Unique Low-Dose Intrathecal Opioid Trial, Still in Need of a Feasibility Check

To the Editor:

It is with great interest that we read the article by Grider et al, "Patient selection and outcomes using a low-dose intrathecal opioid trialing method for chronic nonmalignant pain", published in the 2011 July/August issue of *Pain Physician* (1).

We are much enlightened by the novel approach employed by the authors in conducting their intrathecal (IT) opioid trials. The novelty is that only a fraction of the opioid was utilized during their trials, after a preceding, gradual opioid tapering and a subsequent opioid-free period of 6 weeks. This is very different from neuroaxial trials by others reported in the literature (2). It appears that, as a result of this unusual approach, the authors were able to achieve satisfactory and persistent analgesia with only a minute dose of IT opioid, both during the trials and one year afterwards, without needing dose escalation in the permanent pumps.

The timing of this article is also of significance because the utility of intrathecal opioid trials was seriously questioned. The recently published "Consensus guidelines for the selection and implantation of patients with noncancer pain" recommended reconsideration of the mandatory IT trial, based on the impression that the predictive value of trials was unsubstantiated, the absence of long-term efficacy, and the lack of demonstrated safety sufficient to outweigh trial risks, etc (3). Thus the panel recommended the decision, whether to conduct the trial or not, be left to the treating physician. Additionally, the panel recommended the development of a less expensive pump for IT trial, with a life span of 6-12 months, so that various agents could be tried, to better simulate IT therapy (3).

Although the trialing method introduced by Grider et al (1) represents a revolutionary approach that seems to provide adequate analgesia with much lower opioid dosages, we wonder if it would be a pragmatic approach in our practice. Our concern is how feasible it is to wean patients off any opioid and keep them opioid free for 6 weeks, which was the prerequisite prior to the initiation of the low dose IT trial based on their protocol.

At our tertiary interventional pain clinic, we conduct outpatient continuous epidural opioid infusion trials on a weekly basis (referred to us for IDD therapy from neighboring states). Our patients considered for IT therapies are mostly on a very high dose of systemic opioids (over 500 mg morphine equivalent). We could not conceivably be successful in weaning them off their opioids and keep them opioid free for another 6 weeks as stated in the protocol by Grider et al (1). We commonly utilize "weaning off systemic opioids" as one of the outcome measures during the outpatient continuous epidural infusion trial (10-14 days). With our approach, the success rate of weaning patients off systemic opioids is about 100%. Our question to the authors is: what dose range do their patients fall in prior to their opioid tapering?

Regarding the trial duration, there was no mentioning in the article of the actual duration of the low dose IT trials by Grider et al (1). If our estimation in reading their protocol is correct, their trial duration is roughly 3-5 days. The authors described the termination of the trial about 24-36 hours after obtaining trial efficacy to make sure evaluation of side effects and functional improvement was evident. However, in our own experience, a rather troublesome side effect, i.e., peripheral edema, frequently encountered during trials, may develop a few days later (4,5). Therefore, we believe extending the trial for a few more days (10-14 days), to make sure analgesia remains satisfactory and edema does not occur, is beneficial.

Lastly, we are intrigued by the authors' speculation that the hyperalgesic state associated with low doses of systemic opioids (6) could be avoided with low-dose IT opioid administration, based on their observation of profound analgesia during low-dose infusion. This is an observation worth further investigation. We wonder if "opioid naïve" status rendered at initiation of a low dose IT trial was actually the reason for the profound analgesia. We wonder if re-try of oral opioids was done in some patients by the authors. It would be of both academic and pragmatic value if such studies

were conducted in parallel to the low dose IT infusion trial group.

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References

1. Grider JS, Harned ME, Etscheidt MA. Patient selection and outcomes using a low-dose intrathecal opioid trialing method for chronic nonmalignant pain. *Pain Physician* 2011; 14:343-351.
2. Deer T, Chapple I, Classan A, Javery K, Stoker, V, Tonder, L, Burchiel K. Intrathecal drug delivery for treatment of chronic low back pain: Report from the national outcomes registry for low back pain. *Pain Medicine* 2004; 5:6-13.
3. Deer T, Smith H, Cousins, M, Doleys D, Levey R, Rathmel J, Staats P, Wallace M, Webster, L. Consensus guidelines for the selection and implantation of patients with noncancer pain for intrathecal drug delivery. *Pain Physician* 2010; 13:E175-E213
4. Ruan X, Tadia R, Liu H, Couch, JP, Lee JK. Edema caused by continuous epidural hydromorphone infusion: a case report and review of the literature. *J Opioid Manag* 2008; 4:255-259.
5. Ruan X, Tardia R, Couch JP, Ruan J, Chiravuri S. Severe peripheral edema during an outpatient continuous epidural morphine infusion trial in a patient with failed back surgery syndrome. P*ain Physician* 2008; 11:363-367.
6. Chu LF, Angst MS, Clark D. Opioid-induced hyperalgesia in humans: Molecular mechanisms and clinical considerations. *Clin J Pain* 2008; 24:479-496.