Scientific Paper

Update on Local Anesthetics in Orthopaedics

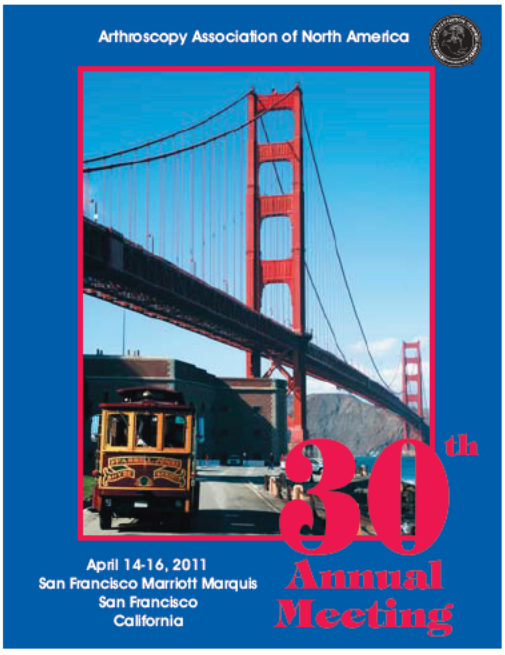
by Constance R. Chu, MD, Albert Fergusson Professor of Orthopaedic Surgery, Director Cartilage Restoration Center, Department of Orthopaedic Surgery, University of Pittsburgh School of Medicine & Michael J. O'Malley, MD, University of Pittsburgh Medical Center, Department of Orthopadic Surgery

Intra-articular use of local anesthetics has received a great deal of attention recently in the orthopaedic literature and in the lay press due to concerns for chondrotoxicity and for being a contributing factor to shoulder chondrolysis associated with the use of continuous infusion pain pumps. Local anesthetics have been an integral part of routine intra-articular injections following arthroscopy, for diagnostic tests, and as a component of therapeutic intra-articular injections ranging from cortisone to hyaluronic acid to biologics such as platelet rich plasma (PRP). Consequently, an awareness and understanding of the potential risks and alternatives to intraarticular local anesthetics is important.

The broader medical literature has long shown that local anesthetics have toxic effects on a variety of cell types to include cardiac myocytes, neurons, and skeletal muscle tissue. Some of these effects lead to life threatening toxicity that can be difficult to treat. Bupivacaine, for example, is known to have severe cardiac effects and systemic administration can cause irreversible cardiac arrest (McLure HA, et al. 2005). Even regional administration result in severe toxicity. There have been reports of cardiac arrest with difficult resuscitation and death during use of 0.75% bupivacaine for epidural anesthesia in pregnant women (Prod Info Marcaine(R), 1991). Bupivacaine has also been implicated in clinical cases of irreversible neurologic injury following spinal anesthesia (Rigler ML, et al. 1991). The mechanisms of toxicity include cell membrane effects and have also been reported to be related to mitochondrial dysfunction resulting in apoptosis and cell death (Irwin W, et al. 2001).

Initial concern for chondrotoxicity of local anesthetics occurred following increasing reports and observations of young patients developing chondrolysis and severe arthroses within a few months after shoulder arthroscopy where pain pumps were used for continuous infusion of bupivacaine (Petty DH, et al. 2004). It was speculated that this clinical observation may be related to intra-articular infusion of bupivacaine. In subsequent studies by Chu et al. (2006, 2008) it was discovered that bupivacaine was exceptionally cytotoxic to chondrocytes in culture, killing 99% of cell after only 15-30 minutes of exposure, and that the chondrotoxic effects of bupivacaine on human chondrocytes was dose and time dependent. Furthermore, Karpie et al. (2007) showed that bovine cartilage when exposed to lidocaine exhibited similar toxicity that increased in a dose and time dependent manner. Other investigators have found similar results with ropivacaine which further suggest that potential chondrotoxicity may be a class effect of local anesthetics (Lo IK 2009, Kim HT 2008). Local anesthetics are often injected in combination with other medications including epinephrine and corticosteroids. Both of these medications have been shown to potentiate the chondrotoxcicity of local anesthetics (Dragoo JL 2008; Seshadri 2009).

In a small animal model the effects of a single intra-articular injection of 0.5% bupivacaine were investigated (Chu CR, et al. 2010). After 6 months there was little gross evidence of arthritis. However, quantitative analysis of histological sections demonstrated a 50% decrease in chondrocyte density in the cartilage of joints injected with 0.5% bupivacaine. This same study showed that a loss of 75% of chondrocytes after injection of a known chondrotoxic agent resulted in a severe progressive arthritis 6 months later. Although this small animal data cannot be directly correlated to humans, it shows that substantial chondrocyte loss results in accelerated loss of articular cartilage and suggests a potential risk for some degree of chondrotoxicity following a single intra-articular injection of bupivacaine.



Cartilage, as a tissue has been shown to have very little capacity to repair and regenerate itself. Therefore any insult that causes damage to cartilage or loss of chondrocytes is likely to contribute to eventual degeneration. The loss of chondrocytes even in the presence of normal appearing cartilage has a detrimental effect on matrix preservation and remodeling. This can result in softer

Continued on page 9

ientific Paper Continued from page 8

and mechanically inferior cartilage that is more susceptible to further damage, degeneration, and progression to osteoarthritis.

The potential risks for chondrotoxicity can be reduced by minimizing the use of local anesthetics. The paradigm that intra-articular administration of local anesthetics is necessary for pain control following arthroscopy was challenged in a recent prospective study by Townshend et al. (2009). They showed that there was no difference in post-operative pain following arthroscopy when patients were given either an intra-articular injection or an extra-articular portal-site injection of bupivacaine. The results of this study provide an example of how intra-articular injection of local anesthetics can be reduced without compromising post-operative analgesia.

There is more to be learned regarding local anesthetics and their future role in orthopaedic surgery. Most studies have been done in small animal and in-vitro models. The important concepts to be gleaned from this work are that local anesthetics are not benign and have potential adverse effects to include a dose and time dependent chondrotoxicity. It is important and prudent for every physician to be aware of these potential risks and consider whether the local anesthetic component of an intra-articular injection is necessary and whether similar effects can be achieved with a lower dose of local anesthetic. Multiple intra-articular injections over a short time period and continuous intra-articular administration of local anesthetics carry the highest potential risks for chondrotoxicity.