REVIEW

IMPLANTABLE SYSTEMS FOR CHRONIC PAIN

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INTRODUCTION

Pain control is a very important issue both for the person suffering and for the socio-economic environment. Physiotherapists and doctors, in general, define pain as an unplesant condition, which causes a lot of suffering, does not allow the affected individual to perform normal activities.

In the case of chronic non-malignant pain, the systematic approach involves a comprehensive evaluation: based on the diagnosis and the mechanisms underlying the pain, the treatment plan is drawn up; the patient is trained; realistic goals are set. The treatment aims to reduce the intensity of pain and thus improve the quality of life.

Pain is associated with lesions in the tissues, it can be a pathological process, it is an unpleasant experience, it persists beyond the evolution of the lesion, the disease. It has nothing to do with cancer. (Argoff C. 2007; Argoff C, 2008; http://www.fsmb.org/pdf/2004_grpol_Controlled_Substances.pdf. Accessed May 22, 2008).

Patient Controlled Anesthesia: PCA (mid-1979s has been shown to be very effective in combating pain. (Evans et al, 1976). Towards the end of the 1970s, the first attempts to control intractable pain are mentioned, when morphine was applied centroaxially using an external infusion system (Onofrio et al, 1981) and then, such a device was implanted (Harbaugh et al, 1982).

The first pump approved for the implant was the Infusaid Model 400; Norwood, MA, SUA. The pump ensures a constant flow of analgesics.

It was then found that patients are affected and the intensity of pain is perceived differently, additional systemic medications are needed in addition to those constantly provided for pain. The goal was to control the ourbursts of pain. One such pump is the one provided by Medtronic, AlgoMed (Medtronic Inc. Minneapolis, MN, USA). The has a deformable tank wich by compression releases a constant bolus through the attached capillary tube. (McMullen et al, 1997). Newer systems have a programmable pump, are used in diabetics to control insulin release. (Erdine et al, 2007). Other pump systems are driven by piezoelectric devices. (Kan et al, 2004).

There are many studies on epidemiology and socio-economic consequences. (Elliott et al, 1999). Based on thes studies, departments were set up with adequate equipment and staff specialized in pain therapy. The benefits of intrathecal therapy (low doses for pain relief, reduced side effects) were also considered.

Implantable systems. Practical considerations

Spinal, epidural infusions are used as an intermediate therapy to relieve pain, to determine the effectiveness of the treatment of chronic pain by neural axial infusions. The systems are needed in prolonged infusions for the treatment of malignant pain and other intractable pain syndromes. (Steven D. Waldman, 2007).

The fully implantable infusion system is also used to relieve pain after doses of intrathecally administered drugs have been tested in patients with a life expectancy of more than 6 months. Patients benefit from pain relief with fewer side effects from continuous infusion of low doses of spinal opioids. (Edgar L. Ross, Edward Michna, 2003).

Procedure

The procedure begins with the placement of the epidural or intrathecal catheter. Implantation and anchoring techniques are different and adapted to the patient's specifics and catheters are of two types. Some epidural catheters are fitted with Dacron sleeves to reduce the risk of infection, but implantable systems (Port-a-Caths epidurals) can

reduce the risk of infection for long-term infusions. (Bennett G, Burchiel K, et al. 2000;Blackshear PJ et al. 1979). Great attention must be paid to the placement of the catheter. Accidental catheterization of the epidural veins can lead to intravascular injection of morphine and its accumulation in the cerebrospinal fluid leads to respiratory depression many hous after the injection. (Edgar L et al. 2003). In the case of an external catheter, infection is a constant risk and proper care is required. (Coffey RJ, Burchiel K. 2002; David E. et al. 2018).

Intrathecal systems provide low doses of drugs directly into the spinal fluid. The systems are represented by a small programmable pump, powered by batteries and a catheter placed at the intrathecal entry site. The pump is placed in the abdomen in the subcutaneous tissue and connected to the catheter. The pump must be refilled at regular intervals.

Exceeding the filling time can compromise the function of the pump and the patient may go into withdrawal. The use of bolus or continuous doses did not provide evidence of clinical efficacy. (Gradet TL et al. 2003).

Patient selection

Patients who need intrathecal medication can be divided into two categories: patients with terminal illnesses such as cancer, and patients with chronic non-malignant pain. Patients with malignant pain generally respond well to intrathecal opioids. Chronic pain that is not related to cancer, can occur without an obvious cause, has a functional character, persists after the usual evolution of the disease or lesions, may or may not be associated with a pathological process. (Argoff C. 2007).

In patients with psychiatric comorbidities, specialized treatment is required because the risk of substance abuse is high. (Carter C et al. 2003). The treatment plan is made according to the diagnosis and the mechanisms underlying the pain and the realistic setting of goals.

METHOD

The implantable systems used to control pain aim to improve the quality of life. An impediment to achieving this goal is given by side effects of drugs. These effects are identified by testing before implantation. (Argoff C. 2007; Pomm HA, Tenzer P. 2005; Butler SF et al. 2008). Invasive therapy is used if patients react well to opioids, but have developed increasing pain and unwanted side effects, despite oral opioids. For terminal patients with should be considered if patients have responded well to opioids, but have developed increasing pain and unwanted side effects, despite oral opioids. For terminal patients with a life expectancy of less than six months, the benefits of this procedure over the risks must be considered. (Sebastiano Mercadante, 2007). A metastasis in the spinal canal could block the inseration of the catheter, the diffusion of the analgesic into the liquid space. (Butler SF et al. 2008).

In chronic non-malignant pain , behavioral, physical and physiological factors have led to controversy regarding the use of implantable systems. In order to be successful in therapy a multidimensional approach is required (cognitive and self-relaxation therapies, psychological and behavioral counseling, pharmacotherapy, acupuncture, minimally invasive interventions: epidural and transforminal injections). (Deer T et al. 2007).

When conservative therapies have failed, surgery is excluded, medical contraindications are eliminated (coagulopathies, infections), there is no active or untreated addiction, after psychological counseling, implantable therapy is indicated. (Antonio Aldrete, 2007).

Complications and management

As a result of the implantation of an intrathecal system a series of complications may occur. The most serious are surgical complications: bleeding, fluid leakage, neurological damage, infections. Bleeding may occur when local hemostasis is ineffective (patients treated with anticoagulants are excluded from this procedure). Bleeding in the epidural or intrathecal space (it is very severe and extremely rare) is associated with increased neurological morbidity (paraplegia). (Edgar L. Ross, Edward Michna, 2003). Spinal tumors can be sources of bleeding during surgery. Postoperatively, patients may experience increasing back pain that progresses to neurological deficits, motor weakness and sphincter dysfunction. The use of fluoroscopy is essential. In this situation, the emergency neurosurgical evacuation of the epidural hematoma formed and confirmed by CT is required. (Gradert TL et al. 2003).

The neurological lesion may also occur due to an inflammatory reaction at the catheter tip and may be associated with the administration of the drug. Lesions of the spinal cord or nerve roots may occur (Harney et Victor, 2004; Huntoon et al, 2004) or skin

lesions. (Levin et Tabor, 2005). Moreover, failure to diagnose this condition could lead to permanent neurological damage. (Coffey et Burchiel, 2002; Langsam, 1999).

To these are added mechanical complications (fractured or cut catheters, subcutaneous placement that may interfere with or prevent certain movements. These are a common cause of failure in drug delivery. (Dickerman et al. 2003).

Less serious complications are given by catheter leakage and side effects of medications (vomiting, nausea, itching, urinary retention, sedation, respiratory depression). These effects are transient and can be treated symptomatically. (Edgar L et al. 2003).

To prevent granuloma from forming at the tip of the catheter (usually a few months after intrathecal administration of the opioid), patients are given non-opioid intrathecal infusions such as baclofen. (Yaksh et Coffey, 2004; Miele et al, 2006). Also, clonidine associated with opioids and maintaining a low concentration of drugs could reduce the incidence of this complication. (Coffey et Burchiel, 2002). It was noted that there is a casual relationship between intrathecal infusion of morphine sulfate and the formation of inflammatory masses at the tip of the catheter. (Gradert et al, 2003; Yaksh et al, 2003; Yaksh et al, 2002).

Infections are prevented by keeping sterile techniques, using antibiotics, monitoring patients. Antibiotics are used preoperatively and intraoperatively (antibiotic irrigation is practiced intraoperatively). (Paice et al, 1996). Most surgeons recommend the use of vancomycin or cephalosporin (staphylococcal infections predominate). (Gyssens 1999).

Surgical implantation of the synchromed ii infusion system

After selecting patiens for the implant, the implantation system is checked carefully following the manufacturer's recommendations. for pump preparation is essential. The patient is taken to the operating room, placed in a supine position and covered with sterile fields. Half an hour before the incision, the antibiotic is sadministered and it is continued with three doses postoperatively. Fluoroscopically check the position of the catheter that anchors to the lumbar fascia and check also the CSF flow. Place the pump, not too deep to allow refilling. Particular attention is paid to hemostasis to prevent bleeding and the risk of postoperative infection.

After the procedure, the patient is brought from the operating room and kept in the postoperative surveillance area by staff trained for this type of intervention. The pump is scheduled to release the prescribed amount of the drug (morphine hydrochloride 20 mg/cc, adminstered at a continuous rate of 1 mg/day).

Patient monitoring

Patient monitoring consists of monitoring vital sings, internal functions, pain intensity, side effects, opioid dose and additional systemic opioid use. Follow respiratory status (apnea and oximetry). Side effects vary in type and magnitude, depending on the patient's specifics (nausea, vomiting, pruritus, urinary retention, respiratory depression). In such situations, the medical staff intervenes promptly.

Regarding complications, no surgical infection, cerebrospinal fluid (CSF) leakage, or spinal serum was observed, without headache, hematoma or skin erosions.

Hair and postoperative antibiotics were used at the implantation of the pump for any subsequent surgical procedure.

No mechanical complications related to the procedure or to the catheter (tilt, leakage, rupture, partial or complete occlusion, catheter displacement or migration), adverse effects related to morphine (clinically significant or fatal overdose) or system rejection were found..

RESULTS AND DISCUSSIONS

Patients had a reduced score from severe to mild pain (mean VAS < 2.8) compared to preoperatively. The benefit of therapy with implantable systems was important and clinically significant (reduction of fatigue and depression), and this was supported by regular examination.

Increased analgesic efficacy of low doses of intrathecally administered opioids, accompanied by reduced systemic exposure, has decreased the frequency and severity of opioid side effects.

Patients initially rated their pain at an average VAS of 4.5/10 and required periodic dose adjustments. The dose administered increased steadily until two months when it reached an average of 1.8 mg morphine hydrochloride/day. At that time, it was decided to combine anticonvulsant drugs such as pregabalin (Lyrica) 300mg/day, oral medication, and the pain level decreased to an average VAS of 2.7. This average dose remained at this level for two years of clinical follow-up.

Patients did not experience side effects from therapy (drowsiness, constipation, nausea, vomiting). After intrathecal medication, most patients (92%) no longer needed any oral medication for pain and were satisfied that they had regained their cognitive abilities. They are seen in the clinic periodically, either when they show up to refill the pump or as needed and evaluated according to the protocol.

After selecting the patients for implantation, special attention is paid to the complications of catheter and pump implantation, of the prevention measures. Leakage of cerebrospinal fluid (careful checking of the catheter, location, anchoring, record), infection (maintenance of sterile conditions), bleeding or hematoma (effective hemostasis, fluoroscopic guidance, rapid evacuation of the hematoma), mechanical dysfunctions (bending of the catheter, disconnection, rupture or failure of the pump), or complications related to opiate overdose.

The depth of the implant should be no more than 2.5 cm from the surface of the skin (to allow access to the reservoir or catheter).

The mechanical complications, described above, would require surgical overhaul and/or pump replacement.

The position of the catheter tip was confirmed in all cases by intraoperative fluoroscopy.

Following the evaluation of patients with cronic pain, the recommendation for the implant is made if, following the intervention, the pain is reduced by least 20%, optimally by 50%. The doctor and the patient agree on the expected results and the evaluation method.

The clinician, patient, family or caregiver must define what constitutes success. Pain relief is essential, it is the major goal of this procedure. Assessing pain relief (VAS, numerical pain assessement, percentage pain improvement) becomes a key element of the process.

In patients with malignant pain, the medical efficacy of the implantable pain delivery system is well known, has great potential, fewer side effects have been observed compared to systemic opioids.

Stabilized locoregional cancer has a dominant nociceptive character through its necrotic and inflammatory invasive phenomena. The location of the cancer, the mode of evolution, the oncological treatment (predominantly by irradiation), the postoperative locoregional evolution, greatly increase the pain through the neuropathic components, increase the level of the nociceptive paintful background.

By combining intrathecal morphine with pregabalin, a dose reduction and a mixed control (neurophatic-nociceptive) for chronic malignant pain are obtined. Neurophatic pain is known to be resistant to opioid therapy, but can be relieved by intrathecal administration of opioids or combination therapy.

In chronic non-malignant pain, intrathecal administration of opioids is controversial in neuropathic pain.

CONCLUSIONS

Implantable systems ensure the supply of low doses of morphine directly into the cerebrospinal fluid both in patients with nociceptive refractory oncological pain from locoregional stabilized cancer, but also in patients with chronic non-malignant pain.

Opioid drugs for intrathecal therapy may be combined with low dosesof non-opioids to be effective against malignant pain, including neuropathic components

Patient selection for intrathecal medication to treat chronic pain, goal setting and management are key to a successful outcome.

ABSTRACT

Chronic malignant and non-malignant pain requires an effective and well established treatment that is performed with implantable systems for intrathecal therapy.

The devices used can be: mechanical pumps (ensures a constant flow) or electronic pumps with variable flow, the release of the bolus being controlled by the patient. Electronic pumps are preferred because they allow rapid dose determination and individual pain control. They are well tolerated and accepted by patients.

The drugs available for intrathecal therapy are in line with the polyanalgesic effect and implantable electronic devices (containing the analgesic) have been significantly improved. New technologies are being developed focused on rechargeable devices and diaphragm pumps.

Complications are various. The most serious are surgical, mechanical. Less severe are catheter leakage and drug side effects. These are transient effects and can be treated symptomatically.

Intrathecal therapy is focused on the use of new drugs with minimal side effects, catheters, pumping technologies and improved surgical techniques.

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