Maturitas 81 (2015) 394–397

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Aspirin is associated with reduced cartilage loss in knee osteoarthritis: Data from a cohort study

Anita E. Wluka[a,*], Changhai Ding[a,b], Yuanyuan Wang[a], Graeme Jones[b], Donna M. Urquhart[a], Flavia M. Cicuttini[a]

[a] Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Victoria 3004, Australia
[b] Menzies Research Institute Tasmania, Hobart, Australia

ARTICLE INFO

Article history:
Received 9 March 2015
Received in revised form 21 April 2015
Accepted 23 April 2015

Keywords:
Aspirin
Osteoarthritis
Cartilage
Cohort study

ABSTRACT

Objectives: Aspirin, widely used in the prevention of cardiovascular disease, in low dose, has anti-inflammatory and vasculoprotective effects: both of these processes contribute to the pathogenesis of osteoarthritis. We examined whether use of low dose aspirin affects change in knee cartilage volume in osteoarthritis.
Methods: Participants from the Melbourne osteoarthritis cohort were classified as users and non-users of aspirin, according to baseline use (≤300 mg/day). Their knees were imaged twice over 2 years. Tibial cartilage volumes were measured and change calculated.
Results: Twenty one (18%) of 117 eligible participants were aspirin users. Annual change in medial tibial cartilage volume was −43 mm^3 (95% confidence intervals (CI) −93, 10) in aspirin users and −101 mm^3 (95% CI −125, −77) in non-users ($p = 0.043$ for difference) after adjusting for age, gender, BMI and radiographic severity. Similar results were seen for annual percentage loss (1.9% vs 5.4%, $p = 0.034$). No difference was observed for lateral tibial cartilage change and annual change ($p = 0.98$, 0.87 respectively)
Conclusion: Low dose aspirin use was associated with reduced medial tibial cartilage loss over 2 years in people with knee osteoarthritis. This data is hypothesis generating and clinical trials are required to confirm efficacy. If this hypothesis is confirmed, low dose aspirin may be used to reduce the progression of knee osteoarthritis.

1. Introduction

Osteoarthritis (OA), the most common form of arthritis, often affects the knee and is a major cause of disability. Therapy is limited to providing symptomatic relief with analgesics, physiotherapy and, when symptoms are severe, joint replacement. The rate of joint replacement, an effective but expensive therapy, is escalating worldwide. Thus the need for interventions to prevent and reduce disease progression is important.

There is increasing evidence that knee OA is a complex disease, the end result of many different pathological processes, including trauma and biomechanical factors, but also systemic factors. For example, the mechanisms by which obesity leads to knee OA is through both increased loading at the knee and meta-inflammation associated with increased fat mass [1]. There is also evidence for a role for inflammation [2] and vascular disease [3] in the pathogenesis of OA. Thus interventions that affect inflammation or cardiovascular risk may provide novel strategies for the prevention and therapy of knee OA.

Low dose aspirin (<300 mg per day) is commonly prescribed in older adults for the primary and secondary prevention of cardiovascular disease. Its effect on the joint, particularly at this dose is unknown and has not been studied. Studies of high dose aspirin (3 g per day) in humans and animals have provided conflicting results [4,5]. Low dose aspirin has a multiplicity of actions, including anti-inflammatory effects [6], effects on platelet function (both anti-thrombotic and anti-inflammatory) [7] and lipids [8], all of which may affect the progression of OA [2,9].

Whilst OA is a disease of the whole joint, disease progression is characterized by the loss of articular cartilage which can be assessed directly using magnetic resonance imaging (MRI).

Abbreviations: OA, osteoarthritis; BMI, body mass index; SD, standard deviation; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

* Corresponding author at: Department of Epidemiology & Preventive Medicine, School of Public Health & Preventive Medicine, Monash University, The Alfred Centre, Commercial Road, Melbourne, Victoria 3004, Australia. Tel.: +61 3 9903 0994; fax: +61 3 9903 0556.
E-mail addresses: anita.wluka@monash.edu, anita.wluka@med.monash.edu.au (A.E. Wluka).

http://dx.doi.org/10.1016/j.maturitas.2015.04.015
0378-5122/

Cartilage volume has been shown to be a valid measure when compared to anatomical specimens [10] and is clinically relevant, as it is associated with increased pain [11] and a higher risk of joint replacement [12].

In the current study we examined whether the use of low dose aspirin affected knee cartilage loss over 2 years in a cohort of people with mild to moderate symptomatic radiographic knee OA.

2. Materials and methods

2.1. Study population

The Melbourne OA study is a prospective cohort study in which participants with symptomatic knee OA were recruited by advertising through local newspapers, the Victorian brand of the Arthritis Foundation of Australia as well as via musculoskeletal clinicians [13]. Baseline and follow up measures were conducted approximately 2 years apart (1.95 years, SD 0.21), from 1997 to 2000. The study was approved by the Human Research Ethics committees of the Alfred and Caulfield hospitals, Melbourne Australia. All participants provided informed consent. One hundred and thirty two participants meeting the inclusion criteria of age >40, knee pain (pain >20% on at least one pain dimension of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [14] and osteophytes present (i.e. ACR clinical and radiographic OA [15]). Exclusion criteria were the presence of any other form of arthritis, contraindication to MRI, poor functional status or planned joint replacement [13].

2.2. MRI assessment

The symptomatic knee of each participant was imaged in the sagittal plane on the same 1.5T whole body MR unit (Signa Advantage HiSpeed General Electric Medical systems, Milwaukee, WI) at baseline and 2 years later [13]. Tibial cartilage volume was measured using image processing on an independent work station using Osiris, a software program, by 2 independent observers [13]. Images were scored unpaired and blinded to subject identification and timing of MRI by both observers, with their averaged results used. Where results differed between observers by >20%, the measurements were repeated until they were within 20%. The coefficients of variation for the measurement of medial and lateral cartilage volumes in our hands are 2.1%–3.4% [13]. Tibial plateau area was measured as described [13]. Measures were made blind to clinical information.

2.3. Low dose aspirin use

Information was collected regarding regular medication use at baseline. Aspirin users were defined as those who reported taking regular dose aspirin (<300 mg per day) at baseline.

2.4. Other measures

At baseline demographic information was collected; body mass index was calculated from measured weight and height [13]. Knee pain was assessed with the WOMAC pain scale (VAS, 0–500) with lower scores indicating less pain [13]. A weight bearing anteroposterior knee radiograph was performed from which the radiographic features of tibiofemoral OA were graded on a 4-point scale (0–3) in each compartment for osteophytes and joint space narrowing using the OARSI atlas [13,16].

2.5. Statistical analysis

Descriptive statistics for participant characteristics were tabulated, with differences described using unpaired *t* tests or chi square test, as appropriate. Annual change in medial and lateral tibial cartilage volume was calculated as (follow up cartilage volume – initial cartilage volume)/time between scans. Annual percentage change was obtained by dividing annual change by initial cartilage volume, expressed as a percentage. Principal outcome measures were the annual change and annual percentage change in cartilage volume. These outcome measures were normally distributed, and were thus compared in those who did and did not use aspirin using Student's *t* tests and estimated marginal means, adjusted for other potential confounders (age, gender, body mass index, osteophyte grade). All analyses were performed using IBM SPSS Statistics version 20.

3. Results

One hundred and seventeen participants of the 132 participants in the cohort study were eligible and completed the aspirin osteoarthritis cohort study. Baseline data regarding medication use was unavailable for 6 participants. Participants were lost to follow up for the following reasons: two moved from the study center, 3 were too busy, 2 underwent knee surgery, 1 was too ill, and 1 died. There were no significant differences between those who completed the study and those who did not. Twenty one participants reported taking aspirin at baseline (Table 1). None reported taking aspirin at a higher dose. Although those taking aspirin tended to be older than those who did not ($p = 0.06$), there were no significant differences between the 2 groups at baseline.

Change in cartilage volume in aspirin users was compared to non-users (Table 2). Annual medial tibial cartilage loss and percentage cartilage loss in aspirin users was approximately half that seen in non-users ($p = 0.067$ and $p = 0.054$, for difference, respectively). These differences became more significant after adjusting for age, gender, body mass index, and baseline radiographic severity ($p = 0.048$ and $p = 0.03$, respectively). There were no significant differences in annual loss and percentage loss of lateral tibial cartilage, or when pain was included in the model. Similar results were obtained when aspirin users were defined as those participants taking aspirin at 2 or more time points, at least 6 months apart, during the study. These results remained after adjusting for baseline levels of exercise (data not shown).

Table 1
Participant characteristics.

	Aspirin ($n = 21$)	No aspirin ($n = 96$)	p for difference[a]
Females (%)	12 (57%)	56 (58%)	0.92[b]
Age, years	66.6 (6.9)	63.0 (10.8)	0.06
Body mass index, kg/m^2	29.4 (5.6)	28.7 (5.0)	0.58
WOMAC pain (0–500)	73 (36)	83 (45)	0.30
Kellgren Lawrence >2	15 (58%)	52 (58%)[c]	0.99[b]
Cartilage volume, mm^3			
Medial tibial	1801 (450)	1724 (480)	0.50
Lateral tibial	2013 (751)	1903 (531)	0.43
Tibial plateau bone area, mm^2			
Medial tibial	2146 (451)	2070 (381)	0.41
Lateral tibial	1410 (271)	1361 (244)	0.40

Data presented as mean (SD) or number (%).
[a] Student's *t*-test unless otherwise indicated.
[b] Chi square.
[c] Kellgren Lawrence score available for 95.