



Intra-articular injection *versus* portal infiltration of 0.5% bupivacaine following arthroscopy of the knee

A PROSPECTIVE, RANDOMISED DOUBLE-BLINDED TRIAL

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The administration of intra-articular local anaesthetic is common following arthroscopy of the knee. However, recent evidence has suggested that bupivacaine may be harmful to articular cartilage. This study aimed to establish whether infiltration of bupivacaine around the portals is as effective as intra-articular injection.

We randomised 137 patients to receive either 20 ml 0.5% bupivacaine introduced into the joint (group 1) or 20 ml 0.5% bupivacaine infiltrated only around the portals (group 2) following arthroscopy. A visual analogue scale was administered one hour post-operatively to assess pain relief. Both patients and observers were blinded to the treatment group. A power calculation was performed.

The mean visual analogue score was 3.24 (SD 2.20) in group 1 and 3.04 (SD 2.31) in group 2. This difference was not statistically significant ($p = 0.62$).

Infiltration of bupivacaine around the portals had an equivalent effect on pain scores at one hour, and we would therefore recommend this technique to avoid the possible chondrotoxic effect of intra-articular bupivacaine.

Intra-articular bupivacaine is widely used as a local anaesthetic in arthroscopic surgery, either as a single agent or to supplement regional or general anaesthesia. A growing number of laboratory studies have demonstrated the potential toxicity of bupivacaine to articular cartilage. Most recently, Chu et al¹ demonstrated that exposure of human chondrocytes *in vitro* to 0.5% bupivacaine for just 15 minutes resulted in cell viability of only 41%. Gomoll et al² examined a rabbit shoulder *in vivo* and showed significant histopathological and metabolic changes in articular cartilage following continuous intra-articular infusion of bupivacaine. Recent reports have also implicated the use of bupivacaine in post-operative chondrolysis in the human glenohumeral and ankle joints.³⁻⁵

Intra-articular bupivacaine provides effective post-operative pain relief following arthroscopic knee surgery compared with a placebo.⁶ However, the potential for damage to healthy articular cartilage in a young population raises concern. We therefore designed a study to examine whether extra-articular infiltration of bupivacaine around the portals provides equivalent post-operative analgesia to intra-articular injection.

Patients and Methods

The study was a double-blind prospective, randomised clinical trial. Consecutive

patients attending for arthroscopy of the knee as a day-case were considered eligible. Patients with inflammatory arthritis, radiological evidence of osteoarthritis, osteochondral fracture or defect or a previous diagnosis of a pain syndrome were excluded. Patients were randomised by sealed envelope into two groups. Following arthroscopy, group 1 received 20 ml of 0.5% bupivacaine introduced into the joint via an arthroscopic cannula, and group 2 received 20 ml 0.5% bupivacaine infiltrated subcutaneously around the portals, avoiding intra-articular injection. Prior to commencing the study it was established that when using a fully inserted 25 G needle (2.5 cm in length), the joint space would not be entered. This is in keeping with the findings of Jackson, Evans and Thomas.⁷ A standard general anaesthetic protocol was agreed which included fentanyl 1 µg/kg, propofol, a laryngeal mask, sevoflurane and oxygen. No additional long-acting analgesic agents were given. The arthroscopy was performed using a thigh tourniquet by either a consultant orthopaedic surgeon or a specialist registrar under supervision. Pain is a highly subjective phenomenon and difficult to quantify.⁸ We attempted to overcome this by using a visual analogue scale (VAS),⁹ which is unidimensional and has been shown to be

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Table I. Patient demographics and operative procedures for the two groups

	Group 1 intra-articular injection	Group 2 (portal infiltration)	
Number	68	69	
Mean age (range)	45.1 (29 to 69)	47.0 (26 to 66)	p = 0.342*
Gender			
M:F	45:23	45:24	p = 0.906†
Diagnostic arthroscopy	5	3	
Partial meniscectomy	63	64	
Removal of loose body	0	2	

* Pearson's chi-squared test

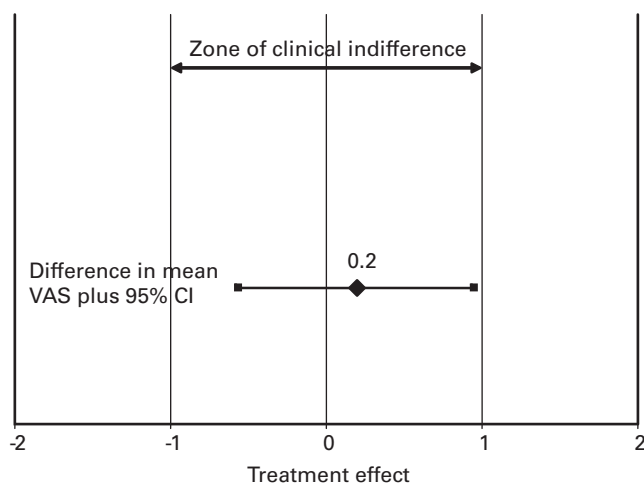
† Student's two-tailed paired *t*-test assuming equal variances

Fig. 1

Graph showing the equivalence test (VAS, visual analogue scale 95% CI, 95%, confidence interval).

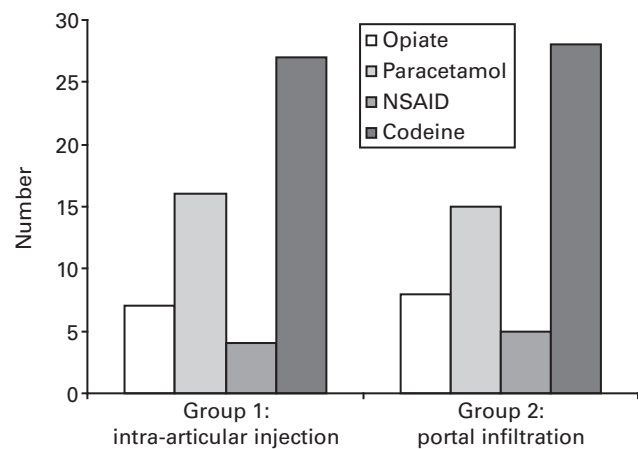


Fig. 2

Bar chart showing the additional analgesia for each group by type (NSAID, non-steroidal anti-inflammatory drug).

versatile, easy to use, reliable and valid in the assessment of acute pain.¹⁰ The VAS was administered one hour post-operatively by a blinded member of the recovery staff using a 10 cm linear scale where 0 represented no pain and 10 the most severe. The need for additional analgesia was recorded. This study was approved by the local ethics committee.

Statistical analysis. A power calculation was performed to calculate the sample size based on the SD of the VAS following knee arthroscopy reported in a recent study.¹¹ It has previously been shown that the minimum clinically detectable change in the VAS is 1.3 points.¹² To demonstrate an effect size of one VAS point with 80% power and a p-value of 0.05 would require a minimum of 128 patients. The chi-squared test, Student's two-tailed *t*-test and equivalence test were used as appropriate to assess for statistical significance. Analysis was performed using SPSS version 12.0

(SPSS Inc., Chicago, Illinois). Statistical significance was accepted with a p-value of < 0.05.

Results

A total of 137 patients were recruited: 68 were to receive an intra-articular injection (group 1) and 69 to receive portal infiltration (group 2). The demographics and operative procedures were similar in each group (Table I). The mean VAS in group 1 was 3.24 (SD 2.20) and in group 2 was 3.04 (SD 2.31) (p = 0.62). Assuming a clinically significant difference of one VAS point, it is possible to perform an equivalence test. The difference in means plus 95% confidence intervals (CI) lie within a range of -1 to +1 (Fig. 1), indicating that there is clinical equivalence between the two techniques of administration of local anaesthetic. In total, 33 patients in group 1 and 34 patients in group 2 required additional analgesia

($p = 0.93$). The distribution of analgesia by type was similar (Fig. 2), but the numbers are too small to perform a meaningful statistical subgroup analysis.

Discussion

The exact mechanism of chondrotoxicity from bupivacaine is not well understood, but is thought to be via an inflammatory process initiated by the production of nitric oxide.¹³ Exposure to a single intra-articular injection of bupivacaine in a rabbit model has been shown to cause histopathological changes in articular cartilage similar to those associated with the development of osteoarthritis.^{2,14} Chu et al¹ reported a dose- and time-dependent effect. Exposure of human and bovine articular chondrocytes to 0.25% and 0.5% bupivacaine solutions demonstrated toxicity which was greater after 30 minutes than after 15 minutes. In an earlier study, Chu et al¹⁵ also demonstrated that a defect in the articular surface led to a more profound chondrotoxic effect.

Despite the strong laboratory evidence for chondrotoxicity, there is an apparent low incidence of chondrolysis following intra-articular administration of bupivacaine in clinical practice. Several studies have demonstrated a strong link between chondrocyte injury or death and the development of osteoarthritis in various models, including humans,^{2,16} and it may be several years between an insult to the cartilage and the onset of clinically apparent osteoarthritis. To our knowledge, no formal clinical evaluation of bupivacaine and chondrolysis has ever been conducted. There have been case reports of chondrolysis in the glenohumeral and ankle joints linked to the use of intra-articular local anaesthetic, although the cause remains unproven.^{3,5} Smaller joints may be at more risk because of thinner cartilage and a smaller volume of post-operative haematoma. It is difficult to extrapolate the findings of laboratory studies to clinical practice. However, many of our patients attending for arthroscopy of the knee are young and with healthy articular cartilage, and we should be aware that there is the potential, albeit based on experimental evidence, to do

harm. This double-blinded, randomised study has demonstrated equivalence between two modes of administration of bupivacaine local anaesthetic following arthroscopy. By avoiding intra-articular infiltration and choosing to infiltrate around the portals, the possible chondrotoxic insult can be avoided without compromise in post-operative analgesia.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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