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BMJ 2002;324:1306-1307
doi:10.1136/bmj.324.7349.1306

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Funding: Health Technology Assessment programme (project number 95/29/04). The opinions expressed therein are those of the authors and not necessarily those of the NHS Executive. DM was supported in the preparation of this paper by an unconditional grant from Merck Sharpe and Dohme. SEH and HAWN acknowledge grants RG2000025 and RG93008 from the British Heart Foundation.

Competing interests: None declared.

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(Accepted 11 December 2001)

Fluoroquinolones and risk of Achilles tendon disorders: case-control study

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BMJ 2002;324:1306-7

Fluoroquinolones have been associated with tendon disorders, usually during the first month of treatment,¹⁻⁵ but the epidemiological evidence is scanty. We did a nested case-control study among users of fluoroquinolones in a large UK general practice database to study the association with Achilles tendon disorders.

Participants, methods, and results

We obtained data from the IMS Health database (UK MediPlus), which contains data from general practice on consultations, morbidity, prescriptions, and other interventions in a source population of 1.2 million inhabitants. The base cohort consisted of all patients aged 18 years or over who had received a fluoroquinolone. We excluded people with a history of Achilles tendon disorders, cancer, AIDS, illicit drug use, or alcohol misuse. We identified potential cases by reviewing patient profiles and clinical data and excluded tendon disorders due to direct trauma. We randomly sampled a group of 10 000 control patients from the study cohort.

We defined four categories of exposure to fluoroquinolones: current use, recent use, past use, and no use. We defined current use as when the tendon disorder occurred in the period between the start of the fluoroquinolone treatment and the calculated end date plus 30 days, recent use as when the calculated end

date was between 30 and 90 days before the occurrence of the disorder, and past use as when the calculated end date was more than 90 days before the occurrence of the disorder. We used unconditional logistic regression analysis to calculate adjusted relative risks and 95% confidence intervals for Achilles tendon disorders, using the no use group as the reference. We adjusted for age, sex, number of visits to the general practitioner, use of corticosteroid, calendar year, obesity, and history of musculoskeletal disorders.

The cohort included 46 776 users of fluoroquinolones between 1 July 1992 and 30 June 30 1998, of whom 704 had Achilles tendinitis and 38 had Achilles tendon rupture. Four hundred and fifty three (61%) of the cases were women, and the mean age was 56 years. Cases visited the general practitioner significantly more often than did controls (mean 20 *v* 17). Cases and controls were similar with respect to indications for use of fluoroquinolone. Age, number of visits to the general practitioner in the previous 18 months, gout, obesity, and use of corticosteroid were determinants of Achilles tendon disorders. The adjusted relative risk of Achilles tendon disorders with current use of fluoroquinolones was 1.9 (95% confidence interval 1.3 to 2.6). The risk for recent and past use was similar to that for no use. The relative risk with current use was 3.2 (2.1 to 4.9) among patients aged 60 and over and 0.9 (0.5 to 1.6) among patients aged under 60 (table). In patients aged 60 or over, concurrent use of

corticosteroids and fluoroquinolones increased the risk to 6.2 (3.0 to 12.8).

Comment

Current exposure to fluoroquinolones increases the risk of Achilles tendon disorders. This finding is in agreement with a smaller study, in which we found an association between tendinitis and fluoroquinolones.⁵ Our results indicate that this adverse effect is relatively rare, with an overall excess risk of 3.2 cases per 1000 patient years. The effect seems to be restricted to people aged 60 or over, and within this group concomitant use of corticosteroids increased the risk substantially. The proportion of Achilles tendon disorders among patients with both risk factors that is attributable to their interaction was 87%. Although the mechanism is unknown, the sudden onset of some tendinopathies, occasionally after a single dose of a fluoroquinolone, suggests a direct toxic effect on collagen fibres. Prescribers should be aware of this risk, especially in elderly people taking corticosteroids.

We acknowledge the cooperation of IMS Health United Kingdom.

Contributors: PDvdL, MCJMS, and BHChS formulated the design of the study. PDvdL carried out the analyses. PDvdL, MCJMS, and BHChS wrote the paper, and RMCH and HGML edited it. BHChS and HGML are guarantors for the paper.

Funding: Dutch Inspectorate for Health Care.

Competing interests: MCJMS is a consultant for Lundbeck (France) and Beaufour (UK) and has previously been a consultant for Pfizer (USA), Roche (Switzerland), and Novartis Consumerhealth (Switzerland). None of these consultancies related to quinolones. MCJMS is responsible for research conducted with the integrated primary care information database in the Netherlands, which is supported by project specific grants from GlaxoSmithKline, AstraZeneca, Merck Sharp & Dohme, Pharmacia & Upjohn, Bristol-Myers Squibb, Eli Lilly, Wyeth, and Yamanouchi. MCJMS has conducted research projects on use of antibiotics for Merck & Co (USA) and Bayer (Italy), but none was related to the adverse effects of quinolones.

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Relative risk of Achilles tendon disorders associated with use of fluoroquinolones according to age

	Cases	Controls	Crude relative risk (95% CI)	Adjusted relative risk (95% CI)*
All Achilles tendon disorders				
Age <60: (n=423)	(n=6058)			
No use	308	4387	1.0	1.0
Current use	13	174	1.1 (0.6 to 1.9)	0.9 (0.5 to 1.6)
Recent use	19	240	1.1 (0.7 to 1.8)	1.0 (0.6 to 1.7)
Past use	83	1257	0.9 (0.7 to 1.2)	0.9 (0.7 to 1.1)
Age ≥60: (n=319)	(n=3942)			
No use	211	2797	1.0	1.0
Current use	33	124	3.5 (2.3 to 5.3)	3.2 (2.1 to 4.9)
Recent use	15	182	1.1 (0.6 to 1.9)	1.0 (0.6 to 1.7)
Past use	60	839	0.9 (0.7 to 1.3)	0.8 (0.6 to 1.1)
Achilles tendon ruptures				
Age <60: (n=21)	(n=6058)			
No use	18	4387	1.0	1.0
Current use	—	174	—	—
Recent use	—	240	—	—
Past use	3	1257	0.6 (0.2 to 2.0)	0.6 (0.2 to 2.0)
Age ≥60: (n=17)	(n=3942)			
No use	8	2797	1.0	1.0
Current use	3	124	8.4 (2.2 to 32.2)	7.1 (1.7 to 29.1)
Recent use	2	182	3.8 (0.8 to 18.2)	3.5 (0.7 to 17.3)
Past use	4	839	1.7 (0.5 to 5.5)	1.4 (0.4 to 4.8)
Achilles tendinitis				
Age <60: (n=402)	(n=6058)			
No use	290	4387	1.0	1.0
Current use	13	174	1.1 (0.6 to 2.0)	1.0 (0.5 to 1.8)
Recent use	19	240	1.2 (0.7 to 1.9)	1.1 (0.7 to 1.8)
Past use	80	1257	1.0 (0.7 to 1.2)	0.9 (0.7 to 1.2)
Age ≥60: (n=302)	(n=3942)			
No use	203	2797	1.0	1.0
Current use	30	124	3.3 (2.2 to 5.1)	3.1 (2.0 to 4.8)
Recent use	13	182	1.0 (0.6 to 1.8)	0.9 (0.5 to 1.6)
Past use	56	839	0.9 (0.7 to 1.2)	0.8 (0.6 to 1.1)

*Adjusted for sex, age, visits to general practitioner, calendar year, use of corticosteroid, history of musculoskeletal disorders, and obesity.

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(Accepted 9 January 2002)

The surname I do not have

I come from the south of India—Chennai in Tamil Nadu—and am currently working as a senior house officer in the NHS. I am writing this article to address the problem of surnames facing several Tamil doctors abroad. My name (one and only name) is Radhika. Until I got married, I was called M Radhika. The initial usually denotes the first letter of your father's name or native place—in my case it was the first letter of my father's name, Murugesan (his one and only name). After I was married, I became Radhika Ramkumar, which was fine.

When I came to Britain I was asked to give my surname wherever I went, but there is no concept of surnames in Tamil Nadu. Not knowing what to do, I gave my husband's name as my surname: he, in fact, uses his father's name as his first name and his own name as his surname (I later found out this is a common practice among Tamil doctors). Everything was fine until people started calling me Dr Ramkumar, which is really my husband's name. Back home, I would have been Dr Radhika to patients, or possibly Dr Radhika Ramkumar, but definitely not Dr Ramkumar.

I did some research on this subject. In every other state in India, people have surnames, so they don't have a problem. In Tamil Nadu in the olden days people added their caste names (such as Pillai, Mudaliar, Iyer, etc), which served as "surnames." However, this has been given up by most people (for the best, since there may be up to 50 Pillais in one area of Chennai).

I am at a loss at what to do. Do I have to take up my caste name (which will rekindle the old flames of the caste system among non-resident Indians) or just refuse to give a surname? A name is a very personal thing, and I just cannot accept being called Dr Ramkumar. I welcome comments on this issue from doctors facing similar problems.

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