.

MATERIALS AND METHODS

Details of the Tampere Aging Male Urological Study population have been described elsewhere.[8] It is a population based prospective study in comprehensive sample of men born in 1924, 1934 or 1944 and residing in Pirkanmaa district in Finland in 1994. Information on the target population (3,143) was obtained by a mailed self-administered questionnaire comprising items on sociodemographic status, lifestyle factors, medical conditions, and medications and erectile problems. The study protocol was approved by the Tampere University Hospital committee of research ethics.

A total of 2,198 men (70%) completed baseline questionnaires during the first quarter of 1994. Of this number 257 were excluded from study, 244 due to missing data regarding erectile function and 13 as the respondents were insti-

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tutionalized or unable to respond independently. Therefore, 1,941 men (62%) were included in the study at baseline. Similar questionnaires were sent 5 years later in May 1999 to 2,864 men and 2,133 (75%) returned the questionnaires.

Overall 1,683 men (59% of those alive and eligible) responded to baseline and followup inquiries. Of them 241 were excluded from analysis because of missing data on erectile function in either study round, and 1,442 were included in the followup sample. A total of 312 men with moderate or complete ED and 4 who underwent radical prostatectomy at baseline were also excluded from the analysis, and 1,126 men free from moderate or complete ED at baseline were included in this analysis.

Erectile dysfunction was assessed by 2 questions on subjects' erectile capacity: "Have you had problems getting an erection before intercourse begins?" and "Have you had problems maintaining an erection once intercourse has begun?" For both questions 4 response options were "never," "sometimes," "quite often" and "intercourse does not succeed." Moderate or complete dysfunction (ED in this study) was defined as frequent failure of intercourse ("quite often" or "does not succeed" in at least 1 of the 2 questions).

The term arthritis was used to describe all disorders that cause joint pain, namely osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. Information on arthritis and on regular analgesic use and the type of drugs was collected in the questionnaire by separate and independent questions on medical history and medication. The question for analgesic use was "Do you use regularly analgesics?" List the names and doses of your drugs. The data on the types and doses were not complete. The reported types of analgesics were acetylsalicylic acid (aspirin), acetaminophen, ketoprofen, indomethacin, ibuprofen, phenylbutazone, naproxen and tenoxicam.

The incidence of ED was calculated by dividing the number of new cases of moderate or complete ED occurring between baseline and followup surveys by the number of person-years of followup. Person-years were estimated by multiplying the number of men in whom ED did not develop by 5 years and the number of those in whom ED developed by 2.5 years.

A multivariate Poisson regression model was used for analysis. Age, smoking, diabetes, cerebrovascular disease, depression, cancer, cardiovascular disease, mental medications, cardiovascular drugs, and urinary and hormonal medicines were included in the multivariate model as confounders. The final models were limited to age and the variables associated with ED at $p < 0.10$ in the age adjusted models.

RESULTS

Men free of moderate or complete ED with complete followup were on average slightly younger than the baseline population free of ED (mean age 56.4 vs 57.0 years). They reported a slightly lower frequency of nonsteroidal anti-inflammatory drug use compared with the baseline sample (9.0% vs 10.2%, respectively, table 1).

A total of 101 (9.0%) men used nonsteroidal anti-inflammatory drugs and 256 (22.7%) reported arthritis. Most (58%) men who used NSAIDs reported arthritis whereas in men with arthritis only 23% were NSAID users (table 2). The incidence of ED per 1,000 person-years was 93 (95% CI 67-127) in users of NSAIDs and 35 (95% CI 30-40) in nonusers. The incidence of ED was higher (61, 95% CI 48-78) in men with than in those without arthritis (33, 95% CI 28-39). In multivariate analysis controlled for the effects of age, smoking, medical conditions and medications, the relative risk of ED was 1.8 (95% CI 1.2-2.6) in men who used NSAIDs compared with men who did not report the use. Adjusting for the effect of arthritis had only a marginal effect on the relative risk (1.9 without and 1.8 with controlling for arthritis).

TABLE 1. *Background characteristics of men free from ED*

	No. Baseline	(%)	No. Followup	(%)
Age:				
50	675	47.0	557	49.5
60	511	35.6	420	37.3
70	250	17.4	149	13.2
Medical history:				
Hypertension	371	25.8	290	25.8
Arthritis	340	23.7	256	22.7
Heart disease	196	13.6	141	12.5
Pulmonary disease	133	9.3	101	9.0
Depression	121	8.9*	85	7.9*
Cerebrovascular disease	75	5.2	53	4.7
Diabetes	69	4.8	48	4.3
Cancer	33	2.3	24	2.1
Medication:				
Cardiovascular	360	25.1	268	23.8
NSAIDs	146	10.2	101	9.0
Mental	53	3.7	35	3.1
Hormonal	10	0.7	8	0.7
Urinary	10	0.7	7	0.6

* Among men without missing data.

The incidence of ED was low (31 per 1,000 person-years) in men who did not use NSAIDs and were free from arthritis. This was less than the incidence of ED (52 cases per 1,000 person-years) in men who had arthritis and did not use NSAIDs. The incidence of ED was 87 cases per 1,000 person-years in men who used NSAIDs but did not have arthritis, and 97 in those who had arthritis and also used NSAIDs.

Among men free from arthritis, the age adjusted relative risk of ED was significantly higher in those who used NSAIDs (IDR 2.4, 95% CI 1.4-4.1), compared with men who did not use NSAIDs. Moreover, among men with arthritis, the relative risk of ED for the use of NSAIDs (IDR 2.3, 95% CI 1.4-3.6) was the same as in men who were free from arthritis. In men who did not use NSAIDs, arthritis itself increased the risk of ED (IDR 1.3, 95% CI 0.9-1.8) only marginally.

In multivariate analysis the effects of age, smoking, medical conditions and other medications were controlled, and the relative risks were compared with the incidence in those without arthritis and who did not use NSAIDs. The relative risk of ED was still higher in men who used NSAIDs but were free from arthritis (IDR 2.0, 95% CI 1.2-3.5), and was similar to those who had arthritis and used NSAIDs (IDR 1.9, 95% CI 1.2-3.1). Compared with men free from arthritis and without the use of NSAIDs, the relative risk of ED in men with arthritis but not using NSAIDs (IDR 1.3, 95% CI 0.9-1.8) was not affected by the adjustment, and was less than the risk in those who did use NSAIDs.

Subjects may be prescribed a low or moderate dose of aspirin for its cardioprotective effect. To rule out the possi-