Intra-articular bupivacaine: potentially chondrotoxic?

The management of acute postoperative pain after orthopaedic surgery is a challenge for anaesthetists and surgeons. The administration of local anaesthetic drugs into the joint space, either by single injection or by continuous infusion, has become a well-recognized technique for postoperative analgesia, in particular after arthroscopic surgery. Bupivacaine is commonly used for intra-articular analgesia because of its long duration of action. Other local anaesthetics used for intra-articular analgesia include ropivacaine and lidocaine. Intra-articular use of these drugs has been widely regarded as safe, and adverse effects of local anaesthetic agents in the joint space have been reported only rarely. Peak plasma concentrations of bupivacaine are sufficiently low after intra-articular injection such that systemic toxicity is extremely unlikely. However, overdose or inadvertent intravascular injection may result in central nervous system and cardiovascular toxicity.

Despite their widespread use, the effects of intra-articular local anaesthetic agents on joint structures have not been fully elucidated. Early evidence from animal experiments suggested that bupivacaine acutely inhibits the synthesis of articular cartilage. A later study found that intra-articular bupivacaine 0.5% resulted in articular cartilage inflammation and synovial membrane changes in rabbit knee joints. However, overdose or inadvertent intravascular injection may result in central nervous system and cardiovascular toxicity.

Chondrolysis is a condition in which extensive loss of articular cartilage occurs over a relatively short period of time. After arthroscopic shoulder surgery, the consequences of postoperative glenohumeral chondrolysis are clearly devastating. The condition typically occurs in young athletes and effective treatment options are limited. The pain and reduced mobility associated with chondrolysis tend to progress to severe osteoarthritis, which may eventually require joint arthroplasty. The largest series of cases of post-arthroscopic glenohumeral chondrolysis (PAGCL) described 12 cases. The authors state that the common factor in all cases was the postoperative administration of an intra-articular infusion of bupivacaine with epinephrine. In total, 27 cases of PAGCL have been reported, with 25 of these cases having received postoperative continuous intra-articular analgesia with bupivacaine.

Recently, a number of experimental studies have suggested that local anaesthetics may damage articular cartilage. It has been shown that bupivacaine 0.5% is toxic to both bovine articular chondrocyte cultures and bovine articular osteochondral tissue. The effect of bupivacaine on human cartilage has also been analysed. The effects of bupivacaine 0.5%, bupivacaine 0.25%, bupivacaine 0.125%, and saline 0.9% on bovine and human articular chondrocyte cultures were compared. Both bupivacaine 0.5% and bupivacaine 0.25% displayed dose-dependent and time-dependent chondrotoxicity. The toxicity of bupivacaine 0.5% was more marked than bupivacaine 0.25% at all time points. The toxicity of both drugs increased as the duration of exposure increased (from 15 to 60 min) and as the time after exposure increased (from 1 h to 1 week). The effect of bupivacaine 0.125% on bovine and human articular chondrocytes was no different from 0.9% saline. The effects of different concentrations of bupivacaine on bovine articular osteochondral tissue were also compared. Again, both bupivacaine 0.5% and bupivacaine 0.25% demonstrated dose-dependent chondrotoxicity. However, the effect of bupivacaine 0.125% was not different from 0.9% saline.

Although less profound than the effects of bupivacaine, lidocaine 1% and lidocaine 2% also exhibit dose-dependent and time-dependent toxic effects on bovine articular chondrocytes. Ropivacaine is the third local anaesthetic to be associated with chondrotoxicity. The effects of bupivacaine 0.5% and ropivacaine 0.5% on both human articular chondrocyte cultures and human articular...
cartilage explants were compared. Although ropivacaine 0.5% was toxic to chondrocyte cultures, it was significantly less toxic than bupivacaine 0.5%. On exposure of cartilage explants to both local anaesthetic agents, the effect of ropivacaine 0.5% was no different from that of 0.9% saline, whereas bupivacaine 0.5% did demonstrate chondrotoxicity.

Other studies have tested the effects of continuous administration of local anaesthetic agents on intra-articular structures. In an experimental animal model, the 48 h intra-articular infusion of bupivacaine 0.25%, both with and without epinephrine, resulted in significant histopathological and metabolic changes in rabbit shoulder joints after 1 week. However, using the same model, no significant histopathological changes were found 3 months after the 48 h intra-articular infusion of bupivacaine, both with and without epinephrine. Metabolic effects consistent with increased articular cartilage synthesis, which may represent a reparative process, could, however, be demonstrated.

Another study investigated the in vitro effects of the 72 h administration of lidocaine 1%, bupivacaine 0.25%, and bupivacaine 0.5%, each with and without epinephrine, on human articular chondrocyte cultures. All of the local anaesthetic solutions containing epinephrine resulted in significant chondrocyte necrosis at 24, 48, and 72 h. None of the local anaesthetic solutions which did not contain epinephrine caused chondrocyte necrosis at 24 h. However, significant chondrocyte necrosis developed after 48 h exposure to lidocaine 1% and after 72 h exposure to bupivacaine 0.5%.

The pathogenesis and aetiology of postoperative chondrolysis are unclear and the clinical entity remains poorly understood. The condition is rare and only a small number of case series have been published. However, information about PAGCL is widely available in the public domain and a number of lawsuits have been filed in the USA against infusion device manufacturers for personal injury involved in the condition. The putative benefits of continuous intra-articular local anaesthetics must not compromise patient safety. We should be prepared to modify our approach to drug usage in the light of new knowledge of adverse effects.

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