

B.C. INTER-PROFESSIONAL PALLIATIVE SYMPTOM MANAGEMENT GUIDELINES

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DEFINITION

Hiccoughs are repeated, involuntary spasmodic contractions of the diaphragm and inspiratory muscles followed by sudden closure of the glottis.¹⁻⁷ Hiccoughs are categorized according to duration^{2,3,4,5,8,9}:

Acute – Hiccoughs that last < 48 hours and are common, non-pathologic, and self-limited.¹⁰

Persistent - Hiccoughs lasting 2 days or more.

Intractable – Hiccoughs that last more than 1 month and not responsive to treatments.

PREVALENCE

Persistent or intractable hiccoughs often indicate serious underlying pathology and are most common (10-20%)⁴ in those with gastro-intestinal tract, thoracic, or central nervous system disease.^{3,5,9-11} Prevalence is relatively low (~1-9%) in the general palliative population.^{2,9,12-18}

IMPACT

Persistent and intractable hiccoughs can interfere with normal daily activity,^{5,19} significantly reducing quality of life, causing distress for both patient and family.⁴ Potential impacts include: increased anxiety, distress,⁷ insomnia, fatigue,^{5,20} gastrointestinal reflux, weight loss, vomiting, aspiration pneumonia, dehydration, electrolyte imbalance, cardiac arrhythmias,²¹⁻²⁵ isolation, delirium (in the elderly), wound dehiscence (in post-surgery),^{3,9} depression, and in rare situations, death.^{23,26-30}

STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources (<u>Additional resources for management of hiccoughs</u>) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.



Step 2 | Assessment

Hiccough Assessment: Using Mnemonic O, P, Q, R, S, T, U and V⁷¹

Mnemonic Letter	Assessment Questions <i>Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.</i>	
Onset	When did the hiccoughs begin? How long do they last? How often do they occur?	
Provoking /Palliating	What brings them on? What makes them better? What makes them worse?	
Quality	What do they feel like? Can you describe them? Do they change when you change position?	
Region/Radiation	Not applicable	
Severity	How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom (e.g., nausea, anxiety or fatigue)?	
What medications and treatments are you cur using? Are you using any non-prescription treat herbal remedies, or traditional healing practice effective are these? Do you have any side effect medications and treatments? What have you t past? Do you have concerns about side effects treatments?		
Understanding	Do they interfere with your ability to eat, drink, talk or enjoy other activities? Do they interfere with your sleep? What do you believe is causing this symptom? How are the hiccoughs affecting you and/or your family? What is most concerning to you?	
Values	What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family?	



Symptom Assessment: Physical assessment as appropriate for symptom

Diagnostics: consider goals of care before ordering diagnostic testing

Recognize that hiccoughs can be multifactorial in advanced disease and that an extensive workup to find the cause can be harmful. Consider patient status and goals of care in determining extent of diagnostics required.⁸

- Perform a detailed history and physical.^{4,9}
- Review prior surgical interventions; respiratory and gastrointestinal symptoms; infections; and use of alcohol and medications, especially corticosteroids, benzodiazepines, and barbiturates.¹⁸
- Consider CBC, electrolytes, and chest xray.⁹ Include liver ultrasound and liver function tests, serum Calcium,^{10, 26, 31} CT, MRI and electrocardiography, as needed.⁴
- Invasive tests such as lumbar puncture and bronchoscopy, depend on the patient's situation.²⁶

Step 3 Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see <u>Underlying causes of hiccoughs</u> in palliative care)

Over 100 underlying diseases have been associated with hiccoughs.^{1,31} Persistent hiccoughs should be taken seriously as they often indicate underlying pathology.

Common causes of persistent and intractable hiccoughs include^{1,2,4,32,33}

- Gastric stasis and distention (most common)³⁴
- Gastro-esophageal reflux³⁴
- Metabolic disturbances (e.g., uremia, hypercalcemia, low magnesium)¹⁵
- Infection
- Irritation of the diaphragm or phrenic nerve

Step 3 - Determine possible causes continued on <u>next page</u>





Determine possible causes and reverse as possible if in keeping with goals

of care continued

- Hepatobiliary disease/hepatomegaly
- Cerebral causes (e.g., tumour, metastasis, CVD)⁸

Other important causes

- Myocardial Infarction, pericarditis, aneurysm.^{2,7,8,35}
- Medications such as benzodiazepines, opioids, corticosteroids.² Risk with dexamethasone is 25%.^{15,19} (See <u>Underlying causes of hiccoughs in palliative care</u> for a list of medication causes)
- Chemotherapy, radiotherapy, and surgery^{15,18,26,37-39}; nasal, pharyngeal, laryngeal conditions; foreign body in ear canal.²
- Anxiety, stress or over-excitement; psychogenic.^{2,7}

PRINCIPLES OF MANAGEMENT

When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?).

- Hiccoughs may resolve on their own; try simple physical techniques.
- Try non-pharmacological interventions during acute 48 hours "bout" phase, particularly any that the patient has previously found helpful.
- Consider medications when they are persistent, lasting more than 48 hours.
- Consider the patient's general condition to avoid potential side effects.⁸
- Refer to palliative care consultants when refractory or patient unable to swallow.





Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

\bigcirc	Use with confidence: recommendations are supported by moderate to high levels of empirical evidence.
ê	Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence.
	Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study
X	Not recommended: high level empirical evidence of no benefit or potential harm

Non-pharmacological interventions

A wide range of non-pharmacological approaches have been used to treat persistent and intractable hiccoughs; however, their safety and efficacy are unknown as no systematic reviews or clinical trials were found.^{8,13} Most treatments have a physiological basis that interrupts the hiccough reflex arc by stimulation of the vagus or phrenic nerves to interfere with normal respiration, or increase pCO2 levels.⁴

Interventions available in the home and residential care facilities

Breathe holding or drinking in small sips.^{8,13, 33}

- Sip iced water or swallow crushed ice.³³
 - Breathe into a paper bag, particularly if patient is hyperventilating.³³



Behavioral techniques such as distraction, small meals, fasting and vigorous exercise (may not be an option in frail elderly or advanced disease patients).⁹

Non-Pharmacological interventions continued on <u>next page</u>



Non-pharmacological interventions continued



Proof Rub the soft palate (e.g., with a swab) to stimulate the nasopharynx.³³ Caution as this may trigger gag reflex.

Interventions requiring additional equipment or admission to acute care



Nebulized normal saline — 2ml of NaCL 0.9% nebulized over 5 minutes at regular intervals throughout the day and prn at night. 43 Needs more study but safe; permits patient self-care and could be considered before drug treatment where equipment is available. Note: in community, may be able to rent or borrow a home nebulizer machine.



Acupuncture,^{1,9,33} if available and acceptable to the patient.

Surgical treatment has shown benefit when cause is known and possibly removable. Cervical phrenic nerve block, only as last resort.³⁸ Careful patient selection required. Consider implications for overall quality of life. Rarely indicated in the frail elderly⁹ or advanced disease patient.

Pharmacological interventions

A systematic review found little high-level evidence for either non-pharmacological or pharmacological interventions that are effective or harmful.²⁵ Palliative experts lack consensus of medications considered essential for safe and effective hiccough management and acknowledge that additional research is needed.⁴⁴

As hiccoughs often terminate spontaneously,^{25,32,45} drug therapy usually is not indicated unless persistent.

Direct treatment to underlying cause of the condition whenever possible.^{6,9,50,60} Baclofen and gabapentin have a lower risk of long term side effects than neuroleptic agents.⁵⁰ They are now preferred over chlorpromazine which can be poorly tolerated.8,41,51

Baclofen



Supported by two small RCTs,^{40,46} and several case reports.^{38,40,46-48} It is suggested to have the best ability to treat hiccoughs.^{1,9} Has been used in cancer and palliative patients with success. 38,45,47,49

Pharmacological interventions continued on next page



Pharmacological interventions continued

 $\langle = \rangle$ Single doses of baclofen 10 mg have successfully stopped hiccoughs after 0.5 to 3 hours.⁴⁷ This may provide immediate patient comfort if a diagnostic process takes several days.47



Ongoing dosing of baclofen 10 mg bid, up to 10 mg TID, may be indicated for 2 to 5 davs.47

Use for a longer duration is indicated if unable to remove triggering cause.⁴⁷

Gabapentin

May be preferred in hiccoughs related to CNS disease or if neuropathic pain coincides.^{50,51} Has been shown to be effective with advanced cancer patients.¹⁵

Adjunctive therapy



Antiemetics may be required if vomiting accompanies hiccoughs.⁴



Anxiolytics (e.g., midazolam) if hiccough distress is severe.^{25,24} Consider in last days of life.

For more information, see Medications for Management of Hiccoughs.

Patient and family education^{1,8,20,32,33,41,42}



Hiccoughs that last < 48 hours usually resolve on their own.



Hiccoughs are often caused by gastric distention, carbonated beverages, alcohol, hot or cold drinks, anxiety or stress.



Simple non-drug approaches may be helpful, especially if helped in the past.



Draw from strategies identified in non-pharmacological interventions.



Contact healthcare provider for hiccoughs that interfere with sleep, or > 2 days.



ADDITIONAL RESOURCES FOR MANAGEMENT OF HICCOUGHS

Resources specific to Hiccoughs

No additional resources specific to hiccoughs included in this document

General Resources

- Provincial Palliative Care Line for physician advice or support, call **1 877 711-5757** In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
 - → <u>http://www.bc-cpc.ca/cpc/</u>
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
 - → <u>http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care</u>
- BC Palliative Care Benefits: Information for prescribers
 - → <u>http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/plan-p-bc-palliative-care-benefits-program</u>
- National Centre for Complementary and Alternative Medicine (NCCAM) for additional information on the use of non-pharmacological interventions
 - → <u>https://nccih.nih.gov/</u>
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
 - → <u>http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_</u> <u>Guideline1.pdf</u>

Additional resources for management of hiccoughs continued on next page





ADDITIONAL RESOURCES FOR MANAGEMENT OF HICCOUGHS CONTINUED

- Fraser Health psychosocial care guideline
 - → https://www.fraserhealth.ca/media/psychosocial%20care.pdf

Resources specific to health organization/region

- Fraser Health
 - → <u>http://www.fraserhealth.ca/health-professionals/professional-resources/</u> <u>hospice-palliative-care/</u>
- First Nations Health Authority
 - → <u>http://www.fnha.ca/</u>
- Interior Health
 - → https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx
- Island Health
 - → <u>http://www.viha.ca/pal_eol/</u>
- Northern Health
 - → <u>https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.</u> <u>aspx</u>
- Providence Health
 - → <u>http://hpc.providencehealthcare.org/</u>
- Vancouver Coastal Health
 - → <u>http://www.vch.ca/your-care/home-community-care/care-options/</u> <u>hospice-palliative-care</u>

Additional resources for management of hiccoughs continued on <u>next page</u>



ADDITIONAL RESOURCES FOR MANAGEMENT OF HICCOUGHS CONTINUED

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
 - → <u>https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf</u>
- ALS Society of British Columbia 1-800-708-3228
 - → <u>www.alsbc.ca</u>
- BC Cancer Agency: Symptom management guidelines
 - → <u>http://www.bccancer.bc.ca/health-professionals/clinical-resources/</u> <u>nursing/symptom-management</u>
- BC Renal Agency: Conservative care pathway and symptom management
 - → <u>http://www.bcrenalagency.ca/health-professionals/clinical-resources/</u> <u>palliative-care</u>
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
 - → <u>http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/</u>
- Canuck Place Children's Hospice
 - → <u>https://www.canuckplace.org/resources/for-health-professionals/</u>
 - 24 hr line 1.877.882.2288
 - Page a Pediatric Palliative care physician 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
 - → <u>http://www.togetherforshortlives.org.uk/professionals/resources/2434</u>_ <u>basic_symptom_control_in_paediatric_palliative_care_free_download</u>



UNDERLYING CAUSES OF HICCOUGHS IN PALLIATIVE CARE ^{2,5,7,8,38,45}

Table 1 Drugs reported to cause hiccoughs			
Alcohol	Cyclophosphamide	Gemcitabine	Muscle relaxants
Anabolic steroids	Chorionic Gonadotropin	Heroin	Nicotine
Aprepitant	Corticosteroids	Hydrocodone	Paclitaxel
Aripiprazole	Dexamethasone**	Irinotecan	Perphenazine
Barbiturates	Donepezil	Levodopa	Pergolide
Benzodiazepines	Docetaxel	Macrolide antibiotics	Progesterone
Bupivacaine epidural	Doxycycline	Megestrol	Rocuronium
Carboplatin	Ethosuximide	Methotrexate	Sulfonamides
Cefotetan	Etomidate	Methylprednisolone	Triamcinolone
Chlordiazepoxide	Etoposide	Mexiletine	Vinorelbine
Chemotherapy*	Fluoroquinolone antibiotics	Midazolam	Zolpidem
Cisplatinum	Flumazenil	Morphine	

* Chemotherapy may be falsely attributed as a cause because dexamethasone is often used concurrently.⁵²

** May be dose-related; more prevalent at dexamethasone doses greater than 10 mg daily.⁵²



MEDICATIONS FOR MANAGEMENT OF HICCOUGHS

There are no approved medications for hiccough use in Canada; everything is off-label.

Drug, Action	Dose, therapeutic range	Onset, Adverse Effects, Precautions and Dosing Concerns
Baclofen 1 st line	5 to 20 mg PO every 6 to 12	Drowsiness, dizziness, hypotension, confusion, nausea, ataxia.
empiric ^{8,31,38,40,41,50,53,}	hour, up to 40 mg/day	Alcohol and CNS depressants can be additionally sedating.
		Avoid in renal failure, or carefully adjust dose due to risk of delirium, respiratory depression.
		Risk of withdrawal symptoms when abruptly stopped.
		Use caution in patients with epilepsy.
Gabapentin	100 mg TID to	Drowsiness, dizziness, fatigue, ataxia, peripheral
1 st line empiric ^{8,15,51,50}		edema, visual disturbances, clumsiness/ unsteadiness. Adjust dose for reduced renal function.
max		No hiccough treatment studies in renal impairment.
		In extended therapy, when possible, gradually reduce dose over a minimum of one week.
		Very few drug interactions

Medications for management of hiccoughs continued on next page





MEDICATIONS FOR MANAGEMENT

OF HICCOUGHS *CONTINUED*

Metoclopramide 2 nd line empiric ^{32,41,50,55,56}	10 mg PO,IV,SC TID to QID	 Asthenia, headache, drowsiness, fatigue. Serious: tardive dyskinesia, neuroleptic malignant syndrome. Adjust dose for reduced renal function. Avoid concurrent use with: Peppermint water (opposing actions on gastro-esophageal sphincter). Haloperidol due to increased risk of extrapyramidal symptoms. GI hemorrhage, mechanical obstruction, or perforation or if GI stimulation might be dangerous. Parkinson disease. Use caution in patients with epilepsy. Oral metoclopramide is 50-80% bioavailable, consider reducing SC, IV, IM dose by 25-50%. 	
Domperidone 2nd line empiric ^{2,32,50,55}	10 mg TID to QID	Adverse effects; xerostomia, serious is prolonged QT interval, sudden cardiac death, ventricular arrhythmia. Risk of QT interval prolongation at doses greater than 30 mg/day. Check concurrent drugs for QTc risk.	
Pantoprazole ^{41,57}	40 mg daily to BID	Generally safe. Few drug interactions compared to other PPIs. Concomitant use of antacids does not affect the pharmacokinetics of pantoprazole sodium.	
Antacid containing simethicone ³²	10 mL QID		
Gaviscon ⁵⁰	10 mL TID	Give after meals.	



OTHER PROPOSED DRUG TREATMENTS

(Recommended Only After Palliative Care Consultation)

Medication	Dose	Adverse Effects, Precautions and Dosing Concerns
Amantadine ^{58,59}	100 mg PO once or twice daily	Non-sedating. Adjust dose for renal function. Three cases (one was cancer/end of life).
Chlorpromazine ^{5,8,9,41,} 50-52,60,61	25 to 50 mg PO once daily, titrating up to 3 or 4 times daily	Hypotension, sedation, urinary retention, glaucoma, delirium, extrapyramidal symptoms.
		Assess risk of QTc prolongation, often concerning.
		Poorly tolerated in elderly patients.
		Avoid long term due to risk of tardive dyskinesia. Injection discontinued, no longer available in Canada.
		Only 25, 50 and 100 mg tablets available.
Dexamethasone ^{5,33,62}	4 up to 8 mg PO	Fatigue, sleep disturbance, hiccoughs.
daily	daily	Suggested for hepatic or cerebral tumor – to reduce compression/irritation. Few studies.
Haloperidol ^{9,56,63}	0.5 to 5 mg PO TID	Avoid concurrently with metoclopramide
	Or via SC, IV, IM routes	due to increased risk of extrapyramidal symptoms.
		Recommended dosing from references varies widely.
		Older studies used IM route, effectiveness via other routes uncertain, but much less painful.
		Oral haloperidol is 60-70 % bioavailable, consider reducing SC, IV, IM dose by one- third.



OTHER PROPOSED DRUG TREATMENTS CONTINUED

(Recommended Only After Palliative Care Consultation)

Medication	Dose	Adverse Effects, Precautions and Dosing Concerns
Lidocaine 2% viscous	5 mL orally BID to TID	Single case report. Was swallowed in 3 patients; 2 used with baclofen.
		May impair swallowing, enhancing aspiration risk. Avoid food ingestion for 60 minutes.
Lidocaine ^{1,5,41}	1 mg/kg loading dose followed by infusion of 2 mg/ min CSCI	Risk of cardiovascular and neurologic toxicities.
Methotrimeprazine ³²	3 to 6 mg PO,SC,IV HS	Injectable alternative to chlorpromazine or haloperidol
Midazolam ^{5,24,33,56}	5 to 10 mg SC or PO Q4H PRN CSCI: 10 up to 120 mg/ day	Two case reports. Review use and suitability with local palliative care team. Adverse effects include sedation, risk of apnea paradoxical reactions, drug interactions, especially with opioids. reduced elimination in liver or heart failure,
Olanzapine ^{60,65,66}	2.5 to 7.5 mg PO daily	and elderly Three cases reports. In two, used in combination with baclofen as 5 mg
Pregabalin 50,67,68,69	25 to 75 mg PO BID, up to 375 mg/day	baclofen BID, other 10 mg TID. Drowsiness (might be less than gabapentin), dizziness, peripheral edema. Three case reports.
Sertraline 70	50 to 150 mg PO/ day	Single patient case report.
Valproic acid 5,50	15 to 20 mg PO per kg/24 hours, divided in 1 or 3 doses	May increase by 250 mg/week until hiccoughs stop.

Other proposed drug treatments continued on <u>next page</u>





OTHER PROPOSED DRUG TREATMENTS *continued*

(Recommended Only After Palliative Care Consultation)

⁺ Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet, CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan (<u>http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf</u>) provides province-wide drug coverage for many of the recommended medications; check website to confirm coverage. Consider price when choosing similarly beneficial medications, especially when the patient/family is covering the cost.

HICCOUGH MANAGEMENT ALGORITHM

No management algorithm included in this document.

HICCOUGH EXTRA RESOURCES OR ASSESSMENT TOOLS

No extra resources or assessment tools included in this document.

HICCOUGHS REFERENCES

- 1. Kaneishi K, Kawabata M. Continuous subcutaneous infusion of lidocaine for persistent hiccup in advanced cancer. Palliat Med. 2013;27(3):284-5.
- 2. Nausheen F, Mohsin H, Lakhan SE. Neurotransmitters in hiccoughs. Springerplus. 2016;5(1):1357.
- 3. Hiccoughs (Singultus) [Internet]. 2016 [cited Jan 26, 2017]. Available from: <u>http://book.pallcare.info/index.php?tid=10&searchstring=hicc</u>.
- 4. Clark K. Dysphagia, dyspepsia and hiccup. 5th Ed. ed. Nathan Cherny MF, Stein Kaasa, Russell K. Portenoy, and David C. Currow, editor. Oxford Medicine Online: Oxford University Press; 2015. 16 p.
- 5. Dahlin CM, Cohen AK. Dysphagia, xerostomia, and hiccoughs. 4th ed. ed. editor. Oxford Medicine Online: Oxford University Press; 2015. 51 p.

Hiccoughs references continued on <u>next page</u>



HICCOUGHS REFERENCES CONTINUED

- Dahlin CM, Cohen AK. Dysphagia, xerostomia, and hiccoughs. 4th ed. ed. Betty R. Ferrell NC, and Judith Paice, editor. Oxford Medicine Online: Oxford University Press; 2015. 51 p.
- 7. Management of Hiccoughs [Internet]. Medical College of Wisconsin. 2013.
- 8. Agnes Calsina-Berna GG-G, Jesus Gonzalez-Barboteo,, Porta-Sales aJ. Treatment of Chronic Hiccoughs in Cancer Patients: A Systematic Review2012; 15(10).
- 9. Emily Chai DM, Jane Morris, and Suzanne Goldhirsch. Hiccoughs. Emily Chai DM, Jane Morris, and Suzanne Goldhirsch, editor. Oxford Medicine Online: Oxford University Press; 2014. 7 p.
- 10. Marinella MA. Diagnosis and management of hiccoughs in the patient with advanced cancer. J Support Oncol. 2009;7(4):122-7, 30.
- 11. Moretti R, Torre P, Antonello RM, Ukmar M, Cazzato G, Bava A. Gabapentin as a drug therapy of intractable hiccup because of vascular lesion: a three-year follow up. Neurologist. 2004;10(2):102-6.
- 12. Lee GW, Kim RB, Go SI, Cho HS, Lee SJ, Hui D, et al. Gender Differences in Hiccup Patients: Analysis of Published Case Reports and Case-Control Studies. J Pain Symptom Manage. 2016;51(2):278-83.
- 13. Choi TY, Lee MS, Ernst E. Acupuncture for cancer patients suffering from hiccoughs: a systematic review and meta-analysis. Complement Ther Med. 2012;20(6):447-55.
- 14. Potter J, Hami F, Bryan T, Quigley C. Symptoms in 400 patients referred to palliative care services: prevalence and patterns. Palliat Med. 2003;17(4):310-4.
- 15. Porzio G, Aielli F, Verna L, Aloisi P, Galletti B, Ficorella C. Gabapentin in the treatment of hiccoughs in patients with advanced cancer: a 5-year experience. Clin Neuropharmacol. 2010;33(4):179-80.
- Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: relationship to age, gender, and performance status in 1,000 patients. Support Care Cancer. 2000;8(3):175-9.
- Mercadante S, Porzio G, Valle A, Fusco F, Aielli F, Adile C, et al. Orphan symptoms in advanced cancer patients followed at home. Support Care Cancer. 2013;21(12):3525-8.

Hiccoughs references continued on next page



HICCOUGHS REFERENCES CONTINUED

- 18. Ripamonti C, Fusco F. Respiratory problems in advanced cancer. Support Care Cancer. 2002;10(3):204-16.
- 19. Kang JH, Bruera E. Hiccoughs during Chemotherapy: What Should We Do? J Palliat Med. 2015;18(7):572.
- 20. Clinical Practice Guidelines: Hiccoughs [Internet]. VCH Community Palliative Care. 2007.
- Arishima H, Kikuta K. [Disseminated metastatic tumor at dorsal surface of medulla oblongata presenting intractable hiccoughs. A case report]. Rinsho Shinkeigaku. 2011;51(4):279-81.
- 22. Lewis JH. Hiccoughs: causes and cures. J Clin Gastroenterol. 1985;7(6):539-52.
- 23. Phillips RA. The management of hiccoughs in terminally ill patients. Nurs Times. 2005;101(31):32-3.
- 24. Wilcock A, Twycross R. Midazolam for intractable hiccup. J Pain Symptom Manage. 1996;12(1):59-61.
- 25. Moretto EN, Wee B, Wiffen PJ, Murchison AG. Interventions for treating persistent and intractable hiccoughs in adults. Cochrane Database Syst Rev. 2013(1):CD008768.
- 26. Launois S, Bizec JL, Whitelaw WA, Cabane J, Derenne JP. Hiccup in adults: an overview. Eur Respir J. 1993;6(4):563-75.
- Krakauer EL, Zhu AX, Bounds BC, Sahani D, McDonald KR, Brachtel EF. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 6-2005. A 58-year-old man with esophageal cancer and nausea, vomiting, and intractable hiccoughs. N Engl J Med. 2005;352(8):817-25.
- 28. FRIEDGOOD CE, RIPSTEIN CB. Chlorpromazine (thorazine) in the treatment of intractable hiccoughs. J Am Med Assoc. 1955;157(4):309-10.
- 29. McAllister RK, McDavid AJ, Meyer TA, Bittenbinder TM. Recurrent persistent hiccoughs after epidural steroid injection and analgesia with bupivacaine. Anesth Analg. 2005;100(6):1834-6.
- 30. Howard RS. Persistent hiccoughs. BMJ. 1992;305(6864):1237-8.

Hiccoughs references continued on <u>next page</u>



HICCOUGHS REFERENCES CONTINUED

- 31. Tegeler ML, Baumrucker SJ. Gabapentin for intractable hiccoughs in palliative care. Am J Hosp Palliat Care. 2008;25(1):52-4.
- 32. Scotland HI. Scottish Palliative Care Guidelines. Scotland: NHS Scotland; 2014.
- 33. Scotland N. Scottish Palliative Care Guidelines2014 [cited 2016 12/15/2016]. Available from: <u>http://www.palliativecareguidelines.scot.nhs.uk/guidelines/</u> <u>symptom-control/Nausea-and-Vomiting.aspx</u>.
- 34. Turkyilmaz A, Eroglu A. Use of baclofen in the treatment of esophageal stentrelated hiccoughs. Ann Thorac Surg. 2008;85(1):328-30.
- 35. Hassen GW, Singh MM, Kalantari H, Yemane-Merriwether S, Ferrante S, Shaw R. Persistent hiccoughs as a rare presenting symptom of pulmonary embolism. West J Emerg Med. 2012;13(6):479-83.
- 36. Walker P, Watanabe S, Bruera E. Baclofen, a treatment for chronic hiccup. J Pain Symptom Manage. 1998;16(2):125-32.
- 37. Martínez Rey C, Villamil Cajoto I. [Hiccup: review of 24 cases]. Rev Med Chil. 2007;135(9):1132-8.
- 38. Smith HS, Busracamwongs A. Management of hiccoughs in the palliative care population. Am J Hosp Palliat Care. 2003;20(2):149-54.
- 39. Katsinelos P, Pilpilidis J, Xiarchos P, Christodoulou K, Papagianis A, Amperiadis P, et al. Baclofen therapy for intractable hiccoughs induced by ultraflex esophageal endoprosthesis. Am J Gastroenterol. 2000;95(10):2986-7.
- 40. Zhang C, Zhang R, Zhang S, Xu M. Baclofen for stroke patients with persistent hiccoughs: a randomized, double-blind, placebo-controlled trial. Trials. 2014;15:295.
- 41. Woelk CJ. Managing hiccoughs. Can Fam Physician. 2011;57(6):672-5, e198-201.
- 42. Brostoff JM, Birns J, Benjamin E. The "cotton bud technique" as a cure for hiccoughs. Eur Arch Otorhinolaryngol. 2009;266(5):775-6.
- 43. De Ruysscher D, Spaas P, Specenier P. Treatment of intractable hiccup in a terminal cancer patient with nebulized saline. Palliat Med. 1996;10(2):166-7.

Hiccoughs references continued on <u>next page</u>



HICCOUGHS REFERENCES CONTINUED

- 44. De Lima L, Bennett MI, Murray SA, Hudson P, Doyle D, Bruera E, et al. International Association for Hospice and Palliative Care (IAHPC) List of Essential Practices in Palliative Care. J Pain Palliat Care Pharmacother. 2012;26(2):118-22.
- 45. Seker MM, Aksoy S, Ozdemir NY, Uncu D, Civelek B, Akıncı MB, et al. Successful treatment of chronic hiccup with baclofen in cancer patients. Med Oncol. 2012;29(2):1369-70.
- 46. Ramírez FC, Graham DY. Treatment of intractable hiccup with baclofen: results of a double-blind randomized, controlled, cross-over study. Am J Gastroenterol. 1992;87(12):1789-91.
- 47. Mirijello A, Addolorato G, D'Angelo C, Ferrulli A, Vassallo G, Antonelli M, et al. Baclofen in the treatment of persistent hiccup: a case series. Int J Clin Pract. 2013;67(9):918-21.
- 48. Guelaud C, Similowski T, Bizec JL, Cabane J, Whitelaw WA, Derenne JP. Baclofen therapy for chronic hiccup. Eur Respir J. 1995;8(2):235-7.
- 49. Tay SS, Yadav RR. Novel use of baclofen in cancer patients for the treatment of hiccoughs. Ann Acad Med Singapore. 2010;39(2):154.
- 50. Steger M, Schneemann M, Fox M. Systemic review: the pathogenesis and pharmacological treatment of hiccoughs. Aliment Pharmacol Ther. 2015;42(9):1037-50.
- 51. Thompson DF, Brooks KG. Gabapentin therapy of hiccoughs. Ann Pharmacother. 2013;47(6):897-903.
- 52. Kang JH, Hui D, Kim MJ, Kim HG, Kang MH, Lee GW, et al. Corticosteroid rotation to alleviate dexamethasone-induced hiccup: a case series at a single institution. J Pain Symptom Manage. 2012;43(3):625-30.
- 53. Sharma RC. Successful treatment of idiopathic intractable hiccup with baclofen and supportive treatment: a case report. J Neuropsychiatry Clin Neurosci. 2015;27(1):e62-3.
- 54. Chou CL, Chen CA, Lin SH, Huang HH. Baclofen-induced neurotoxicity in chronic renal failure patients with intractable hiccoughs. South Med J. 2006;99(11):1308-9.
- 55. required) s. Micromedex [Available from: <u>www.micromedexsolutions.com</u>.

Hiccoughs references continued on next page



HICCOUGHS REFERENCES CONTINUED

- 56. Twycross R, Wilcock A, Dean M, Kennedy B. Canadian Palliative Care Formulary. Canadian Edition ed: palliativedrugs.com; 2010.
- 57. Takeda. Pantoloc (pantoprazole sodium). Oakville, ON: Takeda Canada Inc.; 2013. p. 18.
- 58. Hernandez SL, Fasnacht KS, Sheyner I, King JM, Stewart JT. Treatment of Refractory Hiccoughs with Amantadine. J Pain Palliat Care Pharmacother. 2015;29(4):374-7.
- 59. Wilcox SK, Garry A, Johnson MJ. Novel use of amantadine: to treat hiccoughs. J Pain Symptom Manage. 2009;38(3):460-5.
- 60. Rizzo C, Vitale C, Montagnini M. Management of intractable hiccoughs: an illustrative case and review. Am J Hosp Palliat Care. 2014;31(2):220-4.
- 61. Gardecki J, Espinosa J, Lucerna A, Bernhardt J. A case of singultus: Avoiding a hiccup in care. Am J Emerg Med. 2016.
- 62. Lee GW, Oh SY, Kang MH, Kang JH, Park SH, Hwang IG, et al. Treatment of dexamethasone-induced hiccup in chemotherapy patients by methylprednisolone rotation. Oncologist. 2013;18(11):1229-34.
- 63. Rousseau P. Hiccoughs in terminal disease. Am J Hosp Palliat Care. 1994;11(6):7-10.
- 64. Neuhaus T, Ko YD, Stier S. Successful treatment of intractable hiccoughs by oral application of lidocaine. Support Care Cancer. 2012;20(11):3009-11.
- 65. Thompson AN, Ehret Leal J, Brzezinski WA. Olanzapine and baclofen for the treatment of intractable hiccoughs. Pharmacotherapy. 2014;34(1):e4-8.
- Alderfer BS, Arciniegas DB. Treatment of intractable hiccoughs with olanzapine following recent severe traumatic brain injury. J Neuropsychiatry Clin Neurosci. 2006;18(4):551-2.
- 67. Matsuki Y, Mizogami M, Shigemi K. A case of intractable hiccoughs successfully treated with pregabalin. Pain Physician. 2014;17(2):E241-2.
- 68. Vandemergel X, Mbeufet M, Renneboog B. Intractable hiccoughs successfully treated with pregabalin. Eur J Intern Med. 2006;17(7):522.
- 69. Nicoletti F, Gradini R, Bassi PF, Rampello L. Lyrica cures the tenor. Clin Neuropharmacol. 2009;32(2):119.

Hiccoughs references continued on <u>next page</u>



HICCOUGHS REFERENCES CONTINUED

- 70. Vaidya V. Sertraline in the treatment of hiccoughs. Psychosomatics. 2000;41(4):353-5.
- 71. Health F. Symptom Guidelines: Hospice Palliative Care, Clinical Practice Committee; 2006 [Available from: <u>http://www.fraserhealth.ca/health-professionals/</u> <u>professional-resources/hospice-palliative-care/</u>]