

EDITORIAL

Intrathecal Opioids for Chronic Pain: A Call for Evidence

The first implanted fixed rate pumps were used in humans in the mid 1980s [1]. In 1991 Medtronic® released the first programmable pump for human use [2]. The majority of the research and reports concern programmable pumps, and the best and most current systematic review of the literature only identified manuscripts on these devices, and only considered chronic non-malignant pain (AKA chronic non cancer pain- CNCP) [1]. Older reviews are available [3–5]. No review, nor our literature search, identified a Randomized Controlled Trial (RCT) of implantable pumps using opioids in CNCP; yet despite such lack of evidence, the devices are commonly used for patients with CNCP. In contrast, there is an FDA drug registry of RCTs available for implantable pumps using ziconotide in CNCP [6]; IntraThecal (IT) baclofen has been assessed for spasticity (but no RCT: see Taricco et al [7].) and in the management of the dystonia of Complex Regional Pain Syndrome [8]. There is a good RCT of implantable pumps using opioids in cancer pain showing modest efficacy but substantial risk [9].

Case reports, open label series and anecdotes abound for opioid pumps in CNCP, but no RCT. The most remarkable feature of this embarrassing situation is that the functionality of the device and the physiological/pharmacological interface actually inherently lend themselves to the randomized controlled trial. Randomization is straightforward. The device can easily be programmed to deliver or not deliver drug, leading to an excellent patient/subject blind. The side effects of delivery could theoretically unblind the subject, but most of these are subtle and cumulative (and that feature can and should be definitively tested, for instance with active controls). Additionally, all operators except the programmer can be blinded, making a “one and a half blind” simple to implement. Why an RCT in a standard chronic pain model with standard methodology has not been performed after 25 years of use is a (partial) mystery. The lack of funding pretext is not rational, as the high profit margin from these devices should be persuasive to industry support for executing definitive efficacy experiments. So what then, is the hold up?

A risk:benefit analysis is difficult to assess in the absence of evidence of efficacy, but reviews of complications raise concerns about the procedure. In the Turner et al. systematic review, the weighted mean suggests that 41% had urinary retention, 37% of who required catheterization “for several days”; nausea/vomiting, 33%; pruritus, 26%; “catheter-related complications” (migration, occlusion, or mechanical failure), 18%; pump “malposition”, 17%;

wound infection, 12%; meningitis 3%; the Perez et al. review of baclofen IT pumps mentions Post Lumbar puncture headache [8], but Turner concludes this is “not . . . common . . .” [1]. 27% of patients required “equipment revisions” (Turner). Many other complications are reported rarely (see Table 5 in Turner et al.) [1]. Serious side effects are reported rarely. There have been 2 overdose deaths reported due to operator error. Other serious documented side effects include intrathecal granulomas with neurologic dysfunction, traumatic syrinx, transverse myelitis, and withdrawal symptoms with pump failure or removal [1]. The cost of IT pumps is very substantial. The original implantation can run \$30,000 to \$40,000, with periodic refills (as often as monthly) running \$500/visit and up. Again, without clear efficacy data it is difficult to assess the cost:benefit ratio.

The rationale for “resorting” to opioid pumps in chronic pain often relies on the argument that pain is “intractable” or “refractory”; however, the available literature indicates that this usually means failure of a modest array of sequential drug trials to provide adequate reported relief, and not optimized efficacious interdisciplinary care [10].

In the spirit of “responsible use and development” we must conclude that there is a critical and immediate need for good science in the use of IT pumps, specifically concerning the common use of opioids in implantable pumps for the management of refractory chronic pain conditions. Until evidence is available, this technology must be considered experimental, and as such the ethics of continuing to use (and bill for) this intervention (after 25 years of empirical use) is highly questionable. The desperation of patients in chronic pain, and the desire for simple, immediate gratification may justify early use of a technology for compassionate reasons, but after a quarter century simple empiricism is no longer tenable.

R. NORMAN HARDEN, MD,^{††§} CHARLES E. ARGOFF, MD,^{¶**}
and DAVID A. WILLIAMS, PhD^{†††}
^{*}Addison Chair in Pain Studies and [†]Director, Center for
Pain Studies, Rehabilitation Institute of Chicago,
Chicago; Associate Professor,
[‡]Departments of Physical Medicine and
Rehabilitation and
[§]Physical Therapy and Movement Sciences,
Northwestern University, Evanston, Illinois;
[¶]Professor of Neurology, Albany Medical College;
^{**}Director, Comprehensive Pain Center, Albany Medical
Center, Albany, New York;

Harden et al.

^{††}*Professor, Anesthesiology, Internal Medicine,
Psychiatry and Psychology;*

^{‡‡}*Associate Director, Chronic Pain and Fatigue Research
Center, University of Michigan, Ann Arbor,
Michigan, USA*

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