MANAGING PERSISTENT HICCUPS IN ADVANCED CANCER 2: TREATMENT

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This is the second in a two-part unit on persistent hiccups in advanced cancer. Part 1 explored the incidence, causes, physiology and adverse effects of hiccups. This part examines both their non-pharmacological and pharmacological management.

LEARNING OBJECTIVES

1. Know about non-pharmacological approaches that may be considered to manage persistent hiccups.
2. Be able to identify drugs that have been used in managing this symptom.

TREATMENT OPTIONS

Treatment of hiccups focuses on disrupting the hiccup reflex arc by blocking transmitting nerve impulses, counteracting stimulating impulses or affecting the cause (Friedman, 1996). When an underlying cause has been identified, it would be logical to target treatment accordingly, for example, by correcting any metabolic imbalance or reviewing the need to continue with hiccup-inducing medication (Smith and Busracamwongs, 2003).

However, in patients with advanced cancer, treating the underlying cause may not be possible or practical. When no underlying cause is apparent, careful consideration must be given about whether it is appropriate to subject patients to potentially burdensome investigations (such as chest X-ray, gastroscopy or CT scan).

The management of persistent hiccups can be challenging. Often patients have undergone numerous interventions in an attempt to control hiccups and it is important to note what has already been tried. Although a wide range of treatments are reported in the literature, proof of effectiveness is mostly in the form of anecdotal evidence and case reports.

The rarity of persistent hiccups makes scientific study difficult and, to date, no treatment can be regarded as standard. Best practice is that, in the absence of an identified, reversible cause, the initial approach to management is by the least invasive methods.

NON-PHARMACOLOGICAL APPROACHES

A ‘gate control’ theory has been proposed, whereby the impulses produced following pharyngeal stimulation act to block the hiccup impulse (Friedman, 1996). Many traditional cures are based on this principle, including swallowing dried bread, rapid ingestion of two spoonfuls of granulated sugar and swallowing crushed ice (Twycross and Regnard, 1998). Medical variations of this approach include:

- Inserting a nasal catheter 8–12cm so it rests opposite the second cervical vertebra. By rapidly moving the catheter to and fro, a stimulus is produced that can lead to an immediate cessation of hiccups (Salem et al, 1967);
- Massaging the anterior of the soft palate in the midline for approximately one minute with a cotton-tipped swab (Goldsmith, 1983);
- Administering nebulised saline over five minutes every two hours (De Ruyscher et al, 1996).

Other reported methods include pressing a finger firmly into each ear for approximately 20 seconds (with or without drinking a glass of water through a straw; such a technique may result in the stimulation of the auricular branch of the vagus nerve, momentarily blocking afferent impulses from the diaphragm (Thomas and Thomas, 2006).

Gastric aspiration via nasogastric tube may provide rapid relief from hiccups when associated with an overly distended stomach. The insertion of a nasogastric tube may also serve to stimulate the pharynx or induce gagging, which in turn disrupts the hiccup reflex arc (Sarhill and Mahmoud, 2007).

Hiccup frequency is suppressed or modulated by the inhalation of carbon dioxide (Newsom-Davis, 1970). Measures such as breath-holding and re-breathing into a paper bag act by increasing the partial pressure of carbon dioxide. This has a central depressant effect that blocks the central component of the hiccup reflex arc (Morris et al, 2004).

Other reported non-pharmacological techniques include acupuncture (Liu et al, 2005), hypnosis, digital rectal massage, phrenic nerve block (Schuepfer et al, 2003) and positive pressure ventilation (Lierz and Felleiter, 2002).

The appropriateness of any intervention must be carefully considered, as even the least demanding technique may prove too strenuous for patients with advanced cancer. For this reason, a pharmacological approach is often required in the management of persistent hiccups.

PHARMACOLOGICAL APPROACHES

Many drugs have been suggested in the management of persistent hiccups. However, the benefits of one drug over another are rarely clear and their mechanism of action is often vague.

Gastric distension is considered to be the most likely cause of hiccups in patients with advanced cancer. Therefore, the initial approach to drug management often aims to relieve distension and promote gastric emptying (Sarhill and Mahmoud, 2007; Hardy, 2003).
Drug mechanisms

**Metoclopramide** is a potent dopamine antagonist that is thought to have a peripheral and central action (Friedman, 1996). Its effect is to tighten the lower oesophageal sphincter and hasten gastric emptying. Metoclopramide can cause extrapyramidal side-effects and its use is best avoided by patients with Parkinson’s disease.

**Domperidone** is an alternative prokinetic agent that does not cross the blood-brain barrier, so is less likely to cause extrapyramidal side-effects (Watson et al, 2005a).

**Simeticone** is a defoaming agent found in preparations such as Asilone. It may be given in conjunction with metoclopramide when used to treat hiccups (Watson et al, 2005b). Peppermint water is a common remedy for gastric distension. However, this facilitates belching by relaxing the lower oesophageal sphincter so concurrent use with metoclopramide would not seem logical (Twycross and Wilcock, 2001).

**Baclofen** is a gamma-aminobutyric acid (GABA) analogue and its use in managing hiccups is well cited (Smith and Busracamwong, 2003; Gueland et al, 1995; Launois et al, 1993). GABA is an inhibitory neurotransmitter and its activation by baclofen is thought to block the hiccup stimulus (Friedman, 1996). Baclofen must be used with caution in patients with renal impairment as serious neurotoxicity has been reported (Chou et al, 2006).

**Nifedipine** is a calcium channel blocker that has been used successfully to end bouts of persistent hiccups (Quigley, 1997). Its mode of action is unclear but it is thought to reverse abnormal depolarisation within the hiccup reflex arc. Unless corrected, hypotension may limit the use of nifedipine.

**Dexamethasone** is a corticosteroid that may control hiccups associated with central irritation, for example in intracranial tumour or encephalopathy, by reducing oedema and inflammation (Watson et al, 2005b). However, corticosteroids have also been associated with causing hiccups and their use may need to be discontinued should hiccups occur (Errante et al, 2005; Ross et al, 1999).

**Chlorpromazine** has been widely used in the management of hiccups for over 50 years (Friedgood and Ripstein, 1955). The dopamine-antagonistic effect of chlorpromazine is thought to block the central component of the hiccup reflex arc (Friedman, 1996). Although efficacious, its use in patients with advanced cancer tends to be avoided as the required doses to achieve hiccup control often results in intolerable side-effects such as sedation and postural hypotension (Sarhill and Mahmoud, 2007).

**Haloperidol** is an alternative dopamine antagonist that has been reported to control persistent hiccups (Phillips, 2005).

A number of other drugs have been reported occasionally in the management of persistent hiccups, including gabapentin (Petroianu et al, 2000).

No drug has been identified as controlling persistent hiccups in all cases. Indeed, published case reports show that for every example of a particular drug being used successfully, there are many other instances where its use did not bring benefit.

**CONCLUSION**

Treatments for persistent hiccups range from traditional cures to medical procedures and drug therapies. The wide range of treatments to consider reflects the challenge persistent hiccups can present. The rarity of this symptom renders scientific evaluation of its management difficult.

**KEY REFERENCES**


- The full reference list for this unit is available in Portfolio Pages at nursingtimes.net

Anecdotal evidence and case reports form the basis of much of the supportive literature. Currently, no intervention can be regarded as standard treatment.

When considering management in patients with advanced cancer, the burden and benefit of any proposed intervention must be taken into account. Often, such patients are debilitated and many non-pharmacological techniques may prove too demanding. The potential side-effects of drug therapy must also be considered.

Gastric distension is reported to be the most common factor underlying persistent hiccups. In the absence of any other identifiable cause, the logical first approach is to reduce distension and promote gastric emptying by the use of an anti-foaming agent (such as Asilone) and a prokinetic (such as metoclopramide).

Although uncommon, the effects of persistent hiccups can be extremely distressing and far reaching. It is a challenge for healthcare professionals not only to find a successful clinical approach to resolve patients’ persistent hiccups but also to provide them with meaningful support tailored to their needs.