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Do Intra-Articular Steroid Injections Increase Infection Rates in Subsequent Arthroplasty? A Systematic Review and Meta-Analysis of Comparative Studies

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ABSTRACT

Intra-articular steroid injections are widely used in joint arthritis. The safety of such injections has been questioned as they may increase infection rates in subsequent arthroplasty. We carried out a meta-analysis of studies examining the relation between intra-articular steroid injections and infection rates in subsequent joint arthroplasty. A literature search was undertaken. Eight studies looking at hip and knee arthroplasties were analyzed. Meta-analysis showed that steroid injection had no significant effect on either deep (risk ratio = 1.87; 95% CI 0.80–4.35; $P = 0.15$) or superficial infection rates (risk ratio = 1.75; 95% CI 0.76–4.04; $P = 0.19$) of subsequent arthroplasty. Further large cohort studies would be of value in further examining whether steroid injections close to the time of arthroplasty are safe.

Intra-articular steroid injections are widely used to control pain and inflammation in arthritic joints. In addition they may be used as a diagnostic tool in distinguishing between pain originating from the arthritic joint and referred pain. There have been clinical concerns that such injections may predispose to infection if an arthroplasty procedure were to be subsequently performed in the injected joint [1–4]. Given the potentially devastating consequences of arthroplasty infection, determining whether such a relation exists is of high clinical importance. Several clinical studies have examined this issue previously but have given conflicting results, which may be partly attributed to the relatively small numbers of cases included in those studies. Pooling of such studies with a meta-analysis could provide more robust evidence.

This study is a systematic review and meta-analysis of comparative cohort studies examining the relation between intra-articular steroid injections and infection rates in subsequent joint arthroplasty.

Materials and Methods

A search of the PubMed, Excerpta Medica Database (EMBASE), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Cochrane central register of control trials (CENTRAL), was conducted from their year of inception to February 2014, with the following combinations of key words: “Injection”, “replacement”, “infection”, and “Injection”, “arthroplasty”, “infection”. There was no language limit. The Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) [5] methodology guidance was employed. Full texts were reviewed for relevant articles, or where a decision regarding inclusion could not be made from the title and abstract. The reference lists of selected articles were also examined for any additional articles not identified from the database search. The included articles were appraised critically using the revised and validated version of Methodological Index for Non-Randomised Studies (MINORS) [6] and scored out of 24. Authors of included studies were contacted if further information was needed. Studies (published in full or abstract form) were included if they compared the infection rates of joint arthroplasties in cohorts of joint arthroplasties that had previous intra-articular steroid injection, with the infection rates in cohorts of joint arthroplasties that had no previous steroid injection. Single case reports, reviews, and non-comparable studies were excluded. Data were extracted in a standardized manner.

Statistical Analysis

Deep infection rate was the primary outcome of the study and superficial infection rate the secondary outcome. Meta-analysis was performed using a random-effects model. Summary risk ratios and 95% confidence intervals (CIs) were calculated and reported for each

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outcome. Heterogeneity was assessed using tau^2, I^2, Q and *P* values. Publication bias with respect to infection rates was estimated using a funnel plot. Data were analyzed with Comprehensive Meta-analysis version 2 (Biostat; Englewood, NJ, USA). Zero total event studies (studies with zero infections in both injected and non-injected groups) were excluded from meta-analysis as previously recommended [7].

Results

The search identified 3249 articles by title; 67 were initially selected based on information gathered from the title, and their abstracts were reviewed. A full text review of 13 studies was performed of which 8 [2–4,8–12] met the inclusion criteria and were used for analysis (Fig. 1). The authors of one study which was only published in abstract form [10] was contacted for more information regarding data and clarifying the definition of infection. The included studies evaluated infection rates in total knee (TKA) and total hip (THA) arthroplasties (Table 1).

The deep infection rates for each of the analysed studies in the injected group varied from 0 – 10% and in the control group from 0–1.3%, with most of the studies having a rate <1.5% (Table 2). Similarly, the superficial infection rates for each of the analysed studies in the 2 groups varied from 0–22.2% in the injection group and from 0.4–11.1% in the control group, with most of the studies having a rate <5% (Table 2). Meta-analysis showed that steroid injection prior to joint arthroplasty had no significant effect on either deep infection rates (Fig. 2: risk ratio = 1.87; 95% CI 0.80–4.35; $P = 0.15$; heterogeneity: tau^2 = 0, I^2 = 0%, Q = 4.6, df = 5, $P = 0.465$) or superficial infection rates (Fig. 3: risk ratio = 1.75; 95% CI 0.76–4.04; $P = 0.19$; heterogeneity: tau^2 = 0.651, I^2 = 65.7%, Q = 14.6, df = 5, $P = .012$). There was limited evidence of publication bias, with a broadly symmetrical funnel plot of studies assessing deep infection rates (Fig. 4). A separate analysis of only those studies examining infection rates in THA [2,4,7–11] was also performed. The overall deep infection rate in THAs that had a previous steroid injection was 12/809 (1.5%) as compared to 17/1686 (1%) in those that had no previous joint injection. Similarly, the overall superficial infection rate in THAs that had a previous steroid injection was 27/721 (3.7%) as compared to 20/1598 (1.3%) in those that had no previous joint injection. Meta-analysis showed that steroid injection prior to THA had no significant effect on either deep infection rates (risk ratio = 1.59; 95% CI 0.66–3.83; $P = 0.31$; heterogeneity: tau^2 = 0, I^2 = 0%, Q = 3.0, df = 4, $P = 0.557$) or superficial infection rates (risk ratio = 1.91; 95% CI 0.48–7.56; $P = 0.36$; heterogeneity: tau^2 = 1.39, I^2 = 77.7%, Q = 13.5, df = 3, $P = 0.004$).

Critical appraisal of the included studies using MINORS criteria [6] are summarised in Table 3. The studies were retrospective cohort matched series. A clearly stated aim could be observed in almost all. Three studies included consecutive series of patients and 5 studies included reports where infections were matched to cases where no infections occurred. Unbiased assessment of outcomes was not seen in any of the studies, as one of the authors was involved in the final assessment of endpoints.

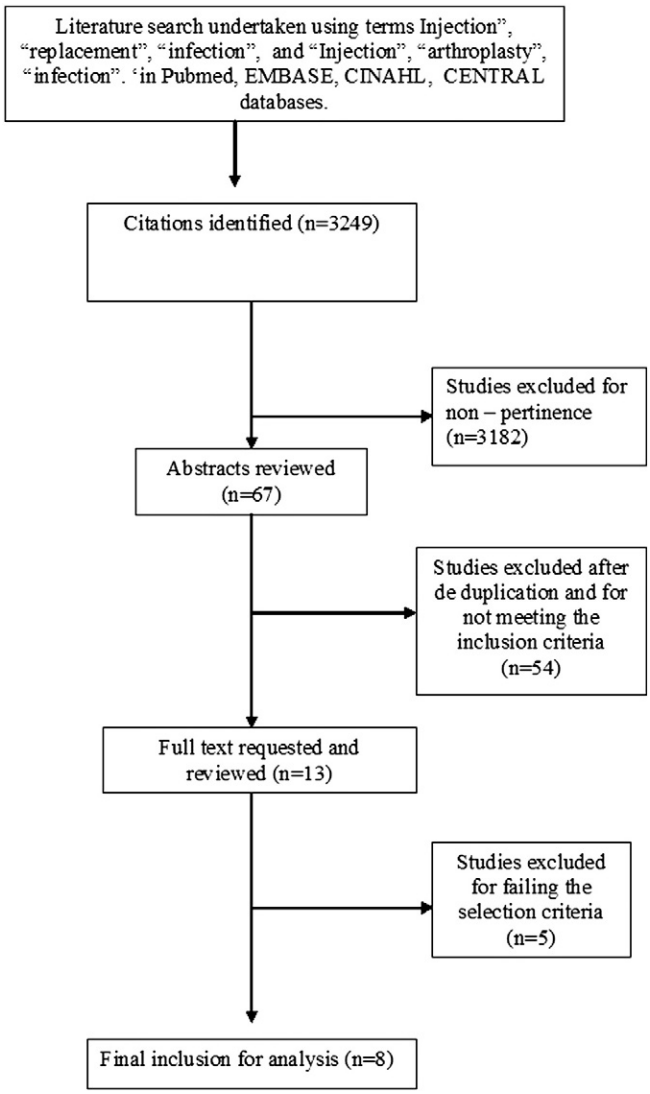

Fig. 1. Literature search and methodology of selection.

Discussion

The safety of intra-articular steroid injections prior to joint arthroplasty has been previously questioned with some clinical studies suggesting that they may lead to increase arthroplasty infection rates [1–4]. This may be due to failure of the steroid to dissolve which may thus persist and cause local immunosupression following joint arthroplasty [2,3]. Alternatively, it may be related to contamination of the joint by the injection process, as the sterility precautions taken are often variable [13]. Other studies, failed to demonstrate an association between previous steroid injections and subsequent joint arthroplasty infection [8–12]. As infection of joint arthroplasty is an infrequent event [14–16], it is possible that failure of some studies to demonstrate such association [8–12] may be related to the small number of patients included and hence low statistical power. A systematic review and meta-analysis of such studies would allow larger number of cases to be pooled and statistically examined.

The most important finding of the present study was that intra-articular steroid injection had no statistically significant effect on the superficial or deep infection rates of subsequent joint arthroplasty, suggesting that such practice is justifiable. This lack of effect was seen both when TKA and THA were combined for analysis but also when THAs were analysed in isolation. Although the incidence of deep infection was the primary outcome of this study, there seems to be a more dramatic difference in the superficial infection rate. There is no proposed mechanism which can safely explain how an injection may increase the risk of superficial infection.

Two of the analysed studies [3, 9] looked only into TKAs. The first study by Papavasiliou et al. [3] showed a statistically higher deep infection rate ($P < 0.025$) in TKAs that had a previous steroid injection (5.5%) as compared to those who had no previous injection (0%). With these results they concluded that the administration of steroid injection prior to a TKA should not be taken lightly. The second study by Desai et al. [9] showed no increased incidence of deep or superficial infection in TKAs after a prior steroid injection as compared