Treatment of osteoarthritis of the hip and knee: A comparison of NSAID use in patients for whom surgery was and was not recommended

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Abstract

Objective

To determine if NSAID use was different between OA (hip and/or knee) patients treated surgically to those treated medically.

Methods

We conducted a case control study, in which cases (n = 433) had had a total joint replacement within a two-year period, while controls (n = 195) had seen a rheumatologist or orthopedic surgeon, and not been recommended for surgery. Current and previous NSAID use was surveyed.

Results

Cases were older than controls (70 vs. 64 years, $p < 0.0001$), and were more likely to have OA in the hips (45% vs. 21%, $p < 0.0001$), to have severe OA ($p < 0.0001$), and to be male (42% vs. 28%, $p < 0.0008$). Potential confounding variables were statistically adjusted using logistic regression. Although disease duration was similar in cases and controls (9.8 years), cases had tried fewer NSAIDs (1.3 ± 0.05 vs. 2.3 ± 0.08 in controls, $p < 0.0001$). Cases were less likely to have taken any NSAID (86% vs. 94% of controls; OR 0.40, $p < 0.007$) or to have had intra-articular steroids (OR 0.19, $p < 0.0001$). Two or more NSAIDs were used (ever) in 38% of cases vs. 70% of controls ($p < 0.0001$); and 3 or more NSAIDs in 5% vs. 38% ($p < 0.0001$). Women were less apt to have obtained total joint replacements (OR 0.62, $p < 0.0001$), including TKRs even when adjusting for severity of OA.

Conclusions

NSAIDs are used less by orthopedic surgeons than rheumatologists in our centre. Some subjects were offered a joint replacement without even a failure of medical management. The reasons for differences in prescribing trends are unknown. Referral biases may exist.

Key words

Osteoarthritis, NSAIDs, treatment, orthopedic surgery.

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Introduction

Osteoarthritis (OA) affects approximately 15% of the world's population (1-5), and affects the majority of the population older than 55 years (6). With advancing age, OA of the hip and knee are more common in women (7). OA is often treated by nonsteroidal anti-inflammatory drugs (NSAIDs), which account for major treatment costs (8, 9). In Canada, OA patients who see a specialist cannot self refer. Thus, in general, patients with more advanced symptoms or disease (signs) are sent either to a rheumatologist or an orthopedic surgeon when the primary care physician deems necessary.

Our intent was to determine the pharmacologic therapies of OA patients treated medically (control group) vs. those recommended to have surgery (cases). We suspected the surgically treated group would have exhausted more medical options.

Methods

Following ethics approval, a chart review of all potential cases was performed at the London, Ontario hospitals for those who had received a total hip or knee replacement over a two-year period. The controls were outpatients, seen by the London rheumatologists and orthopedic surgeons, who had hip or knee OA (selected by the billing code 715), where surgery was not recommended, and radiographs available. OA was defined as radiographic evidence of joint space narrowing without evidence of other rheumatic diseases. All OA was symptomatic as it had necessitated referral. Those with secondary OA, inflammatory arthritis, or who refused to complete the questionnaire were excluded.

Joint radiograph interpretations were used to determine severity of OA(mild, moderate or severe joint space narrowing) at time of surgery. All subjects were mailed a questionnaire to assess: demographics, subject's onset of OA, use of intra-articular steroid or viscoelastic injections and extensive NSAID use by name (all available, listed by generic and trade names), identified as current use and 'ever' use. Possible confounding data were queried, including: diabetes, hypertension and reasons for not using NSAIDs. During this study period, glucosamine and chondroitin were uncommon therapies, and were not assessed. Aspirin data were excluded, as aspirin was often used for indications other than OA.

The number of NSAIDs used in each group was compared; odds ratios were calculated using JMP statistical software. NSAID use was categorized as: ever used (≥ 1 NSAIDs), ≥ 2 NSAIDs used, or ≥ 3 NSAIDs used; and then into hip or knee OA. Patients with both areas affected were included in each analysis. A list of confounders was developed *a priori*. The frequency of all variables was studied; when rates were different between groups, the variable was adjusted for in a multivariate analysis. Age and gender were adjusted for. A secondary analysis stratified the two groups by radiographic severity of OA.

Results

715 charts were reviewed for NSAID use and radiographic grade of OA. Of the 628 eligible for this study, 235 had hip OAand 411 knee OA(18 had both). There were 433 cases (surgically treated) and 195 controls (medically treated). Nearly all of the controls came from the rheumatologists. The mean age was greater ($p < 0.0001$) in patients receiving joint replacements than in the controls. More women were seen with OA, but women were under-represented in the surgical cases. Thus, there were proportionately more men in the surgically treated OA group, 42% vs. 28%, ($p < 0.0008$).

The surgical cases were more likely than controls to have OA in the hips, 45% vs. 21% ($p < 0.0001$). However, more TKRs were done but a larger proportion of knees were treated medically compared to hips. The cases had more severe OA on radiographs, 77% vs. 43% ($p<0.0001$). Family history of OA was increased in the controls (66% vs. 54%, $p < 0.03$). Comorbidity was higher in medically treated controls and may have influenced the decision against surgical replacement occasionally. Allergies, past steroid use and other conditions (fibromylagia, MVA injury, or

Table I. Baseline characteristics of surgically and medically treated OAsubjects over 2 years. Results are presented as the number of subjects positive for the characteristic with the percentage in parentheses or, where applicable, as the mean ± SEM. OR values are for surgically treated compared to medically treated. Some subjects did not answer every question.

Characteristic	Cases of total joint replacement	Controls treated medically	p-value	Odds ratio (OR) (surg vs. med)	95% Confidence interval for OR
No.	433	195			
Female	250 (58)	140 (72)	0.0008	0.54	(0.38, 0.78)
Age (years)	69.8 ± 0.4	64.5 ± 0.9	0.0001		
Duration of OA(years)	9.7 ± 0.4	9.8 ± 0.8	0.85		
Severity (N with severe OA)	330 (77)	82 (43)	0.0001	4.46	(3.11, 6.40)
Hip OA	194 (45)	41 (21)	0.0001	3.05	(2.06, 4.52)
Knee OA	251 (58)	160 (82)	0.0001		
Family Hx of OA	120 (54)	67 (66)	0.03	0.59	(0.36, 0.96)
Hypertension	210 (48)	58 (30)	0.0001	2.22	(1.55, 3.19)
Cardiovascular disease	93 (21)	30 (15)	0.07	1.50	(0.96, 2.36)
Psychiatric disorder	10 (2)	10 (5)	0.07	0.44	(0.18, 1.07)
Diabetes	49 (11)	15 (8)	0.16	1.53	(0.84, 2.80)
Cancer	24 (6)	12 (6)	0.76	0.89	(0.44, 1.82)
GI Ulcers	52 (12)	17 (9)	0.22	1.43	(0.80, 2.54)
Alcohol consumption	4 (1)	4 (2)	0.26	0.44	(0.11, 1.80)
Drug Allergies	58 (16)	40 (27)	0.004	0.52	(0.33, 0.81)
Intra-articular steroid use (ever)	69 (27)	85 (66)	0.0001	0.19	(0.12, 0.31)
Anemia	14 (3)	3 (2)	0.22	2.14	(0.61, 7.52)
Other significant conditions	311 (72)	160 (82)	0.006	0.58	(0.36, 0.85)

Table II. Baseline factors that are statistically different between subjects with hip OAand knee OA, in all subjects treated medically or surgically. Results are presented as the number of subjects positive for the characteristic with the percentage in parentheses or, where applicable, as the mean ± SEM. Some subjects did not answer every question. OR values are for hip OAcompared to knee OA.

Characteristic	Hip OA	Knee OA	p-value	Odds ratio (OR)	95% Confidence interval for OR
No.	235	411			
Duration of OA(years)	7.8 ± 0.6	11.0±0.5	0.0001		
Severity (N with severe OA)	191 (82)	235 (58)	0.0001	3.34	(1.83, 6.09)
OAfamily history	66 (50)	127 (63)	0.016	0.57	(0.36, 0.89)
Intra-articular steroid use (ever) to any joint	36 (25)	124 (49)	0.0001	0.34	(0.21, 0.53)

All other factors examined are shown in Table I.

previous joint replacement) occurred more often in the controls (Table I). History of peptic ulcers was reported infrequently in each group (12% cases; 9% controls), $p < 0.2$, and does not support differential prescription of NSAIDs between groups.

Hip OA

In subjects with hip vs. knee OA, no medical conditions examined were statistically different between the groups. Subjects with hip OA were: less likely to have a family history of OA, with 50% vs. 63%, $p < 0.014$; less likely to have received intra-articular steroids, with 25% vs. 49%, $p < 0.0001$; less likely to have a longer OAdisease duration (7.83 years ± 0.62; and 11.03 years ± 0.48), $p < 0.0001$. However, subjects with hip OAhad more severe OA(82% vs. 58%), $p < 0.0001$.

Within the subset of subjects with hip OA ($n = 235$; 18 hip and knee), age (61.5 ± 2.2 years, medical vs. 69.4± 0.7, surgical), severity of OA (48% severe in medical vs. 90% in surgical; $p < 0.0001$) and a history of intra-articular steroid use for any joint (56% medical vs. 21% surgical; $p < 0.0014$) were different between cases and controls (Table III).

Knee OA

These same demographic variables: age, severity of OA and history of intra-articular steroid use, along with the additional variable of gender, were found to be different between cases and controls within the knee OAsubset ($n = 411$) (Table III).

Differences between NSAID use (ever) by controls and surgical cases were examined within the total group, as well as hip and knee OAsubsets. Cases were less likely to have taken any NSAID (86% vs. 94%, $p < 0.003$); ≥2 NSAIDs (38% vs. 70%, $p < 0.0001$); or ≥3 NSAIDs (5% vs. 38%, $p < 0.0001$).

Table III. Baseline demographic characteristics for surgically treated (cases) vs. medically treated (controls) within the subsets of subjects with hip OA, and of subjects with knee OA. Results are presented as the number of subjects positive for the characteristic with the percentage in parentheses or, where applicable, as the mean ± SEM. Some subjects did not answer every question.

Characteristic	Cases of total joint replacement	Controls treated medically	p-value	Odds ratio (OR)	95% Confidence interval for OR
Subjects with hip OA					
No.	194	41			
Age (years)	69.4 ± 0.7	61.5 ± 2.2	0.0001		
Male	86 (44)	16 (39)	0.5319	1.24	(0.62, 2.48)
Female	108 (56)	25 (61)			
Severity (N with severe OA)	172 (89)	19 (48)	0.0001	9.05	(4.20, 19.52)
Duration of OA	7.4 ± 0.6	10.1 ± 2.3	0.1550		
OAfamily history	53 (48)	13 (56)	0.4664	0.72	(0.29, 1.77)
Intra-articular steroid use (ever)	26 (21)	10 (56)	0.0014	0.21	(0.07, 0.58)
Subjects with knee OA					
N	251	160			
Age (years)	70.4± 0.5	65.5 ± 0.9	0.0001		
Male	100 (40)	42 (26)	0.0043	1.86	(1.21, 2.87)
Female	151 (60)	118 (74)			
Severity (N with severe OA)	169 (68)	66 (43)	0.0001	2.92	(1.93, 4.43)
Duration of OA	11.4 ±0.6	10.3± 0.9	0.2875		
OAFamily History	70 (59)	57 (69)	0.1521	0.65	(0.36, 1.18)
Intra-articular Steroid Use (Ever)	46 (34)	78 (67)	0.0001	0.25	(0.15, 0.42)

Table IV. Surgically treated subjects (cases) who used NSAIDs compared to patients treated medically rather than by surgery (controls). OR was calculated for cases (surgically treated) compared to controls (medically treated). P-values are presented for the unadjusted model, as well as adjusted for age, gender and severity of OA.

	% of surgically treated (no.)	% of medically treated (no.)	Odds ratio (OR)	95% Confidence interval	P-value (adjusted)	P-value
Total OAgroup (knee & hip)						
1 or more NSAID(s)	86 (366)	94 (176)	0.40	(0.21, 0.77)	0.003	0.007
2 or more NSAIDs	38 (164)	70 (133)	0.26	(0.18, 0.39)	0.0001	0.0001
3 or more NSAIDs	5 (20)	38 (72)	0.08	(0.05, 0.14)	0.0001	0.0001
Subjects with hip OA						
1 or more NSAID(s)	88 (168)	92 (36)	0.61	(0.17, 2.14)	0.41	0.05
2 or more NSAIDs	40 (76)	56 (22)	0.51	(0.25, 1.02)	0.06	0.13
3 or more NSAIDs	4 (8)	28 (11)	0.11	(0.04, 0.30)	0.0001	0.0008
Subjects with knee OA						
1 or more NSAID(s)	84 (210)	93 (145)	0.41	(0.20, 0.82)	0.008	0.02
2 or more NSAIDs	39 (96)	73 (114)	0.23	(0.15, 0.36)	0.0001	0.0001
3 or more NSAIDs	6 (14)	40 (62)	0.09	(0.05, 0.17)	0.0001	0.0001

The mean number of NSAIDs tried in cases was 1.3 ± 0.05 vs. 2.3 ± 0.08 in controls, $p < 0.0001$.

Decreased NSAID exposure in cases

The tendency of decreased NSAID exposure amongst cases was evident in hip and knee OA subsets, though not always statistically significant. Within the hip subset, an average of 1.4 ± 0.07 NSAIDs had been tried in cases vs. 2.1 ± 0.16 in controls, $p < 0.0001$. When adjusted for age, OA severity and gender, cases were more likely to be NSAID naïve, $p < 0.05$. In the knee OA group, 84% of cases had tried at least one NSAID, compared to 93% of controls ($p < 0.008$); 39% vs. 73% ≥ 2 NSAIDs ($p < 0.0001$), and 6% vs. 40% ≥ 3 NSAIDs ($p < 0.0001$). The average number of NSAIDs tried was 1.3 ± 0.07 (cases) vs. 2.3 ± 0.09 (controls), $p < 0.0001$. No significant dose response between disease duration and number of NSAIDs was found in the study sample, or in either the case or control groups alone ($p < 0.14$).

Potential confounders were adjusted for (separately and together) in the analyses using logistic regression and results were virtually unchanged (Table IV). NSAIDs were still used more often in the controls ($p < 0.007$). Individual NSAIDs were analyzed, and all individual agents were prescribed less often in cases. Overall, 14% of the cases were completely NSAID naive.

Discussion

Surgically treated patients with hip or knee OA are less apt to have been exposed to NSAIDs, and if exposed, they had used fewer NSAIDs. It may be that they were not treated as aggressively medically or, perhaps, because they are innate NSAID "non-responders", so not as many are tried. Due to older age in surgical cases, perhaps a definitive procedure is done in lieu of trying NSAIDs; however, disease duration was equal in both groups. Our analyses found no relationship between disease duration and number of NSAIDs tried, although intuitively, an individual with long-standing OA may have tried more NSAIDs than one with a more recent diagnosis. Perhaps there is a referral bias from the family doctors of which we were unaware. A significant number of patients referred for total knee replacement (TKR) were NSAID naive. It could be that their severity of pain and functional limitation was worse, and therefore, they were "fast-tracked" into surgical treatments. However, as the waiting lists in London are long (and disease duration was similar), this seems not to be the case. Intra-articular steroid use (ever) was more common in controls than cases; thus, even in those for whom NSAIDs may have been thought to be unsafe, other treatments were tried less often.

One would have anticipated that due to more severe disease (radiographically), the total NSAID exposure would have been higher in those treated surgically. Surprisingly this was not the case. Perhaps controls were reluctant to have surgery and vice versa. All subjects were symptomatic or they would not have been referred to a specialist. The selection of medically treated subjects as controls may have been biased. They could be in a different state of the disease (they had slightly less severe radiographic changes). No single NSAID "stood out" as having increased use in the cases. Conversely, one could assume that there could be a self-selection of severe OAto obtain solely arthroplasties as the risk/benefit ratio of NSAIDs in severe disease could be different.

Hawker *et al*. reported that women in Ontario were less apt to have hip replacement surgery compared to men; our study confirms these data for hip and knee replacements (statistically significant in TKRs only) (10). OA is more common in women and they have more procedures, though not as many as the prevalence would predict (10). In this study, men were 1.85 times more likely to be treated surgically for OA. The reasons for this are uncertain but women had less severe radiographic OA. Perhaps men have more symptomatic OA (at the same grade), or perhaps women are denied referrals to orthopedic surgeons or are less apt to be offered joint replacement surgery. Hawker *et al*. found women had worse symptoms and greater disability so it is unlikely that in our study, women had less pain or disability (10). Other studies have found under-representation of women for bypass graft surgery.

The treatment differences between rheumatologists and orthopedic surgeons are vast. Surgeons recommend surgery, while rheumatologists also tend to recommend medical treatment options. This study may have simply found the practice differences between the specialties. Radiographic severity of OA and/or more advanced age may be triggers for recommending joint replacements; thus, if this is the case, the differences in NSAID use could be spurious. Perhaps orthopedic surgeons recommend surgery after a certain age, regardless of past treatments. Age also increases the risk of OA.

Our study design was flawed; there were fewer controls, and the controls were younger and had less severe OA, so this was not a matched case control study. Obesity was not compared; the groups were not randomized and may have had an unequal distribution of known and unknown confounders. We cannot confirm the duration of NSAID exposure; but if the NSAID(s) didn't work well or for long in the surgical cases, one would anticipate that they would have tried more NSAIDs (switching to find one that would work). We did not find different particular NSAIDs used within the groups. A large proportion of the controls were recruited from the rheumatologists and the cases from the orthopedic surgeons and differences in the prescribing practices in the two groups and may not be generalizable outside of our area. However, all cases were ascertained, and through billing codes, most controls seen by rheumatologists over the same 2 years were captured. Also, 43% of controls had severe OA radiographically. One could speculate that NSAIDs have beneficial effects on cartilage thus those with more NSAIDs had less severe OA; another explanation could be that family physicians may refer more severe disease to orthopedic surgeons, but would usually try treatment prior to a referral as mean disease duration was greater than 9 years.

Despite the limitations, it appears that orthopedic surgeons offered total joint replacements for OAof the hip or knee after trying an average of only 1.3 ± 0.05 NSAIDs, compared to 2.3 ± 0.08 in controls during the same time frame. Some patients certainly had not failed medical management at time of surgery. Women have more hip and knee OA but receive disproportionately less total joint replacements.

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