MEDICAL PRACTICE

Contemporary Themes

Syringe driver in terminal care

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Abstract

Continuous subcutaneous infusions of drugs by syringe driver are used often and successfully in the terminal care of patients when drugs cannot be given orally. Diamorphine is the opioid of choice because of its high solubility. If other drugs such as antiemetics, anticholinergics, sedatives, or steroids are required they may also be given by syringe driver. This method is particularly useful for domiciliary care, where the practical difficulties of providing regular parenteral analgesia are otherwise formidable.

Introduction

The syringe driver is used to give continuous subcutaneous opioid infusions to patients who are terminally ill, particularly at home. This method is widely used and general practitioners and hospital doctors now find it recommended for their dying patients.

Syringe pumps used to be cumbersome, mains powered, expensive, and suitable for bedridden hospital patients only.[1] The volume of fluid that was required to operate these devices precluded subcutaneous administration. Syringe drivers for continuous subcutaneous infusions are small and battery operated. They were developed initially for subcutaneous desferrioxamine treatment of patients with thalassaemia,[2] and their use with opioids was first described in 1979.[3] They have since gained wide acceptance for use with both adults and children.[4] Almost all hospice services, many district nursing services and general hospital wards, and some general practices have bought syringe drivers. Other uses include postoperative analgesia, insulin for diabetic patients, cancer chemotherapy, heparin, neostigmine for myasthenia gravis, and hormone treatment of infertility.[5]

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Indications for use

The inability of the patient to swallow or absorb drugs is the major indication—for example, during intestinal obstruction; persistent vomiting; dysphagia; mouth, throat, and oesophageal lesions; unconsciousness; and malabsorption.[6-10] Other less widely accepted indications include an unsatisfactory response to oral drugs, administration of high dose oral morphine (>150 mg/4 h), and use during the last 24 to 48 hours of life.

The syringe driver is thus a valuable alternative to the less pleasant methods of drug administration, such as suppositories and intramuscular injections, when oral drugs are contraindicated or unsatisfactory. In the chronic pain of cancer analgesics need to be given regularly and prophylactically. Regular injections, which are an ordeal for the cachectic, dehydrated patient with bed sores, are difficult to organise satisfactorily at home, and it is inconvenient and time consuming for nurses to give them.

Machines and syringe

Though a variety of machines are available that offer different features, in Britain the Graseby Medical MS series is most widely used. These are usually refilled daily, but some models run for up to 37 days without repriming.[11] The whole apparatus, including the battery, weighs less than 200 g and is about the size of a cigar packet. It may be placed in a shirt or pyjama pocket, under a pillow, or in a pouch slung around the neck.

An electronic timer intermittently advances a bracket, which drives the syringe plunger. The machines are calibrated in mm/h not in ml/h because they take many types of syringe. Thus when making up the syringe it is the length of the contents, not the volume, that is critical. For example, if a speed of 2 mm/h is selected a typical 10 ml syringe with a loaded barrel length of 50 mm will deliver its load in 25 hours.

The speed cannot be altered accidentally. The rate adjusters are flush with the surface of the machine, and are altered with a small screw driver. There is a soft whirring sound with each emission, and some models also have a flashing light. Patients seem to find the regularity of the sound and light

comforting rather than disturbing. Some models are fitted with an alarm to indicate if the machine is malfunctioning. Single use or rechargeable batteries may be used and last about six weeks.

A test button allows a single emission with accompanying sound and light. This feature may also be used to give an extra dose.[12] Sometimes pain relief is adequate while the patient is at rest but the patient has pain when moving, opening the bowels, or having dressings changed, for instance. In such cases an extra dose is very helpful but needs to be given 15 to 20 minutes before the painful procedure. The number of pulses required to give an extra dose may be calculated. In the Graseby MS series each pulse advances the syringe plunger about 0·33 mm—if 48 mm solution contain 180 mg diamorphine for delivery over 24 hours then each extra pulse will deliver $180 \div 48 \times 0{\cdot}33 = 1{\cdot}25$ mg, or four pulses will deliver an extra 5 mg. If the system is to be used in this way the syringe will run out in less than the calculated time so extra volume and drug should be allowed.

The syringe is held in the driver by a rubber strap which hooks onto the machine. The patient is connected to the syringe by a 60-100 cm fine plastic tube. This has a small (25 G) butterfly needle, which is inserted subcutaneously into the anterior chest, abdominal wall, arm, or thigh. The insertion is almost painless, and thereafter the needle is completely painless. A couple of loops should be coiled on the skin to protect against accidental withdrawal and secured with tape such as Micropore. A transparent dressing such as Opsite or Tegaderm allows the needle site to be seen.

The results of a recent study indicate that needles need resiting on average every three to four days.[13] No difference was noted in irritation at the injection site in patients who had additives to the diamorphine solution compared with those who did not. The larger the diarmorphine dose, however, the more often the needle site needed changing. The site on the body, age, sex, type of cancer, and degree of emaciation were not significant. Eight of 50 patients needed to have the site changed on alternate days, and in four the syringe driver was abandoned because of doubts about the absorption of the drugs.

To make up the drug solution the required dose of diamorphine is dissolved in a small volume of water or physiological saline, other drugs added, and the whole mixture diluted until the volume is such that the barrel can be withdrawn to the required length. When a new catheter is connected allow for a dead space of about 0·5 ml.

When starting a subcutaneous infusion it is important to explain it to the patient and family. Inevitably, many patients will die soon after starting this regimen, and some families may perceive it as a sign of approaching death. It should be presented as an alternative method of giving the drugs that the patient already requires.

The machines are robust and reliable. They have been used successfully for desferrioxamine treatment in children and adolescents in Italy.[14] As use spreads district and ward nurses are becoming familar with them, but it is helpful to be able to turn to a hospice or home care service for advice. Relatives and even patients could sometimes draw up the drugs and change the syringe.

Drugs for the syringe driver

OPIOIDS

Diamorphine, which is more water soluble than morphine, is the opioid of choice. When diamorphine is unavailable, as in the United States, morphine may be used[15]; 1 g diamorphine hydrochloride can be dissolved in 1·6 ml water to give a solution with a volume of 2·4 ml (415 mg/ml), but the maximum suggested concentration is 250 mg/ml.[16] Subcutaneous opioid absorption approaches 100% even in patients with fluctuating blood pressure and peripheral perfusion. In a study of 13 ventilated postoperative patients serum morphine concentrations were no lower in nine patients who were given morphine by continuous subcutaneous infusion than in four given the same amount by intravenous infusion.[17]

The effectiveness of a given dose of intramuscular diamorphine is equivalent to three times the dose of oral morphine,[7] and a similar formula is found for subcutaneous infusions. Since regular oral morphine is the preferred method while patients can still swallow few patients will start on a syringe driver as "morphine virgins." The equianalgesic dose of subcutaneous diamorphine, therefore, corresponds to one third of the total daily dose of oral morphine, whether in solution or sustained release tablets (MST Continus, Napp Laboratories). If a patient is receiving intramuscular diamorphine the same total daily dose should be given in the pump. For example, one patient's pain was controlled with morphine elixir 30 mg in 10 ml four hourly—that is, six doses a day. The total oral morphine dose is therefore 180 mg per 24 hours, and the equivalent parenteral dose of diamorphine is a third of that—that is, 60 mg diamorphine a day—in the syringe driver.

If the analgesic requirement is not known the following protocol is recommended[18]:

(1) Start injections every four hours of 2·5 or 5 mg diamorphine, or if the patient has already been taking opioids a dose that is equivalent to the last dose.

(2) If this is unsatisfactory increase this dose in 50% increments until the patient reports even a little pain relief.

(3) Calculate the 24 hour requirement by multiplying by six, and start the infusion at this level.

(4) Increase the 24 hour dosage in the pump by 50% increments until the pain is controlled. Note that requirements may vary from less than 20 mg to more than 5 g per 24 hours.

When starting an infusion it is important not to allow any breakthrough pain. This may be achieved either by starting the infusion more than two hours before the previous oral dose wears off or by giving a loading dose injection of the four hourly requirement.

ANTIEMETICS

Although vomiting is a common reason for giving the infusion, antiemetics are needed less often than might be expected.[8] Firstly, the infusion probably gives steady blood opioid concentrations, avoiding the fluctuations that are thought to produce nausea. Secondly, tolerance to the side effect of the emetic is acquired quickly, and many patients have had previous exposure.

The first choice antiemetic is haloperidol (initially 5 mg/24 h, which can be increased).[19] Haloperidol can easily be added to diamorphine and causes no skin irritation but does not have an opioid sparing effect.[20] If vomiting persists metoclopramide (12·5-50 mg/24 h) or cyclizine (50-150 mg/24 h), or both may be added.[1] Methotrimeprazine (25-150 mg/24 h) and hyoscine are also effective but cause more sedation. Prochlorperazine and chlorpromazine cause skin irritation and should therefore be avoided. A continuous infusion of metoclopramide has produced better control of the nausea and vomiting associated with cisplatin treatment than a conventional intermittent dose, possibly owing to more stable therapeutic blood levels of the drug.[21]

Intestinal obstruction, a common indication for using the pump,[10] often requires both analgesics and antiemetics, but metoclopramide and domperidone should be avoided, as they are ineffective and may worsen the associated colic. The use of the syringe driver has considerably improved the control of vomiting in this condition.[10]

Antiemetics (metoclopramide or prochlorperazine) are sometimes given by separate injections to avoid a risk of drug precipitation and consequent blockage of the cannula or skin irritation.[8] This seems to defeat the purpose of the syringe driver. The compatibility and stability of diamorphine with various antiemetics have been investigated.[22,23] Diamorphine concentrations dropped by less than 10% after 24 hours. In the high concentration solutions required for infusions that last several days cyclizine or haloperidol may precipitate, metoclopramide mixtures become discoloured, but mixtures of hyoscine and diamorphine appeared to be stable.

HYOSCINE

Hyoscine is used in terminal care as an antiemetic to relieve the colic of intestinal obstruction[10] and to abolish death rattle in the moribund patient.[24] In these circumstances a syringe driver is commonly used, and hyoscine may usefully be given in this way alone or with diamorphine. Pinpoint pupils are one of the best signs of morphine poisoning, and it is important to be aware that anticholinergic drugs such as hyoscine may mask this.

CORTICOSTEROIDS

Dexamethasone is commonly added at this hospice. The diamorphine solution is made up with as much water as the calculation of volumes will allow. Then other additions are made. The dexamethasone is drawn slowly into the syringe and finally inverted a few times to mix. Decadron (Merck Sharp and Dohme) seems to be the best brand for this. Skill is required to prevent precipitation. There is no clinical evidence that either drug is made less effective. The chemical compatibility is being studied. If steroid diminishes the tissue reaction around the infusion site it may reduce the incidence of skin reactions and allow better absorption of drugs.

Conclusion

The continuous subcutaneous infusion of drugs by syringe driver is a major advance in the terminal care of patients at home.[8,13,19,25,26] The syringe driver was developed as an alternative route of

administration for familiar drugs when it is impossible or difficult to give drugs by mouth. It permits convenient, adequate, and comfortable parenteral drug treatment in the patient's home.

Pain is controlled in nearly all cases, though the treatment of nausea and vomiting has been less successful. Symptoms of intestinal obstruction have been greatly alleviated.[10] The dose of diamorphine varies from 7·5 mg to 6 g per 24 hours and the duration of treatment from less than 24 hours to over a year. Pump failure has not been a problem, though flat batteries, blockage of the cannula, disconnection, poor absorption, and inflamed sites sometimes occur, the last two being the main problems.

Machines that need refilling less often are being developed. This extra convenience should provide more time for the doctor to spend with his patients and their families rather than depriving them of medical and nursing contact. The competent use of drugs is, after all, only a part of good terminal care.

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A woman has had a subtotal colectomy followed by a mucosal protectomy and ileal anal anastomosis for ulcerative colitis. She suffers from some faecal incontinence. What treatment is advised?

Considerable clinical information on mucus and faecal leakage after restorative proctocolectomy with ileoanal anastomosis is now available. There appear to be two major factors: firstly, the motility and capacitance characteristics of the small bowel above the anastomosis and, secondly, the function of the anal sphincter mechanism. The relation between leakage and resting anal canal tone postoperatively has been shown,[1] as has an appreciable fall in anal tone comparing preoperative and postoperative values.[2] The current presumption is that this is due to the anal dilatation occurring while constructing the ileoanal anastomosis. Although the manometric evidence suggests that resting tone remains lower in the long term, clinical improvement in the function occurs during the first year or so after closure of the ileostomy. This includes a reduction in frequency of defecation, improvement in continence (whether mucoid or faecal), and the consequent improvement in perianal skin soreness. Since the patient has had the operation three years previously, the hopes for this improvement do not apply.

It would be helpful to know (1) whether a reservoir was constructed or not, (2) if so, the type of reservoir used, (3) function frequency and mode of evacuation (whether spontaneous or catheter assisted), (4) the severity of the incontinence (minor or major leakage, day or night, or both, urgency or not), (5) present values of resting and voluntary contraction anal pressure, and (6) whether the repair made any difference. From the description given symptomatic treatment could probably be improved. The regular use of loperamide would be advisable since it is often effective in reducing frequency of defecation, is better than propantheline, and is well tolerated by patients. An ileostomy barrier cream such as aluminium chlorohydrate (Chiron) should be more effective than those already tried and it should be combined with washing and careful drying of the perianal skin after defecation. Incidentally, an examination should be carried out to make sure that the patient does not have a lesion other than excoriation which could produce soreness—for example, a fissure. If despite a further reduction in frequency of defecation and the use of a barrier cream symptoms remain intolerable it must be decided whether further surgery should be tried or an ileostomy established. This decision depends partly on the type of reconstruction already performed but mainly on the personal wishes of the patient. If a straight ileoanal reconstruction without a reservoir has been carried out and anal sphincter function is reasonable then conversion to a reservoir reconstruction would have a good chance of improving continence. If the patient has had an S type reconstruction with a long distal ileal segment and anal sphincter function is reasonable an operation to remove the distal ileal segment and join the reservoir directly to the anal sphincter may again improve the conditions. Both these procedures entail another abdominal approach with the risk of breakdown of a newly constructed ileoanal anastomosis and therefore the possibility of failure. Under these circumstances, the patient's wishes in the matter are paramount.—R J NICHOLLS, consultant surgeon, London.

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A man in his 30s has suffered from a unipolar disorder, predominantly mania, for 14 years. Remissions may last for up to two years but episodes are severe, requiring admission to hospital despite adequate long term serum lithium concentrations. Is there any adjuvant treatment that might prevent relapses so ruinous to his previously promising career?

The response to prophylactic lithium varies from complete (50%), when no further morbidity is observed, to partial (30%), when the severity and duration of episodes is reduced, to failure to respond (20%), when morbidity continues unabated. This patient seems to have a bipolar illness, as unipolar mania is a random form of bipolar illness. His remissions for up to two years show that it is not a rapid cycling illness (having four episodes or more a year). Rapid cycling illness is invariably poorly responsive to lithium. Before supplementary or alternative treatments to lithium are considered the reasons for incomplete response[1] should be investigated, including non-compliance, a common cause for the failure of lithium treatment, and the need for adjusting lithium dosage serum concentration to find the optimum dosage and level for this particular patient. Moreover, patients who have relapses often have personality difficulties that might be helped by psychological treatment.[2] Supplementary or alternative treatments for this patient might include long acting neuroleptic medication[3] and carbamazepine.[1] The latter drug prescribed in dosages to achieve plasma concentrations within the anticonvulsant therapeutic range is an effective supplementary or alternative prophylactic medication in patients with bipolar illness, including those with rapid cycling illness who have failed to respond to lithium.—M T ABOU-SALEH, senior lecturer in psychiatry, Liverpool.

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