The use of Scopoderm in palliative care

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The drug hyoscine has several indications for symptom control for patients with end-stage disease. The transdermal preparation, Scopoderm, is most widely used to control excess salivary secretions but it can also have a role in the management of terminal secretions and in the control of nausea.

The usefulness of hyoscine in palliation relates mainly to its effects on the gastrointestinal and respiratory systems. The evidence base supporting the use of hyoscine (Scopoderm, Novartis Pharmaceuticals, UK) patches for symptom control in patients with advanced incurable disease is weak and much of the rationalization for its use with these patients has been extrapolated from studies done in the general medical and surgical population.

The use of Scopoderm to control salivary flow is relatively undisputed and has several uses for palliative care patients. However, the role of Scopoderm as a means of controlling terminal secretions or 'death rattle' is less clear. The role of Scopoderm in the management of nausea has attracted some attention but few studies have been done comparing its effectiveness with other antiemetic regimens in patients requiring palliative care.

PHARMACOLOGY

Hyoscine is a naturally occurring belladonna alkaloid and is a competitive inhibitor of the muscarinic receptors of acetylcholine. It has antispasmodic and antisecretory properties and it is the most potent single agent in the control of motion sickness (Ferris et al, 1991). It has a short duration of antisecretory action and the side effects include dry mouth, drowsiness, blurred vision and mydriasis. The severity of the central side effects is mainly dose related but paradoxical agitation and toxic psychosis has been seen, especially with repeated administration of the drug (Clissold and Heel, 1985).

Hyoscine is available in two different salts: hyoscine hydrobromide, and hyoscine butylbromide (Buscopan, Boehringer Ingelheim, Bracknell, UK) which has poor oral bioavailability and does not cross the blood–brain barrier. Scopoderm is a transdermal preparation of hyoscine hydrobromide which releases hyoscine at a rate of approximately 5 μg per hour after a priming dose of 140 μg has saturated the skin receptors. Kinetic studies have shown that blood levels of hyoscine reach steady state within 24 hours, and functionally, the Scopoderm patch appears to be the equivalent of a 72-hour slow intravenous infusion (Clissold and Heel, 1985).

DOSAGE AND ADMINISTRATION

It is recommended that, for adults, a single transdermal hyoscine patch is applied to the postauricular area and replaced at intervals of 72 hours. The skin in the postauricular area has been shown to be more permeable than skin in other body areas and thus a lower hyoscine content is required to achieve saturation of skin receptors and steady state flux across the epidermis. It has also been shown that changes in temperature of the skin have little effect on drug delivery (Shaw and Chandrasekaran, 1981).

For motion sickness and for the control of postoperative emesis it is recommended that the patch be applied at least 4–6 hours before the antiemetic effect is required (Clissold and Heel, 1985). In the palliative care setting, where it is less usual to be pre-empting symptoms, the initial application of the hyoscine transdermal patch could be supplemented with subcutaneous bolus doses of hyoscine for the first 4–6 hours. Clearly more than one Scopoderm patch may need to be used in certain situations; however, the benefit to side-effect ratio has to be balanced in each case.

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SALIVARY SECRETIONS

Antimuscarinic drugs in general reduce the volume of gastric secretions and of saliva. The receptors mediating the effects on salivary flow appear to be extremely sensitive to cholinergic blockade (Clissold and Heel, 1985). While this property causes the troublesome side-effect of dry mouth it can also be used to advantage in palliation of symptoms. Patients with intractable swallowing difficulties, e.g. head and neck cancers, oesophageal cancers or cerebral disease causing inhibition of swallow and gag reflexes, can often have problems with drooling or choking owing to the normal production of saliva. In such patients the transdermal route is an ideal way of administering medication and the Scopoderm patch can reduce the production of saliva to a more manageable level.

To date no published studies have been done in the palliative care setting to compare the effectiveness of Scopoderm with subcutaneous bolus or continuous injection of either hyoscine hydrobromide or hyoscine butylbromide. It is suggested, however, that the Scopoderm patch could have advantages over the subcutaneous route in terms of patient acceptability, invasiveness and also health professionals' time, especially in the community setting.

TERMINAL SECRETIONS

In the hours before death patients who are unable to clear secretions from their upper airways can often have noisy breathing which has come to be known as 'death rattle'. Although no detailed evaluation has been published of the distress caused by death rattle to patients and their carers it is felt that, in clinical practice, it may contribute to restlessness in dying patients. It is often seen also to contribute to the distress of the family, friends and the professional carers at this difficult time.

One retrospective case note audit looking at hyoscine use in the final 48 hours of life showed that the percentage of patients receiving hyoscine by injection or continuous infusion increased from 11.5% at 48 hours before death to 51% in the last 6 hours of life (Bennet, 1996).

Studies have also shown that, in the inpatient palliative care setting, Scopoderm is seldom used and that subcutaneous infusion and injection are the most common means of administering hyoscine in the final hours of life (Lichter and Hunt, 1990; Power and Kearney, 1992). Given that the transdermal route may take 24 hours to achieve steady state blood levels of hyoscine it seems likely that this pattern of use will continue. In the community, however, Scopoderm can play a useful part in controlling terminal secretions over the last 48 hours (Dawson, 1989).

It has been suggested that terminal secretions can be categorized into one of two types:

1. Type 1 secretions are mainly caused by accumulation of saliva when swallowing reflexes are inhibited near to death
2. Type 2 secretions are predominantly bronchial and may accumulate over several days as the patient deteriorates.

The evidence available suggests that hyoscine is unlikely to influence the mechanisms of type 2 terminal secretions (Bennet, 1996). Evidence also suggests that patients who have lost airway reflexes early as a result of cerebral malignancy are more likely to be given hyoscine in the final 24 hours of life (Bennet, 1996). It may therefore be possible to anticipate death rattle with these patients and apply the Scopoderm patch before the onset of the symptom to prevent its occurrence.

NAUSEA AND VOMITING

Acetylcholine is implicated in the generation of the symptoms of nausea and vomiting at various points in the emetic pathway. Centrally acetylcholine is an important neurotransmitter in the nucleus solitarius, the vagal afferent pathways and the vestibular system, all of which influence the vomiting centre, which is a functional entity close to the area postrema on the floor of the fourth ventricle (Twycross and Back, 1998). Peripherally muscarinic cholinergic receptors can be found on mucosal cells in the intestinal lumen as well as within the smooth muscle of the bowel wall (Schuurkes et al, 1986; De Conno et al, 1991). Thus hyoscine hydrobromide can have a central antiemetic effect as well as reducing vomiting and colic in bowel obstruction.

The use of transdermal hyoscine in the control of motion sickness is well established and trials have shown it to be significantly superior to placebo and to oral meclozine in reducing the severity of motion sickness (Clissold and Heel, 1985). It is reasonable to suggest, therefore, that Scopoderm may be a useful antiemetic to try where head movement is noted to be a precipitating cause of the nausea, e.g. labyrynthitis, acoustic neuroma, bone metastases in the base of skull or cerebral/cerebellar disease (Lichter, 1993).

Scopoderm has been shown to be ineffective as a single agent in the prevention of chemother-

apy-induced emesis, but one study suggested that it could provide added benefit when used in combination with the standard antiemetic regimen of metaclopromide and dexamethasone (Meyer et al, 1987).

Another area where Scopoderm may prove useful as an antiemetic in the palliative care setting is nausea produced as a side-effect of narcotic administration. One of the ways in which narcotic analgesics cause nausea is thought to be enhanced labyrinthine sensitivity. This occurs because of the inhibition of breakdown of acetylcholine resulting in increased amounts of the neurotransmitter within the synapse (Gutner et al, 1952).

One study examined the use of the Scopoderm patch in 13 ambulatory oncology patients with nausea since starting opioid analgesics, which was, on movement, refractory to other antiemetics or present on admission to the hospital. A rapid improvement in nausea was shown in 11 (85%) out of 13 patients within an average 1.3 days. In 9 out of the 11 patients it was felt that the response was because of the patch as no other medication changes had been made (Ferris et al, 1991).

CONCLUSIONS

Hyoscine in the form of the transdermal Scopoderm patch has been in general use in the palliative care setting for many years but, despite this, the evidence base supporting its use with this particular patient population remains sparse. Studies in other patient groups allow some justification for its use in the regulation of certain symptoms including: control of salivary flow in patients with intractable swallowing difficulties, the reduction of terminal secretions (type 1 only), the control of nausea where motion is a precipitating factor, and nausea induced by use of opioid analgesics. There is a great need for further studies of efficacy and patient tolerability to be done, specifically within the palliative care patient population. **HM**

Conflict of interest: none.

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KEY POINTS

- The Scopoderm transdermal patch delivers hyoscine hydrobromide and therefore has both central and peripheral effects.
- It can significantly reduce the production of saliva for patients with intractable swallowing difficulties.
- Scopoderm has a limited role in managing 'death rattle' where the secretions are mainly of salivary origin or where it can be anticipated that patients will have difficulty clearing secretions as they deteriorate. It is less useful in controlling bronchial secretions.
- Scopoderm is a useful antiemetic where vestibular mechanisms are involved in the production of nausea.
- Nausea induced by opioid analgesics may partly be the result of enhanced labyrinthine sensitivity and may therefore respond to Scopoderm where the first-line antiemetics (metaclopramide or haloperidol) have failed.
- Studies examining the use of Scopoderm in the palliative care setting are very few and more work is greatly needed in this area.