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REVIEW ARTICLE

Total joint arthroplasty following intra-articular steroid injection : A literature review

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This study aimed to identify, by systematic review of the literature, whether intra-articular steroid injection before total joint replacement confers an increased risk of post-operative deep prosthetic infection. All studies assessing the incidence of deep prosthetic infection in patients who had undergone steroid injection in the same joint were included. A mixed meta-analysis and narrative review of 12 studies with 2068 participants was conducted. Steroid injection prior to total joint replacement was found to confer no increased risk of deep or superficial prosthetic infection (CI = 95%). We found no evidence of a link between injection and deep joint infection, and conclude that this is a safe procedure when conducted with aseptic precautions. We suggest a prospective randomised control trial to provide conclusive data on this question.

Keywords : steroid ; injection ; knee ; hip ; infection ; joint replacement ; arthroplasty.

INTRODUCTION

Osteoarthritis (OA) affects 8.5 million people in the UK (*3*), and causes a significant economic burden, with £850 million spent on total joint replacement, and a loss of economic production of £3.2 billion in 2012 (*6*).

The management of OA ranges from conservative measures (analgesia, physiotherapy, intra-articular steroid injection (IASI) to surgical intervention (mostly joint replacement).

Intra-articular steroid injection has been used as a symptomatic treatment for OA for half a century (*25*), and is known to be effective for short term (up to 24 weeks) relief of symptoms in both knee (*2*) and hip (*28*) OA. When combined with local anaesthetic it can be used to distinguish true hip pain from referred spinal pain prior to further invasive

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treatment (*18*). The American College of Rheumatologists have advocated intra-articular steroid injections in their latest guidelines when a patient does not respond to simple analgesia, although there are no recommendations on the number or frequency of injections (*13*). Intra-articular steroid injection is, however, not without risk and a number of complications have been reported including septic arthritis (*5*), tendon rupture (*36*) and articular cartilage degeneration experimentally (*4*). Therefore, the decision to administer an IASI should not be taken lightly.

There has been debate in the literature as to whether IASI prior to total joint replacement, both of the hip and the knee, causes an increased risk of deep joint infection following surgery. This study aims to review the current literature regarding this question.

MATERIALS AND METHODS

Eligibility

We included all studies assessing the incidence of infection following total joint replacement in patients who had undergone IASI in the same joint. Only studies assessing clinical outcomes of human subjects were included. All potentially eligible studies were included irrespective of study design, language of publication or method/risk of bias.

Search strategy

We performed a PRISMA compliant (*26*) search to identify relevant articles from 1985 to September 2012 using online literature databases.

Study identification

The title and abstract of each study were reviewed. Full text papers were ordered of those studies pertinent to the research question and these were reviewed against the eligibility criteria.

Critical appraisal

The critical appraisal was conducted using a modified version of the Critical Appraisal Skills Programme (CASP) (*15*) tools for case-control and cohort studies.

Data analysis

A meta-analysis was undertaken where there was limited between-study heterogeneity in respect to cohort characteristics, study design, intervention and follow-up assessments. When there was between-study heterogeneity, a narrative synthesis of the study findings was undertaken. When pooled analysis was deemed appropriate, statistical heterogeneity was evaluated using the inconsistency value (I^2) and Chi-squared tests. In instances where I^2 was below 20% and Chi-squared reported p-values of above 0.01, a fixed-effects meta-analysis was undertaken. When these were not satisfied, a random-effects model was utilised.

The primary analysis questions were to investigate the difference in incidence between individuals who received an intra-articular injection (hip or knee) and subsequent deep joint or superficial wound infection post- total hip replacement (THR) or total knee replacement (TKR) respectively. Accordingly odds ratio (OR) analyses were undertaken, with data reported as a ratio and with 95% confidence interval (CI) and p-value data.

All meta-analyses were undertaken on RevMan (Review Manager) [Computer program]. Version 5.1. Copenhagen : The Nordic Cochrane Centre, The Cochrane Collaboration, 2011).

RESULTS

Search Results

Twelve studies from 252 initial studies were included for review. Eight studies investigated the effect of IASI and THR (*7,17,20,22,23,24,33,34*), 4 for IASI and TKR (*9,14,16,29*).

Critical Appraisal

The CASP (*15*) appraisal showed that the studies were generally of a high standard. They all had clearly defined aims, and were structured and conducted appropriately to meet them. The results were precise and able to be applied to the local population. All of the case-control studies took into account confounding factors when matching their cohorts, apart from Papavasiliou *et al* (*29*) where no matching was performed.

Table I. — Cohort Characteristics IASI in THR

Study	Study Design	Study/ Control Group	No of cases	Gender (M/F)	Age (years)	IASI to THR interval (months)	Follow-up (months)	Deep infection	Superficial infection
Chitre *et al* 2007	Retrospective analysis	Study	36	NR	63.7 (30-83)	18 (4-50)	25.8 (9-78)	0	1
Karuppiah *et al* 2007	Retrospective analysis	Study	128	52/76	NR	11	38.4	0	0
Kaspar *et al* 2005	Case control	Study	40	25/15	71.0 (45-87)	11.38 (7.2-14.5)	33.2 (9.9-86.2)	4	N/A
		Control	40		70.6 (46-87)		30.2 (11.8-53.0)	0	N/A
McIntosh *et al* 2006	Case Control	Study	224	93/131	70 (35-94)	3.7 (SD 2.7)	32.4 (SD 16.8)	3	11
		Control	224		69 (41-92)		31.2 (SD 19.2)	1	8
McMahon *et al* 2012	Prospective analysis	Study	49	N/R	69.0 (51-98)	12.1 (SD 5.1)	97.8 (85-117)	1	1
Meermans *et al* 2012	Case Control	Study	182	48/127	66.4 918-86)	5.09	72.1 (12-131)	1	5
		Control	175	50/125	66.6 (18-85)		70.5 (15-129)	1	7
Sankar *et al* 2012	Retrospective review	Study	40	10/30	68.4 (52-83)	6.2 (2-23)	23.2 (11-37)	0	1
Sreekumar *et al* 2007	Case Control	Study	68	15/51	62.2 (32-89)	14	25.3	0	0
		Control	136	32/104	64.1 (39-89)		22.3	1	1

F – female ; IASI - Intra-Articular Steroid Injection ; M – Male ; NR – not reported ; THR – Total Hip Replacement.

Cohort Characteristics

A summary of the cohort characteristics is available in Table I (THR) and Table II (TKR). For the THR studies, a total of 1342 participants were reviewed. Two studies did not state the gender mix of their cohorts (*7*,*23*) ; the other studies included 290 males and 659 females. The mean age of the cohorts ranged from 62.2 years (*34*) to 75.0 years (*20*). Follow-up periods ranged from 22.3 months (*34*) to 97.8 months (*23*).

For the TKR studies, a total of 726 participants were reviewed. Gender mix and mean ages were not reported in two studies (*14*,*29*). The other studies included 127 males and 187 females. Mean ages ranged from 68 years (*9*) to 72 years (*9*). Follow-up periods ranged from 33 months (*9*) to 79 months (*16*).

Clinical Findings

THR deep infection : Four case-control studies (n = 1087) were pooled in this analysis (Kaspar *et al* (*20*) ; McIntosh *et al* (*22*) ; Meermans *et al* (*24*) ; Sreekumar *et al* (*34*)). The odds ratio indicated individuals were twice as likely to develop a deep infection if they received an intra-articular steroid injection prior to THR compared to no injection, but this was not statistically significant (p = 0.12) and therefore may be considered a chance result. The pooled odd ratio was 2.65 (95%CI : 0.79, 8.96 ; Fig. 1).

THR superficial infection : Three case-control studies (n = 1007) were pooled for this analysis (*22*,*24*,*34*)). The meta-analysis indicated no difference in the incidence of superficial infection between those who received an intra-articular steroid injection prior to THR compared to no injection (OR : 1.04 ; 95% CI : 0.52, 2.10 ; Fig. 2).

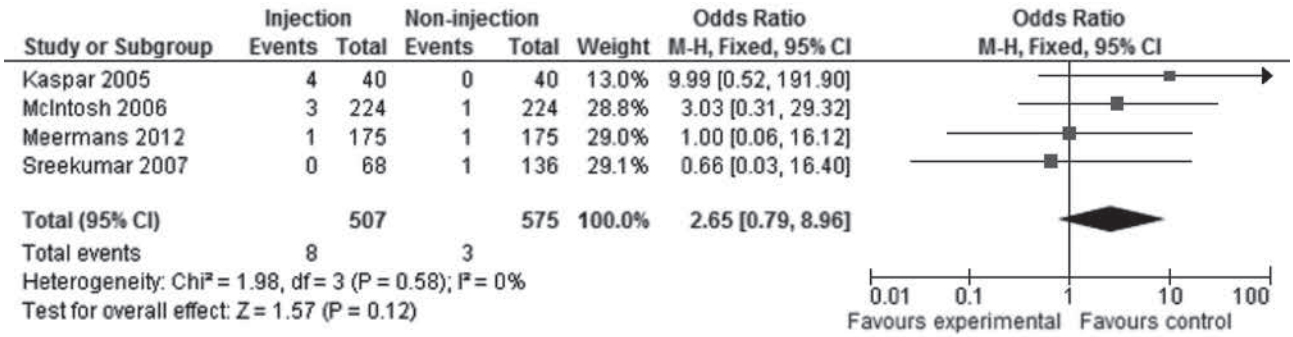
The low incidences of superficial and deep infections are re-iterated across the retrospective cohort dataset. Chitre *et al* (*7*), McMahon *et al* (*23*), Sankar *et al* (*33*) and Karrupiah *et al* (*17*) all reported acceptable deep infection rates.

TKA deep infection : Two case-control studies (n = 414) were pooled in this analysis (Desai *et al* (*9*) ; Papavasiliou *et al* (*29*)). Whilst the odds ratio

Table II. — Cohort Characteristics IASI in TKR

Study	Study Design	Study/ Control Group	No of cases	Gender (M/F)	Age (years)	IASI to TKR interval (months)	Follow-up (months)	Deep infection	Superficial infection	Unspecified infection
Desai *et al* 2008	Case Control	Study	90	26/54	68 (49-87)	NR	33 (12-72)	0	2	NR
		Control	180	74/96	72 (51-88)		48 (12-72)	0	5	NR
Horne *et al* 2008	Case Control	Study	29	NR	NR	16 (1-540)	NR	NR	NR	28
		Control	219	NR	NR		NR	NR	NR	0
Joshy *et al* 2006	Case Control	Study	32	14/18	69 (46-86)	46 (12-121)	79 (22-170)	32	0	NR
		Control	32	13/19	70 (47-86)	59 (13-132)	77 (23-156)	0	0	0
Papavasiliou *et al* 2006	Case Control	Study	54	NR	NR	NR	NR	3	12	NR
		Control	90	NR	NR			0	10	NR

F – female ; IASI – Intra-Articular Steroid Injection ; M – Male ; NR – not reported ; TKR – Total Knee Replacement.



Chi^2 ; Chi-Squared test, I^2 ; inconsistency test, Z ; Z-Score, M-H ; Mantel-Haenszel Test, CI ; Confidence Interval.

Fig. 1. — Forest plot reporting the incidence of THR deep infection between those who received an intra-articular steroid injection prior to THR compared to no injection.

indicated people were twice as likely to develop a deep infection if they received an intra-articular steroid injection prior to TKR compared to no injection, this was not statistically significant (p = 0.64) ; and may be considered a chance result. The pooled odd ratio was 2.24 (95% CI : 0.08, 65.30 ; Fig. 3).

TKR superficial infection : Two case-control studies (n = 414) were pooled in this analysis (Desai *et al* (*9*) ; *Papavasiliou et al* (*29*)). The meta-analysis indicated no difference in the incidence of superficial infection between those who received an intra-articular steroid injection prior to TKA compared to no injection (OR : 0.91 ; 95% CI : 0.07, 11.11 ; Fig. 4).

TKR unspecified infection : Two case-control studies (n = 312) were pooled in this analysis for reported "infection" not specifying whether this was deep or superficial (Horne *et al* (*14*) ; *Joshy et al* (*16*)). The meta-analysis showed no difference in the incidence of IASI prior to operation in TKRs that went on to become infected and those that did not (OR : 1.12 ; 95% CI : 0.56, 2.25 ; Fig. 5).

Joshy *et al* (*16*) specified that their study cohort was comprised of patients with proven deep joint infection, whereas Horne *et al* (*14*) included patients "who had had a readmission with wound healing problems and a suspected infection within six months of TKR or who, at any stage, had revision knee surgery for an infected joint". On narrative

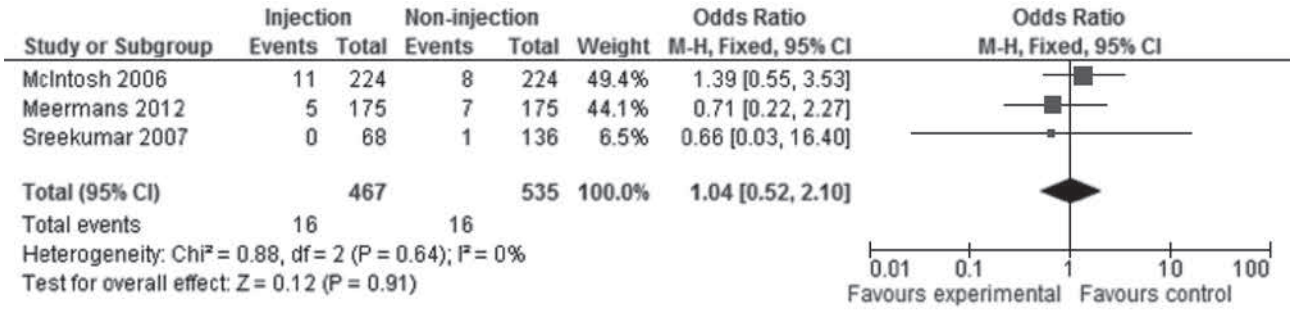


Fig. 2. — Forest plot reporting the incidence of THR superficial infection between those who received an intra-articular steroid injection prior to THR compared to no injection.

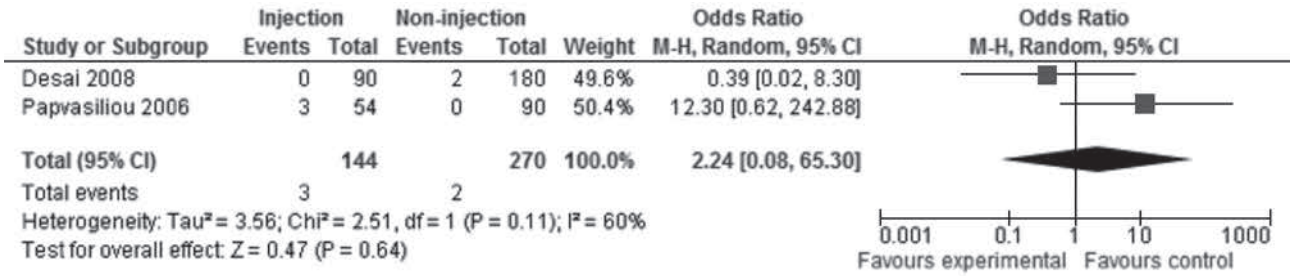


Fig. 3. — Forest plot reporting the incidence of TKA deep infection between those who received an intra-articular steroid injection prior to TKA compared to no injection.

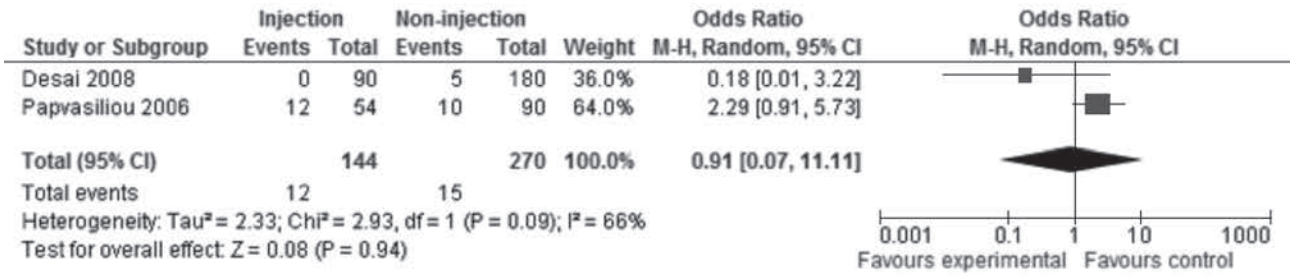


Fig. 4. — Forest plot reporting the incidence of TKA superficial infection between those who received an intra-articular steroid injection prior to TKA compared to no injection.

review, no relationship between IASI and deep or superficial infection was identified by Horne *et al* (*14*) or Joshy *et al* (*16*).

DISCUSSION

Deep joint infection following arthroplasty is a catastrophic event. The incidence is increasing and diagnosis can be challenging (*30*). Revision surgery following infection is associated with longer operative time, more blood loss, and a higher number of complications compared with revisions for aseptic loosening or primary THR, and the mean cost of revision surgery in cases of sepsis was found to be £21,937 compared £11,897 in aseptic cases in the UK (*37*). There is experimental evidence that prior IASI leads to an increased infection risk (*1,11*). However, there are a number of factors known to impact infection risk within an individual patient (*12,21,31, 32,35*).

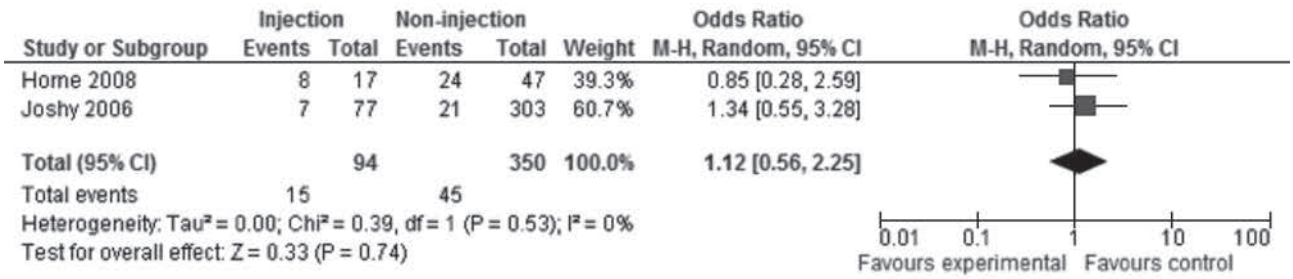


Fig. 5. — Forest plot reporting the incidence of TKA unspecified infection between those who received an intra-articular steroid injection prior to TKA compared to no injection.

Concern regarding the effect of IASI on infection rates in subsequent THR was first raised by Kaspar and de Beer (*18*,*29*). Their study published in 2006 (*20*) found a 10% infection rate in patients who had received an IASI prior to THR. This result appears to have since been refuted by the subsequent studies conducted. It was initially suggested by McIntosh *et al* (*22*) that a short interval between IASI and THR may have had an effect. However, this appears not to be the case as Sankar *et al* (*33*) conducted their study with a mean interval of 6.2 months (2-23) without adverse effect.

The setting of the IASI may be significant. Kaspar *et al* (*20*) report conducting IASIs in a fluoroscopy suite. They describe adequate skin preparation and aseptic technique, however it is not described what the ambient conditions in the suite were, and it has been suggested that pathogenic organisms may be introduced in to the joint at that time. McIntosh *et al* (*22*) also described the IASI being done by members of the radiology department, although it is not specified whether this was in the radiology department or theatres. They found a non-significant increase in deep infection rate (1.3% vs. 0.45%) although both rates were within the historic infection rate reported at the study institution between 1969 and 1996. Subsequent studies have all described the sterility of the environment and procedure undertaken.

Papavasiliou *et al* (*29*) identified a significant increase in deep prosthetic infection following TKR in patients who had undergone IASI. The study did not find any significance in the timing or number of injections. Interestingly, Papavasiliou *et al* (*29*) did not match their control cohort. The control was taken as the consecutive patients within the series who did not receive IASI prior to TKR.

Most IASIs to the knee are conducted in a clinic setting with only a cursory attempt at aseptic technique. Desai *et al* (*9*) conducted injections in the operating theatre with strict aseptic procedures observed, and recorded no deep infections in their series. Horne *et al* (*14*) conducted an interesting retrospective study. Several different health professionals had conducted the IASI (general practitioners, orthopaedic surgeons and rheumatologists), and it can be assumed that the injections were therefore conducted under varying degrees of asepsis, No increased risk of developing postoperative wound problems or deep prosthetic infections was identified. In view of evidence that both smoking (*10*) and diabetes (*27*) increase the risk of wound complications, no increase was detected by Horne *et al* (*14*) although it is suspected that the number of patients admitting to smoking was underreported.

We believe that the current evidence suggests that IASI prior to total joint replacement is safe, when conducted within appropriate aseptic conditions. The documented symptomatic benefits experienced by patients outweigh the small risk of immediate complications, and the large majority of studies show it confers no increased risk of joint sepsis. Our conclusions must be viewed with some caution as they are based on level II evidence. A randomised control trial would provide conclusive evidence with regards to the study question, however we accept that this would be difficult to undertake due to the invasive nature of an IASI.

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