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Background & Pathophysiology

Hiccups, or singultus, are involuntary contractions of the diaphragm, intercostal muscles, and glottis triggered by activation of the phrenic-diaphragmatic reflex. (1)

Hiccups are classified by their duration: Acute (<48 hrs); persistent (>48 hrs); intractable (>30 days). (1)

Persistent and intractable hiccups are listed in the National Organization for Rare Diseases (NORD).

- Rare disorders are diseases or conditions that affect fewer than 200,000 Americans. (2)

Mechanism: (1,3)

Firing of the phrenicdiaphragmatic reflex triggers a hiccup.

Treatment: (3)

Treat underlying etiology, if known. **Empiric treatment:**

- PPIs
- Baclofen, gabapentin
- Acupuncture, hypnosis, psychotherapy
- Phrenic nerve block, vagal nerve stimulation

Hypothesis:

Osteopathic manipulative treatment (OMT) will reduce the frequency of intractable hiccups by addressing somatic dysfunctions in regions anatomically associated with the phrenic-diaphragmatic reflex arc (hiccup reflex).



The hiccup reflex arc is comprised of three limbs: (1) The afferent limb (phrenic, vagus, and sympathetic nerves (T6-T12)), which projects to (2) central processing centers (spinal cord (C3-C5), medulla oblongata, and midbrain structures), which coordinate (3) the efferent limb (phrenic, recurrent laryngeal, and intercostal nerves), which produce coordinated muscle contractions. Irritation at any limb of this reflex-arc can produce a hiccup. Figure adapted from Steger et. al. (3).

IRB Approval and Citations

- 1. Rouse S, Wodziak M. Intractable Hiccups. Curr Neurol Neurosci 2018;18(8):51. 2. "H.R. 4013 — 107th Congress: Rare Diseases Act of 2002." www.GovTrack.us.
- 2002. April 30, 2023 https://www.govtrack.us/congress/bills/107/hr4013
- 3. Steger M, Schneemann M, Fox M. Systemic review: the pathogenesis and pharmacological treatment of hiccups. Aliment Pharm Therap 2015;42(9):1037– 50.

This study was reviewed and approved by the Institutional Review Board (IRB) at Michigan State University (MSU), under study number 00007900.

conditions.

Eligibility submitted by patient.

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OMT as Treatment for Intractable Hiccups: A Case Series

Methods & Study Design

Patient Recruitment: Patients 18 and older with intractable hiccups were recruited through physician offices, online postings, and flyers placed on and around MSU's campus. **Exclusion Criteria**: Fractures, lymphoma/leukemia, rheumatoid arthritis, and other

Symptom Tracking: Hiccups and associated symptoms were tracked via digital surveys for seven days before and after treatment.

OMT Administration: One OMT session was administered by a licensed osteopathic physician following a comprehensive medical history and osteopathic examination. Treatment sessions took place at the MSU Department of Osteopathic Manipulative Medicine.

OMT Modalities: High-velocity, low-amplitude (HVLA) techniques were not used.

Study Timeline:





Figure 1. Total Number of Hiccups Before and After by Patient. Total number of hiccups recorded over a 7-day period before and after treatment for each study participant. Welch's t-test was performed to compare the total number of hiccups before and after treatment for each participant, as it does not assume equal variances. Statistically significant differences (p < 0.05) are indicated with p-values above the brackets.

Average Number of Daily Hiccups Among All Participants Before and After OMT



Treatment

Figure 2. Average Number of Daily Hiccups Among All Participants Before and After OMT. Average number of daily hiccups recorded among all participants for the 7-days before and after osteopathic manipulative treatment (OMT). The bars represent the mean daily hiccups, with error bars indicating confidence intervals. A two-sided independent t-test was performed to compare the average number of daily hiccups before and after treatment. Statistically significant differences (p < 0.05) are indicated with exact p-values inside the brackets.

Patient Demographics, Medical History, & Somatic Dysfunctions

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Region	Dysfunction
Sex	F	F	F	F	F	Cranial	-
Age	18	20	28	19	21	C1	++++
Duration	1 vear	3.5 years	4 months	2 vears	5 vears	C2	++
						C3	++
Assoc. Symptoms	Belching, stomach pain	Reflux, nausea	Belching	N/A	N/A	C4	+
						C5	+++
Triggers	Eating, drinking	Eating, exercise	Spicy food	Eating, drinking, stress	Eating, drinking, stress, excitement, alcohol	C 6	+
						C7	++++
						Rib 1	++++
Pattern	20 + daily, with occasional exacerbations	After meals	After meals	Episodes of 1-5 hiccups	1-3 per hour	T1	-
						T2	_
						Rib 3	+
						Т3	+
РМН	Leg length discrepancy	Tendonitis of both knees	Knee pain	Anxiety, anemia, vertigo	Depression, anxiety, PMDD, GERD, ADHD	T4	-
						Rib 5	+
						T5	++
PSH	Tonsillectomy (8 years old)	N/A	Wisdom teeth removed (22 years old)	N/A	Ureter surgery (infant), adenectomy & tonsillectomy (11 years old)	Rib 6	+
						Т6	++
						T7	++++
						T8	++
						Т9	+++
Meds	Lexapro 50 mg, OCP	N/A	Adderall XR 10 mg & IR 5 mg, Nexplanon implant	Fluoxetine 40 mg	Adderall XR 15 mg	T10	++
						T11	++
						T12	++
						L1	+++
Social Hx	Alcohol, occasional cigarette	Caffeine, alcohol	Caffeine, alcohol	No drug or alcohol use	Caffeine, alcohol,	L2	-
						L3	++
					marijuana	L4	++
Family Hx	N/A	Paternal eosinophilic esophagitis & colon polyps	N/A	N/A	Depression, skin cancer	L5	++++
						Sacrum	++++
						Diaphragm/ Celiac Ganglion	++++
emographic an	d Clinical Charact	eristics of Patients (Lef	t) Table 2. Somatic	Dysfunction Find	ings Among Patients (Right)	Gangilon	
phic and clinica e table includes	l characteristics of s information on a	f the five patients in thage, duration of hiccur	nis Somatic dysfunct os, study. Each "+"	ions by region ar sign indicates th	nong the five patients in thine number of patients who	Pelvis	+++
a symptoms, PMH), past su	triggers, hiccup rgical history (PS	patterns, past medic SH), medications, soc	ial exhibited dysfun ial indicates no soma	ction in the spe atic dysfunctions	ecified region. The "-" signed were found.	UE	++
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Key Takeaways:

Table 1: All participants were young women. Eating and drinking were common triggers for hiccups. Associated symptoms were gastrointestinal in nature.

Table 2: Most patients had somatic dysfunctions in regions linked to the hiccup reflex arc, including C1 (vagal nerve), C5 (phrenic nerve), lower thoracic (sympathetic nerves), and the diaphragm and celiac ganglion (sympathetic hub).

Conclusion

Safe & Effective Treatment: These results strongly suggest that OMT can be an effective treatment for reducing the severity of intractable hiccups.

Mechanism Based Treatment: The treatment is mechanistically motivated, as many of the somatic dysfunctions found were in regions associated with the hiccup reflex arc, including the cervical spine, thoracic regions, diaphragm, and celiac ganglion.

Prevalence: The study indicates that intractable hiccups may not be as rare as previously thought; five patients were identified and enrolled within a two-year period, all within the greater Lansing area.

Future Directions

Expand Sample Size: Future studies should aim to increase the sample size to enhance the generalizability of these findings. Extended Tracking: Track hiccup frequency and associated symptoms over a longer period, both before and after OMT, to provide more comprehensive data on the treatment's efficacy.

Multiple Treatments: Employ multiple treatments over the course of days or weeks to test whether hiccup frequency would fall even further.

Self-Placebo Trial Design: Implement a self-placebo trial design, where patients are randomly assigned to receive either placebo/sham or treatment first, followed by the opposite, to control for placebo effects and strengthen the validity of the results. Multiple Locations: Conduct studies at multiple locations to increase the diversity of the participant pool and further improve generalizability of these findings.



Let's connect!



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