

Bumps in the road to developing long-lasting, single-injection nerve blocks

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Can a new liposomal bupivacaine product provide long-lasting nerve block with a single injection? An initial study in humans shows promise—but also some "confusing results," reports the November issue of *Anesthesia & Analgesia*, official journal of the International Anesthesia Research Society (IARS).

A single injection of liposomal bupivacaine produces femoral [nerve](#) block lasting longer than 24 hours in volunteers, according to a study by Dr Brian M. Ilfeld and colleagues of University of California San Diego. But the results aren't straightforward, with variable responses and a hard-to-explain "inverse relationship" between dose and response.

Liposomal Bupivacaine Shows Evidence of Lasting Nerve Block...

The researchers evaluated a liposomal bupivacaine preparation (brand name Exparel) designed to release local anesthetic over 96 hours after injection. The liposomal bupivacaine product is FDA-approved for use in managing incision pain after surgery, but not for performing peripheral nerve blocks.

Fourteen healthy volunteers received single-injection blocks of the femoral nerve in the upper thigh using different doses of bupivacaine. Responses were evaluated in terms of pain tolerance (sensory nerve block) and muscle movement (motor nerve block).

The results showed significant and lasting responses in terms of both sensory and peripheral nerve block. However, the relationship between dose and response was exactly the opposite of expected, with lower doses of liposomal bupivacaine producing greater responses. "This inverse relationship is biologically implausible and most likely due to the limited sample size and the subjective nature of the measurement instruments," Dr Ilfeld and colleagues write.

In most cases, the nerve block effects peaked within 24 hours after injection, although the total duration of the block was much longer. The duration of motor block was unrelated to the dose of liposomal bupivacaine.

...But More Work Needed to Develop Effective 'Depo-Local Anesthetics'

Femoral nerve blocks are useful in controlling leg pain in several situations—for example, in patients undergoing total knee replacement surgery. With currently available local anesthetics, single-injection nerve blocks provide a maximum duration of effect between eight and 24 hours. Longer-lasting nerve block requires repeated injections or use of a catheter and drug pump.

"An alternative approach is to encapsulate a long-acting local anesthetic within microspheres or liposomes," Dr Ilfeld and coauthors explain. Such "depo-local" formulations could be given in a single injection, and release adequate levels of local anesthetic to maintain effective nerve block over time. Preliminary studies showed promising results with liposomal bupivacaine for this purpose.

The new study adds further evidence that liposomal bupivacaine can provide longer-lasting nerve blocks. And yet some of the findings don't

add up—especially the inverse dose-response relationship. Although the results are "suggestive," Dr Ilfeld and coauthors emphasize that larger trials will be needed before liposomal bupivacaine can be recommended for routine clinical use in performing nerve blocks.

Despite the "confusing results," the study is still intriguing to anesthesiologists, according to an editorial by Dr John C. Rowlingson. He writes, "We need long-acting local anesthetics for injection, be that along an incision or for a variety of [nerve blocks](#)."

Depo-[local anesthetics](#) may be especially valuable in reducing the need for strong opioid (morphine-related) pain medications in patients who require extended pain management. Dr Rowlingson calls on anesthesiologists to "remain patient but for a little while longer" while research continues on "the road to discovery of a dependable encapsulated local anesthetic".

More information: [journals.lww.com/anesthesia-an ...
le_injection.32.aspx](http://journals.lww.com/anesthesia-an-le_injection.32.aspx)

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