

Topical Morphine for Painful Skin Ulcers in Palliative Care A treatment guideline

Introduction

The hypothesis that opioids exert a local analgesic effect is based on several observations:

- 1) Nociceptive afferent nerve fibres contain peripheral opioid receptors which are silent except in the presence of local inflammation (1,2),
- 2) Morphine and its metabolites are largely undetectable systemically when applied topically to skin ulcers (suggesting the analgesic effect is local) (3),
- and 3) Peripheral opioid injections for local analgesia, such as intra-articular morphine after knee surgery, have been found to be effective in several trials (4).

Intrasite Gel® is an aqueous gel that is used as a medium for morphine. When placed in contact with a wound, the gel absorbs excess exudate and produces a moist environment at the surface.

An effective topical opioid analgesic that could be applied to inflamed or open skin lesions would be a useful option for some patients. It is still not known whether local analgesia could decrease the need for systemic analgesics in the first place, or reduce the dose of concurrent analgesics, and, therefore, decrease the associated systemic side effects.

Clinical Efficacy

Several small case series have shown rapid relief using topical opioids in patients with pain due to skin infiltration of tumor, skin ulcers of malignant and non-malignant origin, severe oral mucositis, knee arthritis, and tenesmoid pain (5-20). Most studies have evaluated morphine, although diamorphine and methadone have also shown efficacy (21,22).

The evidence supporting its use still comes from small case studies, poorly designed controlled trials, or uncontrolled open label studies. However, in the palliative care setting, there is a dearth of good evidence to support interventions in the last days of life.

Purpose

This protocol has been developed to aid local healthcare professionals working in the specialist field of palliative care, to safely evaluate and use topical morphine for painful skin ulcers, to enable them to gain experience in its use, to gather useful audit data, and to ensure that this is done in the safest and most standardised way.

Inclusion

All patients **MUST** be assessed by a member of the specialist palliative care team

Terminal or palliative care patients only

Painful superficial chronic wounds <10cm diameter

Non-neuropathic, localised pain

Opioid naïve patients – only where the introduction of systemic opioids would be inappropriate, or is refused by the patient.

Opioid tolerant patients – only where side effects prevent adequate dose escalation of the systemic opioid dose.

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Exclusion

Hypersensitivity (e.g. rash) to morphine or other opioid derivatives.
Hypersensitivity to Intrasisite gel.
More than 2 wounds of <10cm diameter.
Any wound greater than 10cm diameter.
Age <18yrs old.

Cautions

- Intolerance to the systemic side effects of morphine or other opioid derivatives.
- Severe renal impairment or severe hepatic impairment – May actually be used in preference to systemic treatments for this very reason.
- Monitor carefully for signs of opioid accumulation and toxicity over time.
- Care in bleeding or exuding wounds due to reduce ability of the Intrasisite® gel to stick to the wound surface.

Contraindications

- Do not use in or around the eyes because the product is not suitable for such application.
- Do not use in wounds with excessive exudates or bleeding because the gel will not adhere to the wound surface.
- Severe impairment of the central nervous system (e.g. raised intracranial pressure, or head injury)
- Acute respiratory depression
- Concomitant use of MAO-inhibitors or within 14 days after discontinuation of MAO-inhibitors
- Use for patients under the age of 18 is not recommended because of the lack of data in this group.
- Topical management of infected wound (systemic treatment allowed)

Adverse effects

Very few side effects have been reported in the literature regarding the use of transdermal morphine. However, the potential exists for systemic absorption, especially over large areas or with higher concentrations. Patients should be closely monitored for opioid side effects, especially if taking opioids orally/topically concomitantly.

Some patients complain of pruritus with application of the morphine gel. Intrasisite Gel contains propylene glycol, which has been reported to be a potential irritant and sensitizing agent in a small number of patients.

Dose and frequency of application

Initially apply not more than 8ml of morphine 0.125% gel to cover each painful wound once daily for up to 24 hours. The amount of gel applied varies according to the size and the site of the ulcer but is typically 5–8grams (equivalent to 5-8mL). This can be increased to twice or thrice daily depending on response (23).

The Intrasisite® gel should be washed off the wound before reapplying the next dose.

Secondary dressing

Use Activheal® foam dressing over the wound and Intrasisite® gel. If a foam dressing is not appropriate, then Activheal® Film dressing may be used.

Monitoring

Initially patients should be monitored twice daily, using pain scores to measure any

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improvement from baseline prior to initiation. If there has been no response after 3-7 days, treatment should be discontinued. In renal/hepatic impairment especially, monitor for signs of opioid accumulation and toxicity.

Manufacture

No commercially manufactured product for morphine 0.125% in Intrasisite® Gel is available in the UK. Pharmacy compounded the gel as 1 mg preservative-free morphine sulfate per gram of Intrasisite® Gel is produced by some manufacturing units on a 'named patient basis'.

When manufactured outside of a pharmacy compounding unit (e.g. at the patients bedside), the morphine solution should be measured with a syringe, and added to the intrasisite gel in a sterile medium sized plastic container. This should be mixed thoroughly until the morphine solution has been equally mixed and distributed throughout the Intrasisite® gel. This should not be mixed with anything else, and should be used immediately.

To make a 0.125% mixture requires;

Morphine sulphate injection 10mg
Intrasisite® gel 8 gram
Sterile plastic jar large enough to be used for mixing
Small sterile spatula or equivalent

(These quantities are based on the fact that a 1.25% solution requires 1.25g to be added to 100ml i.e. 1250mg in 100ml or 125mg in 10ml. Thus a 0.125% solution requires 100mg to be added to 80ml or 10mg in 8ml)

Stability & Expiry

The morphine component has been shown to be stable for up to 28 days when mixed with a neutral water-based hydrogel with no detectable breakdown products (24). However, when manufactured in any other place than a pharmacy compounding unit, *once mixed the gel should be used immediately and not stored*. This is due to concerns around microbiological contamination following mixing in a non-sterile environment, rather than the physical instability of the mixed gel.

Morphine gel may also be prepared by some compounding hospital pharmacies, or other pharmacy compounding units. Obtaining supplies through this route, especially from manufacturers other than NHS hospitals is very expensive.

Disposal of Controlled Drugs

Local medicines policies cover the disposal of controlled drugs in detail, and the advice below reflects this guidance. The information below was correct at the time of writing, but staff must ensure they are continually familiar with the most up to date version of the local Controlled Drugs Policy (ELHT/C105 Version 1), which is hosted on the ELMMB website.

Part-used vials / ampoules of CDs, as well as the dressing and the gel removed from the patient should be disposed of in an appropriate sharps bin which should be labelled according to the Controlled Drugs Policy (ELHT/C105 Version 1) as "contains mixed pharmaceutical waste and sharps – for incineration". Community nurses should document on the nurses' PDRC/ CDR the quantity of CD administered and the amount disposed of.

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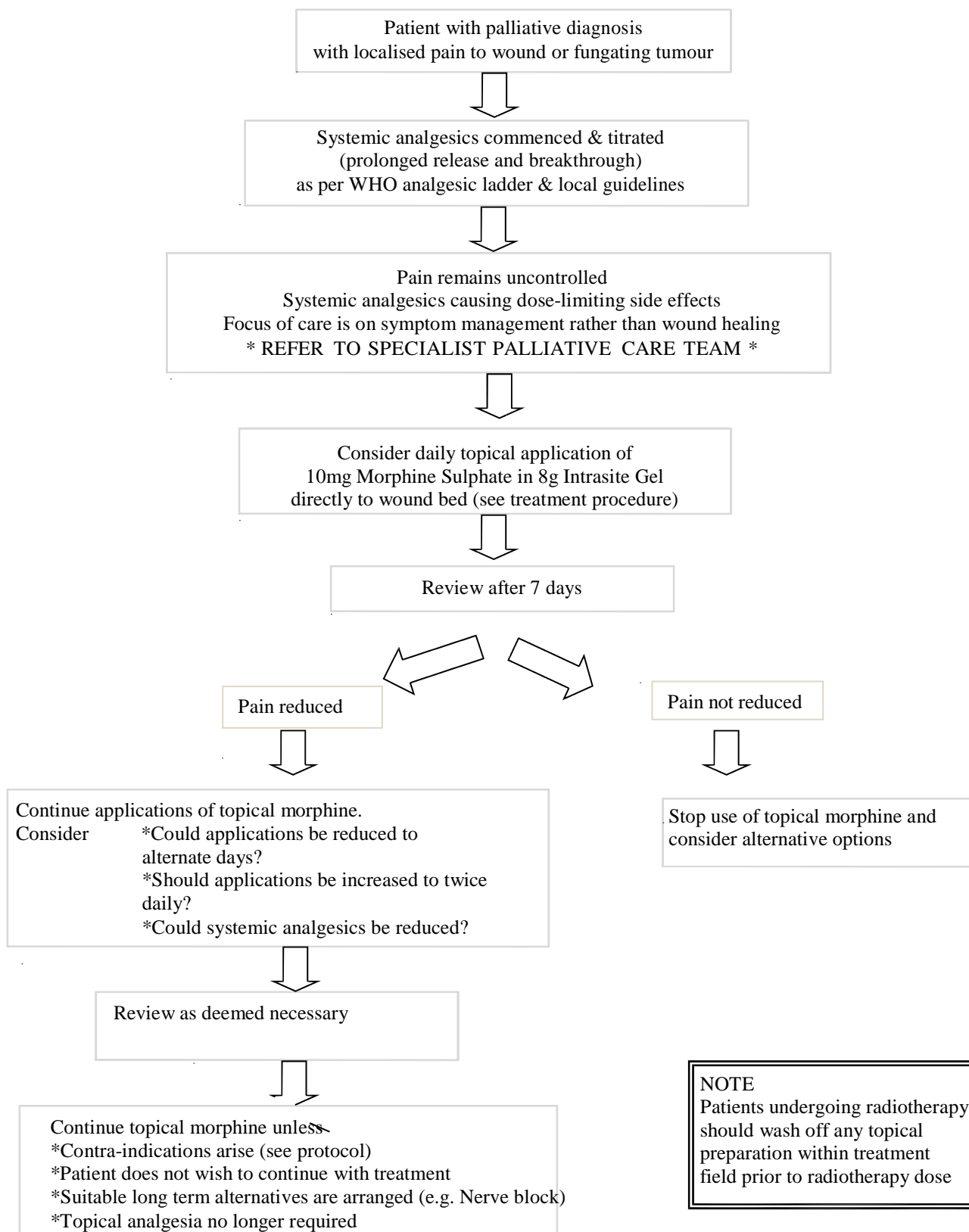
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EAST LANCASHIRE HEALTH ECONOMY TOPICAL MORPHINE GUIDELINES

Algorithm for use in palliative care



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EAST LANCASHIRE HEALTH ECONOMY TOPICAL MORPHINE GUIDELINES

Treatment Procedure

EQUIPMENT REQUIRED

- Sterile dressing pack – containing; plastic tray, apron, gloves, gauze swabs, sterile field, disposable bag.
- 0.9% sodium chloride for irrigating/cleaning wound.
- Activeheal Foam Island dressing or Tegaderm film dressing. If unsuitable use alternative foam dressing from wound care formulary.
- Intrasisite gel 8g.
- Morphine Sulphate injection 10mg.
- 2ml syringe & filter needle
- Plastic probe for mixing gel and morphine.
- Sterile spatula.
- Sharps bin

PROCEDURE

1. Check authorization/prescription and appropriate documentation.
2. Record pain score as reported by patient.
3. Explain and discuss the procedure with the patient and obtain consent to proceed.
4. Prepare clean dressing field area as per Trust guidelines.
5. Draw up morphine sulphate 10mg and mix with Intrasisite Gel 8g in sterile plastic tray.
6. Remove old dressing and irrigate/cleanse the wound with saline.
7. Note size, appearance, odour and exudate from wound to document in notes.
8. Apply intrasisite gel and morphine solution directly to wound bed or onto dressing.
9. Apply secondary dressing to wound.
10. Dispose of any remaining mixture and any items which have been in contact with morphine in sharps bin.
11. Check that patient is comfortable and dressing is secure.
12. Complete documentation.
13. Record pain score 2 hours after dressing change.