Implementing and managing intrathecal pumps

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The use of intrathecal therapy is associated with increase quality of analgesia and a decrease in side effects in patients who have not tolerated oral pharmacological therapy AND have had a successful epidural trial. Steps to achieve a high degree of success are delineated in this article, including ideal catheter tip position, indication and use of medications for the infusion, rate of infusion, etc. Moreover, recommendations to follow before and after a myelogram through the pump are given.

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Polymodal intrathecal analgesia via the administration of an opioid in combination with bupivacaine and/or clonidine has become widespread practice. With the use of neuraxial analgesia, pain relief is obtained in a highly selective fashion with the absence of motor and sympathetic blockade, making these modalities highly adaptable to the home care environment. When first introduced, the philosophy behind neuraxial opioid therapy was that by administering small quantities of opioids in close proximity to their receptors in the substantia gelatinosa of the spinal cord, one could achieve high concentrations at these sites. Thus, analgesia is superior to that achieved when opioids are administered by other routes, and because the total amount of drug administered is reduced, side effects are minimized. Currently, the biggest advantage is the ability to use multiple agents to target multiple receptors, resulting in better neuropathic, somatic, and visceral pain control while minimizing side effects. In general, patients with survival expectancy greater than 3 months will be candidates for intrathecal therapy with a permanent intraspinal catheter and an implanted subcutaneous pump. Conversely, those patients with survival expectancy less than 3 months will require epidural therapy with an implanted system.

If the patient had a successful trial, one may proceed to implant an intrathecal system. We suggest the following protocol to achieve more than 80% success rate:

- Conditions for success
  - Place the tip of the intrathecal catheter in the dermatome corresponding to the area of nociception under fluoroscopy guidance. The epidural trial may be helpful in this regard, as it provides feedback on the success of this approach.
  - For severe somatic pain, combinations of bupivacaine and an opioid will be needed.
  - For neuropathic pain:
    - A. If the tip of the catheter is below L3-4: initial therapy with opioid and clonidine is advisable to avoid motor block associated with doses of bupivacaine greater than 10 mg/d.
    - B. If the tip of the catheter is above L1-2: initial therapy with opioid and bupivacaine.

The doses and drugs that we use in our practice are described in Table 1.

Thus, compounding by a trained pharmacist will be needed. The goal is to concentrate these drugs to twice the daily dose, so that the 20-mL programmable pumps may be programmed to deliver 0.5 mL/h. In this way, patients will need pump refills monthly, and it will not be a burden to their quality of life by having frequent visits to the pain specialist’s office.
Conversion from epidural to intrathecal doses

As noted previously, an epidural trial may be useful in determining not only the medications needed for the successful treatment of the patient’s pain, but also serving as a guide to determine the initial doses for intrathecal therapy. We have used the following approach:

1. If the patient used the 0.12-mg/mL hydromorphone concentration for the epidural trial, at a rate of 2 mL/h, this equals approximately 6 mg/d. Because hydromorphone has an ideal octanol/buffer coefficient for arachnoid penetration, then the same dose is used per day, that is, 6 mg/d as a starting dose. An adjustment in the dose is done based on the bolus dose usage by the patient in the last 48 hours of the epidural trial.

2. If the patients used the 0.06-mg/mL hydromorphone concentration for the epidural trial, at a rate of 2 mL/h, this equals approximately 3 mg/d, and we use the same daily dose intrathecally. Again, an adjustment in the dose is done based on the bolus dose usage by the patient in the last 48 hours of the epidural trial.

3. If the patients used the 0.03-mg/mL hydromorphone concentration for the epidural trial, at a rate of 2 mL/h, this equals approximately 1.5 mg/d, and we use doses between 0.5 and 1 mg/d intrathecally to start therapy. This is particularly true in debilitated elderly patients, and we always consider the possibility that they may need dose adjustments, based on clinical response.

It is noteworthy that all patients will receive bupivacaine, and patients with a strong neuropathic component, or the tip of the catheter in the lower lumbar or sacral area, will always receive clonidine. The dose of bupivacaine above the L2 lumbar area is 15 mg/d to start therapy, and it is titrated to up to 20 mg/d as needed. It is important to guarantee that the intrathecal catheter is located in the posterior intrathecal space to avoid motor deficit. It is also noteworthy that bupivacaine cannot be compounded beyond 40 mg/mL because of the risk of precipitation. The starting dose of clonidine is 250 μg/d, and we titrate daily doses to up to 2 mg/d. It is important to note that clonidine will produce vasoconstriction at doses greater than 750 μg/d, and there are usually no changes in blood pressure at doses between 250 and 600 μg/d.

The starting infusion rate is always 0.5 mL/d, except in situation where the source of nociception exceeds 4 dermatomes. Under these circumstances, we use an infusion rate of 1 mL/d to increase the analgesic area.4

The steps that we use to implement the intrathecal therapy are:

- Step 1:
  - Opioid + bupivacaine:
    - MS 3-25 mg/d or hydromorphone 0.5-15 mg/d,
      - 6 mg of MS per day = 1 mg of hydromorphone per day.
    - Bupivacaine: 6-20 mg/d.
  - Opioid + clonidine:
    - Clonidine: 250-2000 μg/d.

- Step 2: Opioid + bupivacaine + clonidine

- Step 3: Ziconotide:
  - Initiate therapy with ziconotide at a dose of 2.4 μg/d (0.1 μg/h) and titrate to patient response.
  - Rinse the pump with 2 mL of the 25-μg/mL solution 3 times and then fill the pump with the balance (16 mL).
  - Titrations increments should not be more than 2.4 μg/d or more frequent than once per week.
  - Maximum recommended dose: 19.2 μg/d (0.8 μg/h).

- In particular situations, the use of morphine + ziconotide may be an alternative. However, the limitations include the following:
  - There is not the benefit of a trial, as ziconotide may not be administered in the epidural space. Consequently, the patient will need progressive titration once the implanted system is in place.
  - Patients may not allow the practitioner to carry out a titration protocol over 4-6 weeks since:
    - Starting dose for ziconotide is 2.4 μg/d with weekly increases of no more than 2.4 μg/d.
    - Therapeutic effects are not usually seen until a dose of 8-10 μg/d is reached.

Recently, the option to coadminister ziconotide with morphine has emerged. A Phase II, open-label, multicenter study of combined intrathecal morphine and ziconotide as add-on therapy in 26 patients with noncancer pain showed that the mean improvement in pain, as judged by visual analog scale measurements, was 14.5% from baseline to week 5. Moreover, there was a mean decrease in opioid therapy of 14.3% at week 5.7 Treatment-related side effects included mental confusion, dizziness, abnormal gait, hallucinations, and anxiety. Consequently, both the mean pain improvement and the mean opioid-sparing effect produced by the use of this agent were clinically insignificant. However, the maximum dose of ziconotide used in this study was 7.2 μg/d and that may explain the marginal results.

If triple therapy with an opioid, bupivacaine, and clonidine at optimal doses is not working or one considers the need to implement therapy with ziconotine, then evaluation for catheter obstruction, disconnection, catheter migration,
or pump malfunction is a must. In doing so, consider the following possibilities:

- **Pump:** Computer program analysis for volume and the volume present within the pump needs to be within 10% of each other; otherwise, pump failure is suspected because of:
  - Magnetic resonance imaging effects (Medtronic Medical Device Correction, August 2008). There is a potential for a delay in the return of proper drug infusion after an MRI affecting all SynchroMed pumps. Moreover, with SynchroMed II pumps, there is the potential for a delay in the logging of motor stall events after MRI. Although the reported incidence of these phenomena is low (0.014% and 0.11%, respectively), it is important to interrogate all the pumps after the MRI to spare patients from not receiving medication. This is particularly important for SynchroMed pumps, as a “pump memory error” may be generated and the pump will not restart infusing unless it is reprogrammed. In contrast, the SynchroMed II may continue infusing even though the interrogation may show a stall state. In either case, the pump alarm will activate in the face of a stall phenomenon.
  - SynchroMed pump motor stall because of gear shaft wear (Patient Management Information, Medtronic, August 2007).

- **Catheter:** A myelogram performed through the diagnostic port of the pump will be needed to determine whether there is obstruction, disconnection (Medical Device Safety Alert, June 2008: proper connection of sutureless connector intrathecal catheters models affected: 8709SC, 8731SC, 8596SC, 8578), and the position of the tip of the catheter. When performing a myelogram through the diagnostic port of the pump, remember that this only accommodates a 24- or 25-gauge Huber needle. Moreover, consider:
  - **A.** The dead space of the catheter when injecting the contrast medium: 0.196 mL [89 cm total catheter length (81.4 cm for the spinal segment + 7.6 of the catheter interface with the sutureless connector) \( \times \) 0.0022 mL/cm catheter volume for the model 8709 SC].
  - **B.** The need for a bolus dose after the study is completed, as the catheter will be filled with contrast medium. Consequently, at a programmed rate of 0.5 mL/h, it will take 9.4 hours for the pump to clear all this volume, resulting in inadequate pain control and possibly opioid withdrawal symptoms.

When performing pump’s diagnostic port injections, one needs:

- **A.** To withdraw enough amount of therapeutic solution and then cerebrospinal fluid before injection contrast medium to remove all the volume of the drug within the catheter and avoid giving the patient a bolus of the medications in use. If this was not performed, up to 0.196 mL of solution could be pushed alone with the contrast medium. Likewise, we suggest that one should aspirate the fluid with a 3-mL syringe at a very low negative pressure to avoid turbulent flow and the risk of leaving medication within the catheter (cavitations phenomenon). We usually aspirate 3 mL of fluid, as this should contain all the medication left in the catheter’s dead space and some cerebrospinal fluid.

- **B.** A bolus dose should be programmed after the myelogram to clear the catheter’s dead space containing contrast medium at this point. By doing so, one avoids leaving the patient without intrathecal treatment for periods of 16-20 hours, depending on how much catheter was implanted.

### References

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