

# THE INFUSION PUMP: CLINICAL OBSERVATION

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***Abstract.** The use of an implantable infusion pump for the treatment of chronic pain is to provide the patient with approximately 1/10 the dose that the patient is taking at the present time, and this small dose will be given in a steady fashion in the form of drip irrigation. The drip irrigation is through a small plastic catheter and a titanium pump under the skin which drips the pain medication in minute amounts continuously.*

*The infusion pump is usually installed in advanced cancer patients as a palliative treatment. In a small minority of noncancerous patients the use of the infusion pump is indicated for treatment.*

*The use of an infusion pump is the best form of treatment for advanced, severe cases of complex regional pain syndrome (CRPS) as long as the patient and the physician understand that the dosage of Morphine cannot be mixed with other forms of strong pain medications.*

*Descriptors. complex regional pain syndrome (CRPS), infusion pump.*

## INTRODUCTION

The use of the infusion pump was first attempted in the early 1960's for the delivery of insulin(1). In August of 1969 researchers from the University of Minnesota developed the first implantable infusion pump(2). In 1981 the first clinical use of an implantable intrathecal infusion pump for opioid delivery was used for the treatment of chronic pain due to malignancy (3-6).

In chronic pain patients, the infusion pump has been most effective in patients suffering from pain below the shoulder level. The patients who suffer from craniofacial pain usually need a lateral ventricular infusion pump inserted. This is usually given to the patients suffering from crainocervical cancer lesions.

The standard narcotics such as Morphine and Dilaudid have been usually used and in some cases the water soluble Sufentanil has been used.

In our clinic, which consists of a tertiary referral center, we do not get fresh cases of straight forward cervical or lumbar disc herniation, acute, subacute or chronic nerve injuries, or patients with a short history of pain due to different types of injuries.

The patients that we do see are cases that are like a used car, already dumped into the junkyard. These are the patients who, frequently have had multiple operations, have been to multiple pain clinics, have had to be detoxified, and everybody has given up on them.

Even this type of patient is not automatically a candidate for the infusion pump. The patient has to go through the procedures of detoxification, placebo treatment, other types of treatment for chronic pain such as large doses of antidepressants and anticonvulsants, and even then the patient will not be a candidate for an infusion pump.

Just because the patient has subjective complaint of pain, he or she is no candidate for an infusion pump. Just because the patient has been taken off strong medications and still has complaints of pain this does not pass the patient for an infusion pump. Just because the patient has had multiple operations and has a failed back or multiple surgical procedure on damaged nerve areas that does not pass the patient as a candidate for an infusion pump.

If the patient is using their pain as a handle to have a primary or secondary gain, or if the patient has a constant complaint of pain without any objective findings, the patient cannot be considered an infusion pump candidate.

The key to the patient becoming a candidate for an infusion pump is the word “objective.” This usually does not mean a positive MRI or CAT scan or x-ray finding. Already these patients have had multiple operations and any kind of positive abnormality on MRI such as disc herniation has already been repeatedly operated on. So anatomically these patients look very good. In our study of the chronic pain patients, disc herniation is the source of the pain in less than one third of such patients. Our group showed that 26% of the patients had severe intractable pain which was due to disc herniation. Doctor Rosomoff's study showed that 28% of their patients also had severe pain which was due to disc herniation (7).

By objective findings we mean in different forms. The nerve injuries are usually not in the form of impingement or compression by a bone or disc. These usually consist of the following injuries (Table I).

**Table I. Objective findings.**

1. Nerve roots contusions.
2. Spinal canal arachnoiditis.
3. Crush injuries.
4. Ephaptic electric short between the sympathetic and somatic nerves (8).
5. Advanced cases of complex regional pain syndrome (CRPS).
6. Electrical injuries, chemical injuries, or sharp object injuries in the "watershed zones" over the dorsum of the foot or hand or over the ankle, elbow, or knee(8).

The type of patient mentioned above usually has gone through years of treatment for chronic pain. They have had multiple unnecessary operations, and have been tried on every kind of treatment such as spinal cord stimulator (SCS). Unfortunately, the SCS is the stylish form of treatment now a day for such intractable chronic pain patients.

It is going to take a few years before physicians realize that they are adding more sources of pain to the patient's complex chronic pain, and they are wasting everybody's time and money with this SCS.

Many other such patients have undergone procedures such as, rhizotomy, tractotomy, and neurectomy. Such operations may be helpful in advanced fatal cases of cancer just to provide a few months of relief, but they invariably practically always aggravate the chronic pain by becoming a new source of pain in the area of the surgical scar. In such patients the objective signs are not hard to find. The key is the clinical correlation. The patient may have a small electric short between the somatic and sympathetic nerve causing severe pain and yet at the same time, the patient may have an already healed disc herniation that is objectively quite impressive, but is not related to the patient's pain. The conventional wisdom of common practice goes after the disc herniation and removal of an asymptomatic disc in such a patient will only create a new iatrogenic source of pain without fixing the original source of pain.

The key is that the objective findings should generate and reproduce the same pain that the patient is being treated for (Table II).

**Table II. Useful objective tests.**

1. A careful neurologic examination with judicious clinical correlation.
2. Neurophysiologic tests such as EMG, evoked potential, bone scans, infrared thermal imaging (ITI), etc.
3. Proper nerve blocks and test treatments to objectively and physiologically prove or disprove that the patient's pain is related to the abnormalities found on para-clinical tests.

Finally, such patients have to undergo extensive proper treatment for chronic pain which consists of but is not limited to the following forms of treatment (Table III).

**Table III. Proper treatment for patients who suffer from chronic pain.**

1. Discontinuation of narcotics.
2. Discontinuation of Benzodiazepines.
3. Proper use of antidepressants which are the treatment of choice for management of chronic pain.
4. Extensive physical therapy.
5. Treatment with ACTH to stimulate the patient's own endorphins and corticosteroids to counteract the pain.
6. Correction of any other hormonal disturbance such as the use of Estrogen for menopause, the use of Calcitonin for osteoporosis.
7. A proper diet.

In our experience, the use of Stadol or Buprenorphine (Buprenex), both are Morphine agonist-antagonist analgesics, and are not even controlled drugs. Both medications are quite helpful in facilitating the discontinuation of addictive narcotics (9).

Of more than 500 severe intractable noncancerous chronic pain patients that we have reviewed, only 38 so far have passed the above criteria and have become the candidates for infusion pump treatment.

Even then, the infusion pump is tried for 1-5 days on a trial basis with a placebo versus narcotic medications and then if it works the patient undergoes the permanent implant of the infusion pump.

### **WHY INFUSION PUMP**

Why should we use infusion pumps for the treatment of chronic pain? There are two parts to this question that are addressed to us regarding the use of infusion pumps is the fact that we have gone through such a tedious trouble to detoxify the patient and then we recommend a form of narcotic treatment on a permanent basis (infusion pump).

The infusion pump is different from other forms of narcotic treatment due to the fact that:

(i). The use of the infusion pump provides a slow drip continuous small amount analgesic. This form of drip irrigation emulates the way that the endorphins work. On the other hand, other forms of long term narcotic administration such as patient controlled anesthesia (PCA), Duragesic skin patch, IM subcutaneous IV, or oral narcotic administration exposes the patient to a flood irrigation of large doses of narcotic followed by a significant withdrawal after a few hours.

During such withdrawal, the central nervous system is devoid of both exorphins and endorphines with the resultant alarm panic agitation and the sensation of pain even in the absence of any lesion originating the pain.

(ii). Most importantly the patient is being given the equivalent of one and a half to two days of standard narcotic dose in the pump to be dripped in 30 days. As a result, the patient is given 1/15 to 1/20 of the standard dose of narcotic.

This sharp reduction of the intake of narcotics will prevent the inhibitory and suppressive effect that large doses of narcotics have on other CNS hormones such as Estrogen, antidepressants, and hypothalamic hormonal secretions. As a result, the patient does not end up having the side effects of insomnia, depression, suicidal tendencies, a lack of desire for sex, and poor appetite.

Researchers from the Cleveland Clinic have reported that the use of intraspinal narcotic (usually intrathecal morphine) infusions with implanted pumps are increasingly used in patients with intractable chronic pain not caused by cancer. In some patients, pain control is difficult with an infusion pump. Seven patients with diagnoses of arachnoiditis, epidural scarring, and/or vertebral body compression fracture were treated with alternative solutions in an epidural route.

For maximum flexibility, Medtronic implanted programmable infusion pumps with catheters to T6-T10 were used, and pain was monitored by verbal pain scales. In three patients epidural infusions of Morphine in 0.5% Bupivacaine resulted in little or no pain relief without significant side effects (e.g., headache, nausea, or vomiting) (10).

In these same patients epidural infusions of Sufentanil Citrate resulted in pain scale reduction of 92%, 82%, and 40% respectively, with no side effects. Four other patients found more effective pain relief when switched from initial Sufentanil Citrate infusion to Morphine Sulfate- Marcaine. Pain scale reductions (with no side effects) were 92%, 76%, 59%, and 47% in these patients. Pain relief and minimal side effects with Sufentanil Citrate is theorized to result from its higher lipophilicity promoting local transdural diffusion to spinal cord and limiting upward diffusion to the brain stem. Sufentanil Citrate is also advantageous for programmable pumps because it is a hundred times more potent than Morphine and therefore allows long pump refill times and higher infusion doses. Although this study was done on a limited number of patients, Sufentanil Citrate and Morphine Sulfate-Marcaine in epidural infusions used in programmable infusion pumps for noncancer patients provide significant alternative drug combination and routes (10).

### **THERAPEUTIC DOSAGE**

The therapeutic dosage of Morphine in the spinal fluid is anywhere from 3.5mg up to 15.5mg. The therapeutic dosage of Dilaudid is anywhere from 2.6mg up to 8.5mg. If either of these medications is even in a very small amount below the lower limit of therapeutic dosage or above the highest limits of a therapeutic dosage, then the patient will have severe pain. The reason the higher dosage of narcotics causes such severe pain is because of the fact that Morphine or Dilaudid has the tendency to saturate the three endorphin opioid receptors. These are as followed: mu, kappa, and theta receptors. The kappa receptor is the largest of the three. If these medications mentioned above are given in the therapeutic dose, then there is still room for the kappa receptor to receive endorphin secreted in the central nervous system. On the other hand, if the above therapeutic dosages of narcotics are applied, then all the three receptors will be flooded with narcotic and the patient will have severe tolerance and withdrawal pain because of the lack of secretion of the endorphin. The central nervous system is not going to produce and secrete endorphin if the patient is already on large and supratherapeutic doses of such medications. This is a frequent cause of failure of infusion pumps.

The rate of success of the insertion of the infusion pump at the beginning is no more than 80%. With the passage of time, because the patient and doctor become impatient, other narcotics are applied through other routes, then the rate of success drops to less than 40%.

Because the doctors have a tendency to be extremely generous and treat the patient with multiple narcotics such as Duragesic, applied simultaneously with MS Contin, Oxycontin, Methadone, Morphine, etc., the patient is not only in danger of overdose and respiratory arrest, but also the patient will have more severe pain than if they were not on the infusion pump. This is the main reason we see more and more of the infusion pumps being turned off because of the problems mentioned above. It takes at least four to six months to get the pump installed and going.

Even after making sure that the dosage of medication is not sub -or supratherapeutic, still it is important to watch out for other side effects of the narcotics in the spinal fluid. The commonest side effect is a marked edema in the extremities, especially in the lower extremities. This edema is due to suppression of endogenous estrogen in women and endogenous testosterone in men. So, the treatment should be supplemented by providing enough estrogen or enough testosterone to prevent the edema.

### **COMPLICATIONS AND ADVERSE EFFECTS**

In our clinic five of the thirty-eight patients, had superimposed infection in the area of the foreign body insertion. This complicated the use of the infusion pump.

Of the five patients, only three had reinsertion of the pump without any further complication. This was done after several weeks to a few months' interval between the first and second surgery.

Of the other two patients from this group, one patient was not a candidate for reinsertion of the infusion pump due to extensive scar formation that developed forcing the withdrawal of the first infusion pump and the other patient did not want to have the infusion pump reinserted due to the fact that they could not tolerate the medication in the infusion pump.

In three patients, there was a significant degree of intolerance to the medication administered in the infusion pump. In two out of these three patient, other medications such as Dilaudid and Fentanyl were tried and two were successful.

With this, approximately 10% complication adverse reaction and failure of the infusion pump are compared to all the other treatments that the patient has already been exposed to which has been 100% failure.

In thirty-eight infusion pumps that have been inserted in the past nine years and practically half of them have been inserted in the past two years, so the long term effects of the infusion pump have not been completely finalized.

Some other complications have been outlined as headache as a rare complication, meningitis, and in one case the patient had a granuloma formation at the tip of the catheter which was pressing on the spinal cord. This is a rare complication. In this case the removal of the granuloma and replacement of the catheter solved the problem.

Others have reported such complications as infections, catheter complications(e.g., breakage of the catheter), cerebral spinal leaks, bleeding, neurological complications (e.g., damage to the spinal cord or nerve roots), medication errors, and paraplegia(6, 11-14)

Another rare complication that has been associated with the use of infusion pumps has been mortality. In a recent study by Coffey et al, reported nine cases of mortality due to over infusion. Eight of the nine cases had noncancer pain and one patient had cancer pain. Eight of the nine patients died 24 hours after implantation of the infusion pump. One patient died 48 hours after being discharged from the hospital. Seven of the nine patients had a new infusion pump implanted, one patient had an infusion pump replacement and one patient had a catheter replacement(15).

## **BENEFITS OF THE INFUSION PUMP**

The benefit of the infusion pump is not to provide the patient with narcotics but to make sure that the patient does not need narcotics in the future. When the patient gets to the stage that they are not responding to standard treatments for chronic pain and when their CRPS becomes so advanced that neither nerve blocks nor other forms of treatment can control the patient's pain, and when the condition is so advanced that it goes beyond one to two years after the onset of the disease, the only thing that can be offered to relieve the patient from severe pain is the infusion pump. This form of treatment provides a minimal amount of pain medication through a catheter to the spinal fluid. It is in the form of drip irrigation rather than flood irrigation. The flood irrigation would be when the patient takes narcotics by mouth or injection or by the use of a skin patch. On the other hand, the drip irrigation is in the form of infusion pump providing a slow drip of minimal amounts of pain medication.

As a result, the patient will be taking far less pain medication but will have more effective results from it because the analgesic will go directly into the spinal fluid as well as access to the brain. The end result is that the patient will not have withdrawal effect from oral or an intramuscular intake of pain medications. Each time the patient is given strong narcotics by mouth, or intramuscular or with the help of a skin patch, the patient gets a flood irrigation of the medication in the body and as a result after four hours of total relief of pain with strong narcotics the patient has a few hours of severe pain until the next narcotic dose is supplied. This problem gradually accelerates and picks up momentum until the patient has to take the narcotic every two to three hours, and becomes totally addicted to the larger and larger doses of medication. Then the patient will be sleeping all the time or screaming with pain.

The patient does not go through withdrawal every four hours from the pain medication and does not develop the severe withdrawal pain.

The infusion pump stimulates the function of endorphins. The endorphins work in very small amounts but continuously. The infusion pump works the same way by giving proper analgesic coverage of continuous nature without withdrawal and without addiction.

It also guarantees that the patient would not take another strong medication because if the patient gets a hold of any strong pain medication it will cause such an extensive sleep and drowsiness that the patient will end up in the emergency room.

This is the best safeguard in regard to the way the infusion pump works. It is true that the infusion pump has a 5% to 10% chance of complications but it is much safer than any operation that has a much higher chance of complications and a much higher rate of failure.

## **INFUSION PUMP FAILURE**

One of the main reasons for failure of the infusion pump is the fact that the patient does not understand the importance of being very selective and conservative in regards to the pain medications, and as a result while the infusion pump is being tested, installed, and the medication is being gradually increased in dosages, the patient sneaks another narcotic from their relatives, friends, etc. Once the patient starts taking the new narcotic medication, then the infusion pump completely fails.

The following are other causes of failure of the infusion pump. Lack of proper plasticity, meaning that unfortunately the treatment with the infusion pump is done in patients who have had CRPS for more than five years. After five years, the body does not have the power of healing to adjust to the foreign body of the infusion pump so the patient's body rejects the infusion pump. The other causes of failure are infection or excessive scar formation (in less than 2% of such patients) or total intolerance of any dosage of Morphine in the spinal fluid.

Finally, there is another serious problem with the infusion pump in that there have been more tendencies for under supplying the infusion pump with pain medication rather than oversupplying it. We have seen patients who have been tried on 1mg or 2mg Morphine or Dilaudid for several months, sometimes more than a year, with no relief of pain only because the medication has not been raised up to the therapeutic range.

If the physician in charge of the infusion pump is meticulous, careful, selective, and if the physician does not add other types of narcotics, then the results for pain relief in the lumbosacral regions and lower extremities are excellent.

If the pain is originating from the central nervous system, or from the cervico-thoracic regions, not much can be expected in regard to benefit of the infusion pump for pain relief.

## **CONCLUSION**

The use of the infusion pump has been helpful in treating patients who suffer from cancer pain and noncancerous intractable pain for many decades(16,17).

In thirty-eight advanced CRPS patients that we have given this form of treatment to, only five patients had complications and the rest of the patients have been totally pain free. The patients that were helped have become useful to themselves and to their families. They have also been able to return to work with the help of the infusion pump.

The use of an infusion pump should not be tried unless the patient is already detoxified for at least one week from other forms of narcotics.

Most importantly the infusion pump prevents the expensive repeated visit to the neurologist and psychiatrist, and the necessity for expensive and seriously dangerous medications given by mouth or IM.

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