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"Hiccups" with COVID-19 Management

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Abstract

Hiccups, medically referred as singultus, is a condition that results from involuntary contraction of the diaphragm and intercostal muscles. Singultus is usually a self-limiting condition which typically lasts less than 48 hours but in rare cases, can persist greater than 48 hours. This is a case of a 48 year-old male who was prescribed dexamethasone for COVID-19 but developed intractable singultus for two weeks. Patient was unable to tolerate diet due to intractable singultus leading to vomiting. He underwent various non-pharmacological maneuvers and pharmacotherapy without resolution. Dexamethasone- induced hiccups have been reported as an under recognized side effect of dexamethasone. Despite discontinuation of offending agent, patient’s singultus persisted. The patient achieved resolution of singultus with a combination of baclofen and olanzapine. This case provides additional literature during this COVID-19 pandemic while dexamethasone is being used as the first line management.

Keywords

COVID-19, COVID, Dexamethasone, SARS-COV-2, Corona, Virus, Coronavirus, hiccups, singultus

Conflict of Interest Statement

There are no conflict of interest with this case report.

Cover Page Footnote

Authors would like to thank the patient for permission to write this case.

CASE REPORT

"Hiccups" with COVID-19 Management☆

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Abstract

Hiccups, medically referred as singultus, is a condition that results from involuntary contraction of the diaphragm and intercostal muscles. Singultus is usually a self-limiting condition which typically lasts less than 48 h but in rare cases, can persist greater than 48 h. This is a case of a 48 year-old male who was prescribed dexamethasone for COVID-19 but developed intractable singultus for two weeks. Patient was unable to tolerate diet due to intractable singultus leading to vomiting. He underwent various non-pharmacological maneuvers and pharmacotherapy without resolution. Dexamethasone-induced hiccups have been reported as an under recognized side effect of dexamethasone. Despite discontinuation of offending agent, patient's singultus persisted. The patient achieved resolution of singultus with a combination of baclofen and olanzapine. This case provides additional literature during this COVID-19 pandemic while dexamethasone is being used as the first line management.

Keywords: COVID-19, COVID, Dexamethasone, SARS-COV-2, Corona, Virus, Coronavirus, Hiccups, Singultus

1. Case presentation

A 48-year-old male with no significant past medical history initially presented to the Emergency Department (ED) with a dry cough. Symptoms were highly suspicious for COVID-19 and testing returned a positive result. The patient was not hypoxic and was discharged to home with dexamethasone, though the reasoning for this prescription in the absence of hypoxia is unclear from the record. Patient returned to the ED five days later with persistent dry cough and new symptoms of heartburn and singultus. He was thought to have gastritis causing singultus and was discharged with famotidine. Once again, one week later, he presented to the ED with complaints of fever, chills, myalgia, and persistent hiccups. He was instructed to finish his course of dexamethasone and was discharged to home again as he was not hypoxic. He returned three days later with shortness of breath, cough, nausea, vomiting, and persistent hiccups. On this visit, patient was dyspneic and tachypneic, requiring two liters of supplemental oxygen and was admitted.

At the time of admission, the patient had grossly normal lab results, except for an elevated d-dimer. CTA chest showed bilateral infiltrates but no pulmonary embolism. Prior to this admission, patient had been taking dexamethasone as an outpatient for two weeks. The decision was made to continue dexamethasone at 6 mg and Remdesevir as patient was now hypoxic. The patient's singultus was so severe it caused vomiting and he was unable to tolerate a diet. He was given a trial of chlorpromazine 25 mg on the first day, without improvement. He tried various physical maneuvers including breath holding, Valsalva maneuver, pressing on eye orbits, and drinking water without improvement. On the second day, metoclopramide 10 mg was tried without effect. Upon further investigation, dexamethasone-induced singultus was suspected as dexamethasone was the only new medication prescribed and, at baseline, the patient was on no home medications. The patient also recalled his hiccups temporally started shortly after he began the course of dexamethasone, but was he unclear on the exact timing. Thus, dexamethasone was discontinued.

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On the third day, the patient's hiccups persisted despite discontinuation of dexamethasone and trial of baclofen 5 mg was initiated. The next day the patient reported mild improvement on hiccups but continued to have difficulty tolerating oral intake. The baclofen was increased to 10 mg TID and olanzapine 5 mg BID was added. Following the first dose of combined baclofen and olanzapine, complete resolution of singultus was achieved. With resolution of the hiccups, patient no longer required supplemental oxygen. Patient was observed for 24 h without singultus recurrence and was discharged with 10 days of baclofen and olanzapine. Two weeks after discharge, the patient was contacted and reported no recurrence of singultus.

2. Discussion

Hiccups, medically referred to as singultus, is a condition that results from involuntary contraction of the diaphragm and intercostal muscles.[1] Singultus is usually a self-limiting condition which typically lasts less than 48 h but in rare cases, can persist for greater than 48 h. Dexamethasone induced hiccup has been reported as an under recognized condition. Various etiologies of singultus have been reported including central nervous system disorders, vagus or phrenic nerve irritation, medication-induced, toxic-metabolic, and psychogenic.[2–6] This case report identified medication-induced hiccups, most specifically dexamethasone. The pathophysiology of singultus involves the hiccup reflex arc which consists of afferent limb, central nervous system, and efferent limb. Dopamine and gamma-aminobutyric acid (GABA) neurotransmitters have been documented in involvement of central nervous system of the hiccup reflex arc.[7] It has been proposed that dexamethasone decreases the threshold for synaptic transmission in the midbrain resulting in hiccups.[8] The exact pathophysiology and other factors associated with steroid-induced hiccups remain unclear.

In order to treat singultus, both non-pharmacological and pharmacological cases have been reported. Non-pharmacological interventions such as holding breath and Valsalva maneuver have been documented.[9] These maneuvers increase the efferent vagal activity leading to negative feedback of reflex arc involving phrenic and vagal nerve to inhibit diaphragm contraction.[9,10]

The only drug approved by US Food and Drug Administration for hiccups is chlorpromazine. It is believed that chlorpromazine works by blocking the dopamine receptors in the central nervous system. When an approved drug is ineffective, other pharmacotherapy should be considered. Based on a number of studies baclofen, metoclopramide, and gabapentin have shown the most improvement of hiccups, though, again, these drugs are not approved for this indication.[11] Baclofen and gabapentin are GABA analogs, and metoclopramide blocks dopamine receptors affecting the hiccup reflex arc. Olanzapine is a serotonin antagonist, thus possibly leading to the inhibition of the "serotonin augmenting phrenic motor−neuronal activity reflex arcs involved in the generation of hiccups within the spinal cord."[12] Furthermore, olanzapine has a dopamine antagonist effect contributing to the inhibition of the hiccup reflex arc.[13] In this patient, these medications were ineffective but the combination of baclofen and olanzapine resulted in resolution based on a case report of successful treatment in intractable hiccups.[14] It is possible that the combination of a GABA, serotonin, and dopamine antagonist contributed to the resolution of intractable singultus in this patient.

3. Conclusion

Typically, hiccups are a benign condition which can become detrimental if it continues to persist for days. As the use of dexamethasone has increased during the COVID-19 pandemic, it is important to identify potential adverse effects. When refractory hiccups are observed in a patient taking dexamethasone, a combination of baclofen and olanzapine can be considered as an alternative pharmacotherapy.

Conflict of interest

There are no conflict of interest with this case report.

References

1. Cole Justin A, Plewa Michael C. *"Singultus."* *StatPearls*. PubMed: StatPearls Publishing; 2021. http://www.ncbi.nlm.nih.gov/books/NBK538225/.
2. Park MH, Kim BJ, Koh SB, Park MK, Park KW, Lee DH. Lesional location of lateral medullary infarction presenting hiccups (singultus). *J Neurol Neurosurg Psychiatr*. 2005;76(1):95−98. https://doi.org/10.1136/jnnp.2004.039362. PubMed Central.
3. Payne BR, Tiel RL, Payne MS, Fisch B. Vagus nerve stimulation for chronic intractable hiccups. Case report. *J Neurosurg*. 2005;102(5):935−937. https://doi.org/10.3171/jns.2005.102.5.0935. PubMed.
4. Renes SH, van Geffen GJ, Rettig HC, Gielen MJ, Scheffer GJ. Ultrasound-guided continuous phrenic nerve block for persistent hiccups. *Reg Anesth Pain Med*. Oct. 2010;35(5):455−457. https://doi.org/10.1097/aap.0b013e3181e8536f. PubMed.
5. Calsina-Berna A, Gracia-Gomez G, Gonzalez-Barboteo JG, Porta-Sales J. Treatment of chronic hiccups in cancer patients: a systematic review. *J Palliat Med*. Oct. 2012;15(10):1142−1150. https://doi.org/10.1089/jpm.2012.0087. PubMed.

6. Theohar Carl, Patrick McKegney F. Hiccups of psychogenic origin: a Case report and review of the literature. *Compr Psychiatr*. 1970;11(4):377–384. https://doi.org/10.1016/0010-440X(70)90220-8. ScienceDirect.
7. Lee G, Oh SY, Kang MH, Kang JH, Park SH, Hwang IG, et al. Treatment of dexamethasone-induced hiccup in chemotherapy patients by methylprednisolone rotation. *Oncol*. Nov. 2013;18(11):1229–12234. https://doi.org/10.1634/theoncologist.2013-0224. PubMed Central.
8. Chang Full-Young, Lu Ching-Liang. Hiccup: mystery, nature and treatment. *J Neurogastroenterol Motil*. 2012;18(2):123–130. https://doi.org/10.5056/jnm.2012.18.2.123. PubMed Central.
9. Petroianu Georg A. Treatment of hiccup by vagal maneuvers. *J Hist Neurosci*. 2015;24(2):123–136. https://doi.org/10.1080/0964704X.2014.897133. PubMed.
10. Steger M, Schneemann M, Fox M. Systemic review: the pathogenesis and pharmacological treatment of hiccups. *Aliment Pharmacol Ther*. 2015;42(9):1037–1050. https://doi.org/10.1111/apt.13374.
11. Polito NB, Fellows SE. Pharmacologic interventions for intractable and persistent hiccups: a systematic review. *J Emerg Med*. 2017;53(4):540–549.
12. Schmid K, Bohmer G, Merkelbach S. Serotonergic control of phrenic motoneuronal activity at the level of the spinal cord in the rabbit. *Neurosci Lett*. 1990;116:204–209.
13. Stegmeier-Petroianu A, Petroianu G. Hiccups and dopamine. *AJPH (Am J Public Health)*. 2008;65:2092–2094.
14. Thompson AN, Ehret LJ, Brzezinski WA. Olanzapine and baclofen for the treatment of intractable hiccups. *Pharmacotherapy*. 2014;34(1):e48. https://doi.org/10.1002/phar.1378.