

Commentary

Effect of bupivacaine on chondrocyte viability

Jason L. Dragoo, MD*, Stephanie Y. Pun, MD

Department of Orthopedic Surgery, Stanford University, Redwood City, CA 94063, USA

Received 15 October 2009; accepted 16 November 2009

COMMENTARY ON: Lee H, Sowa G, Vo N, et al. Effect of bupivacaine on intervertebral disc cell viability. *Spine J* 2010;10:159–166 (*in this issue*).

We commend Lee et al. [1] for a valuable investigation of the effects of a commonly used local anesthetic, bupivacaine, on intervertebral disc cell viability. The routine use of bupivacaine in popular procedures such as nerve root blockades, facet joint injections, and intradisc injections makes this study clinically important. Given that a subpopulation of intervertebral disc cells possesses a chondrocytic phenotype, this study is particularly relevant in light of recent evidence of the chondrotoxicity of local anesthetics.

The concern regarding local anesthetics on chondrocyte viability was first raised by clinical reports of postarthroscopic glenohumeral chondrolysis that became clinically apparent at approximately 5 months postoperatively. The diagnostic criteria for postarthroscopic glenohumeral chondrolysis include increased shoulder pain, shoulder stiffness, shoulder crepitus independent of range of motion, and radiographic glenohumeral joint space narrowing. The use of intraarticular pain pumps has been associated with glenohumeral chondrolysis. In one case series, Hansen et al. reported that all 12 cases of postarthroscopic glenohumeral chondrolysis involved the use of a high-flow intraarticular pain pump with 0.25% bupivacaine with epinephrine.

The chondrotoxicity of local anesthetics has been demonstrated in a number of recent *in vitro* studies. Chu et al. described the chondrotoxicity of 1% lidocaine and 0.5% bupivacaine on bovine articular chondrocytes in culture and 0.25% bupivacaine on human articular chondrocytes in culture, with significant cell death after as little as 15 minutes of exposure. Dragoo et al. demonstrated that 48-hour exposure to 0.25% and 0.5% bupivacaine in a continuous infusion

pain pump under joint metabolism conditions caused minimal chondrocyte necrosis, but exposure for 72 hours significantly decreased human cultured chondrocyte viability. Furthermore, the addition of epinephrine significantly decreased chondrocyte viability, and the authors concluded that intraarticular use of bupivacaine with epinephrine should be avoided.

In vivo studies regarding the long-term chondrotoxicity of local anesthetics have been less conclusive. Gomoll et al. demonstrated in an *in vivo* rabbit model that although a 48-hour infusion of bupivacaine caused immediate damage to articular cartilage within 1 week of administration, there were no permanent deleterious effects when the cartilage was examined 3 months after administration. These paradoxical longer term results emphasize the importance of further *in vivo* studies to delineate the long-term effect of local anesthetics on articular cartilage.

Given the chondrocytic nature of a subpopulation of intervertebral disc cells, there is concern regarding the potential toxicity of local anesthetics on intervertebral disc cells. The intradiscal space is similar to the relatively avascular intraarticular environment, thereby potentially increasing the effective half-life and toxicity of local anesthetics through decreased blood flow and washout. Similar to the role of chondrocytes in the pathogenesis of osteoarthritis, intervertebral disc degeneration is characterized by disc cell senescence and cell loss. Therefore, preservation of intervertebral disc cells is crucial to maintaining normal intervertebral disc function, and any iatrogenic damage should be avoided.

This *in vitro* study by Lee et al. investigated the effect of bupivacaine on the cell viability of normal rabbit and degenerative human nucleus pulposus and annulus fibrosus cells. A time- and dose-dependent cytotoxic effect of bupivacaine on human nucleus pulposus cell viability was found. These findings are consistent with previous *in vitro* studies of the cytotoxic effects of bupivacaine on articular

DOI of original article: 10.1016/j.spinee.2009.08.445.

FDA device/drug status: not applicable.

Author disclosures: none.

* Corresponding author. Department of Orthopedic Surgery, Stanford University, 450 Broadway, Redwood City, CA 94063, USA. Tel.: (650) 721-7800.

E-mail address: jdragoo@stanford.edu (J.L. Dragoo).

chondrocytes. Like these previous investigations, this study is limited by the in vitro nature of the experiments. Demonstration of bupivacaine's cytotoxicity in vitro does not necessarily imply that bupivacaine is clinically harmful to intradiscal cells. It remains unknown how the cellular response to bupivacaine may differ in the in vivo environment. Cell death is associated with disc degeneration, but as is the dilemma in studies of the pathogenesis of osteoarthritis, it is difficult to separate bupivacaine-induced cytotoxicity from the natural progression of the disease.

The concentrations of bupivacaine investigated and the durations of exposure are consistent with previously published in vitro studies of bupivacaine on articular chondrocytes, but there is little evidence of the propriety of these values. It is unclear whether the chosen concentrations for investigation are biologically relevant, given the size of the intradiscal and intraarticular spaces. The relatively avascular, intraarticular, and intradiscal environments exhibit normal metabolism through diffusion, and it is unclear whether the investigated duration of exposure is the true

duration that bupivacaine would remain in these body environments.

Despite the in vitro nature of this study, Lee et al. have provided insight into the potentially deleterious effects of bupivacaine on intradiscal cells. Given the widespread clinical use of local anesthetics for spine pathology, selective use of such agents should be exercised. The potentially detrimental effects of bupivacaine on cell viability must be weighed against the potential pain relief provided to the patients. Given the evidence of disparate findings between in vitro and in vivo studies of local anesthetic chondrotoxicity, further in vivo studies are also necessary to investigate whether bupivacaine results in clinically detrimental effects on intradiscal cells and disc degeneration.

Reference

- [1] Lee H, Sowa G, Vo N, et al. Effect of bupivacaine on intervertebral disc cell viability. *Spine J* 2010;10:159–66.