

Original Article

The Effect of Gender Differences in Protracted Hiccups

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ABSTRACT

Background: Although little importance is attached to hiccups, they may be associated with several diseases. The purpose of this study was to investigate the effects of gender differences on types of hiccups and the relation with diseases involved in the etiology. **Materials and Methods:** Patients presenting to the Kirikkale University Medical Faculty Hospital with hiccups were investigated retrospectively. Patients' age, sex, duration of hiccups, additional diseases, advanced imaging results, laboratory tests, and clinical follow-up were recorded. Patients were divided into two groups; Group transient hiccup (TH) consisted of subjects with a duration of hiccups less than 48 h, and Group protracted hiccup (PH) of patients with a duration exceeding 48 h. The Chi-square test was used for comparisons, and $P < 0.05$ were regarded as significant. **Results:** Eighty-four patients were enrolled, 44.1% ($n = 37$) in Group TH, and 55.9% ($n = 47$) in Group PH. Male patients comprised 67.5% ($n = 25$) of Group TH and 89.4% ($n = 42$) of Group PH ($P = 0.027$). The conditions most associated with hiccups were gastrointestinal system (GIS) diseases. Correlation was determined between GIS diseases and male gender ($P = 0.034$), no relation between other system diseases and gender. Correlation was determined between GIS diseases and protracted hiccups ($P = 0.037$), but no relation between other system diseases and type of hiccups. **Conclusion:** Protracted hiccups are more common in males. This gender variation applies particularly to hiccups of GIS origin.

KEYWORDS: *Gastrointestinal system, gender, hiccup, male*

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INTRODUCTION

Hiccup is an involuntary, intermittent, and spasmodic contraction of the diaphragm and intercostal muscles that many people experience at least once in their lives.^[1] These contractions are uncomfortable and may number between 4 and 60/min.^[1,2] Hiccups may lead to problems such as malnutrition, dehydration, weight loss, insomnia, listlessness, mental stress, and a decreased quality of life, and maybe a precursor of diseases involving several systems.^[3,4] Hiccups generally assume the form of transient attacks not exceeding 48 h. Attacks exceeding that duration are considered as protracted hiccups. Those exceeding 48 h are classified as “persistent,” and those exceeding 1 month as “intractable.”^[5-7] Transient attacks generally derive from causes such as alcohol intake, stress, excitement, excessive and fast eating, spicy foods, and gastric distension, while persistent/intractable hiccups

may derive from several diseases of different organs and systems.^[1,6,8] To be able to diagnose these diseases, pathologies of the gastrointestinal system (GIS), central nervous system (CNS), cardiovascular system, and the thorax should particularly be investigated, and various causes of vagus or phrenic nerve or diaphragmatic irritation should be considered, in addition to bleeding, thrombus, mass, infection, and toxic and metabolic causes.^[1,6,8-11] Few of these causes may be known in patients presenting to the emergency department with hiccups. However, identification and treatment of underlying causes are of the utmost importance.^[1,9,12] Detailed history, physical examination,

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and investigation accompanied by appropriate tests should, therefore, be performed in cases presenting with protracted (persistent/intractable) hiccups.^[8] Although hiccups have frequently been observed in elderly men in previous studies, the cause of hiccups and the relation between types of hiccups and gender are still unclear.^[3,10]

The purpose of this study was to investigate the effects of gender differences on type of hiccups and the relation with diseases involved in the etiology.

MATERIALS AND METHODS

Study design

Following receipt of Ethical Committee Approval (No. 2017-20/01), this retrospective study was performed with patients presenting to the Kirikkale University Medical Faculty Emergency Department due to hiccups between January 1, 2013, and January 1, 2018.

Patient evaluation and group constitution

All data were obtained from the hospital computer system and archive records. ICD-10 code “R.06.6” was investigated to identify patients presenting with hiccups. Patients’ demographic data (age, sex, body weight, height, history of disease, drugs used, duration of hiccups, numbers of attacks or recurrences, number of hospital presentations due to hiccups, and treatments administered), physical examination findings, laboratory results, polyclinic records, chest X-ray findings, and confirmed endoscopy, computerized tomography, and magnetic resonance imaging reports were recorded. Patients were divided into two groups based on duration of hiccups, and were also investigated regarding whether the causes originated from the CNS or not (non-CNS).

- Group TH: Duration of hiccups <48 h (transient hiccups)
- Group PH: Duration of hiccups >48 h (protracted hiccups).

Patients undergoing advanced diagnostic tests at other health centers after discharge from the emergency department, not attending follow-up visits, with missing data or aged under 18 were excluded from the study.

Statistical analysis

Statistical analysis was performed on SPSS 21.0 (IBM SPSS Statistics 21.0, IBM Corporation, Armonk, NY, USA) software. Normality of data was evaluated using the Shapiro–Wilk test. Parametric data were expressed as the mean \pm standard deviation, and categorical variables as number (n) and percentage (%). The Chi-square test was used for comparisons between the groups. Relations between age and sex in the groups were analyzed using analysis of ANOVA. Values of $P < 0.05$ were considered as statistically significant.

RESULTS

Two hundred and thirty-nine patients with hiccups were identified during the study period. One hundred and fifty-five patients meeting the exclusion criteria were subsequently excluded, and the study was completed with 84 patients. Duration of hiccups attack was <48 h in 44.1% ($n = 37$) of patients, between 48 h and 1 month (persistent) in 36.9% ($n = 31$), and longer than 1 month (intractable) in 19% ($n = 16$). Accordingly, Group TH contained 44.1% ($n = 37$) of patients, and Group PH 55.9% ($n = 47$) [Table 1].

The mean age of all patients was 52.2 ± 21.3 years (range: 19–84). Mean age in Group TH was 51.2 ± 22.8 , and mean age in Group PH was 52.9 ± 20.2 ($P = 0.601$). Men constituted 79.8% ($n = 67$) of all patients, 67.5% ($n = 25$) of those in Group TH, and 89.4% ($n = 42$) of those in Group PH ($P = 0.027$). The mean age of the women in the total patient group was 41.7 ± 19.7 years and that of the men 54.8 ± 20.9 years. Mean ages in Group TH were 54.7 ± 23.2 years for men and 43.9 ± 20.9 for women ($P = 0.180$). Mean ages in Group PH were 54.9 ± 19.8 years for men and 36.4 ± 17.1 for women ($P = 0.042$). Analysis of the relation between types of hiccups and gender revealed that protracted hiccups were more common in men ($P = 0.027$) [Table 1].

The most common cause of hiccups was GIS diseases ($n = 39$), followed by psychiatric diseases ($n = 35$) and neurological diseases ($n = 19$). In addition, 89.8% ($n = 35$) of GIS diseases involved gastritis and gastroesophageal reflux disease (GERD). Eighteen patients with hiccups had diagnoses of cancer; 27.8% ($n = 5$) were newly diagnosed cancer patients, and 22.2% ($n = 4$) were receiving chemotherapy for cancer treatment. CNS-related causes of hiccups were determined in 46.4% ($n = 39$) of patients, and nonCNS-related causes in 53.6% ($n = 45$). No difference was determined between hiccups types (groups TH

Table 1: Age and gender data of hiccup patients

	Mean \pm SD			<i>P</i>
	Group PH (<i>n</i> =37)	Group TH (<i>n</i> =47)	Total (<i>n</i> =84)	
Age (year)	51.2 \pm 22.8	52.9 \pm 20.2	52.2 \pm 21.3	0.601
Male	54.7 \pm 23.2 [†]	54.9 \pm 19.8*	54.8 \pm 20.9	0.180 [†]
Female	43.9 \pm 20.9 [†]	36.4 \pm 17.1*	41.7 \pm 19.7	0.042*
Gender, <i>n</i> (%)				
Male	25 (67.5)	42 (89.4)	67 (79.8)	0.027
Female	12 (32.5)	5 (10.6)	17 (20.2)	0.027

PH=Protracted hiccups, TH=Transient hiccups, SD=Standard deviation

Table 2: Distribution of causes associated with hiccups and polyclinic presentations

Groups	Diseases related hiccups	Diagnosis		Total, n (%)
		New, n (%)	Old, n (%)	
Group CNS	Neurological diseases (n=19)			
	Cerebrovascular hematoma and infarct	3 (15.8)	13 (68.4)	16 (84.2)
	Parkinson disease	-	1 (5.3)	1 (5.3)
	Epilepsia	-	2 (10.5)	2 (10.5)
	Neurosurgical diseases (n=7)			
	Arteriovenous malformation	2 (28.6)	-	2 (28.6)
	Subdural hematoma (operated)	1 (14.3)	-	1 (14.3)
	Epidural hematoma (operated)	1 (14.3)	-	1 (14.3)
	Intracranial mass (operated)	1 (14.3)	-	1 (14.3)
	Epilepsi (after cancer or hematoma surgery)	2 (28.6)	-	2 (28.6)
	Psychiatric diseases (n=35)			
	Anxiety disorder	4 (11.4)	13 (37.1)	17 (48.6)
	Depression	3 (8.6)	15 (42.9)	18 (51.5)
	GIS disease (n=39)			
	Gastritis, and GERD	9 (23.1)	26 (66.7)	35 (89.8)
	Peptic ulcer (including <i>Helicobacter pylori</i> eradication therapy)	2 (5.1)	2 (5.1)	4 (10.2)
	Respiratory system (n=18)			
	Chronic obstructive pulmonary disease	2 (11.1)	9 (50)	11 (61.1)
	Interstitial lung disease	-	4 (22.2)	4 (22.2)
	Obstructive sleep apnea syndrome	2 (11.1)	1 (5.5)	3 (16.6)
	Oncological diseases (n=18)			
	Cancer presence before hiccup (without chemotherapy)	-	9 (50)	9 (50)
	Cancer presence before hiccup (with chemotherapy)	-	4 (22.2)	4 (22.2)
Presence of newly diagnosed cancer, and enlarged lymph nodes	5 (27.8)	-	5 (27.8)	
Group non-CNS	Endocrinological diseases (n=15)			
	Diabetes mellitus (hyperglycemia)	-	12 (80)	12 (80)
	Hypothyroidism	1 (6.7)	2 (13.4)	3 (20)
	Others (n=45)			
	CAD (including myocardial infarction)	2 (4.4)	7 (15.6)	9 (20)
	Atrial fibrillation	1 (2.2)	2 (4.4)	3 (6.6)
	Patient with ICD	1 (2.2)	-	
	Food related (aerofagia, gastric distension)	4 (8.9)	-	4 (8.9)
	Alcohol use	2 (4.4)	-	2 (4.4)
	Obesity	-	2 (4.4)	2 (4.4)
	Chronic renal failure	-	1 (2.2)	1 (2.2)
	Drugs (cisplatin, dexamethasone, opiates)	4 (8.9)	-	4 (8.9)
	Polyclinic presentations			
	Gastroenterology			58 (28.9)
	Psychiatry			34 (16.9)
Neurology			29 (14.4)	
Pulmonary diseases			18 (8.9)	
Oncology			17 (8.5)	
Other (thoracic surgery, endocrinology, neurosurgery, cardiology, and ENT)			51 (25.4)	

GERD=Gastroesophageal reflux disease, ICD=Implantable cardioverter defibrillator; CAD=Coronary artery disease; ENT=Ear, nose, and throat; CNS=Central nervous system; GIS=Gastrointestinal system

and PH) regarding whether or not causes were CNS-related ($P = 0.337$) [Table 2].

At analysis of relations between diseases causing hiccups and gender, the correlation was observed between GIS diseases and male gender ($P = 0.034$), but

none was determined between other system diseases and gender [Table 3]. Examination of the relation between diseases causing hiccups and types of hiccups revealed a correlation between GIS diseases and types of hiccups ($P = 0.027$), but not with other system diseases [Table 4].

Table 3: Correlation between diseases responsible for hiccups and gender

Disease related to hiccups	Male (n=67), n (%)	Female (n=17), n (%)	P
GIS diseases	39 (58.2)	5 (29.4)	0.034
Psychiatric diseases	21 (31.3)	5 (29.4)	0.878
CNS diseases	12 (17.9)	4 (23.5)	0.598
Respiratory system diseases	12 (17.9)	1 (5.9)	0.059
CVS diseases	17 (25.4)	3 (17.6)	0.504
Neoplasm	14 (20.9)	2 (11.8)	0.392

CNS=Central nervous system; GIS=Gastrointestinal system;
CVS=Cardiovascular system

Table 4: Correlation between diseases responsible for hiccups and hiccup types

Disease related to hiccups	Group 1 (n=37), n (%)	Group 2 (n=47), n (%)	P
GIS diseases	11 (29.8)	26 (55.3)	0.037
Psychiatric diseases	8 (21.6)	18 (38.3)	0.153
CNS diseases	8 (21.6)	8 (17.1)	0.780
Respiratory system diseases	6 (16.2)	6 (12.8)	0.757
CVS diseases	10 (27.1)	10 (21.3)	0.610
Neoplasm	5 (13.5)	11 (23.4)	0.279

CNS=Central nervous system; GIS=Gastrointestinal system;
CVS=Cardiovascular system

DISCUSSION

Our results show that protracted hiccups are more common in men and are closely associated with GIS diseases. Previous studies of hiccups have reported no relation between transient hiccup attacks and gender, and that protracted hiccups generally occur in men.^[8,9,13-15] Liaw *et al.* reported that men constituted 76.5% of patients under monitoring due to hiccups. In their study, the great majority of which consisted of patients with long-term hiccups, Cymet reported a male gender rate of 91%.^[11,13] Lee *et al.* performed perhaps the most comprehensive investigation of the relation between hiccups and gender and reported a male gender dominance of 90%.^[9] The incidence of hiccups is lower in women than in men, and onset is also later.^[8,9] Male patients comprised 789.8% of patients in our study. The predominance of male gender was pronounced in both short-term and long-term hiccups and was particularly statistically significant in protracted hiccups. Variation was also determined between the sexes regarding age. Mean age in women was lower than that in men, and the age difference between the sexes was particularly statistically significant in protracted hiccups. These findings are compatible with previous studies reporting a predominance of the male gender, and also provide new information showing that protracted hiccups are more common among older men.

Irrespective of duration, hiccups is an uncomfortable symptom that generally derives from the GIS.^[1] Cymet also reported that hiccups frequently derives from the GIS, and that most patient consultations involve the Gastroenterology Department.^[11] GIS-related hiccups may derive from simple causes such as excessive or rapid eating, spicy foods, or aerophagia, or from fatal diseases such as cancers of the GIS. Gastritis, GERD, and peptic ulcer are the patients of the main focus on this subject.^[1,8] Cabane *et al.* emphasized the importance of GERD in the development of hiccups and showed that the condition could be resolved in these patients with antacid or proton pump inhibitor use.^[5] Orr *et al.* in their study reported that hiccups were triggered by acid overproduction caused by *Helicobacter pylori*, erosion of esophageal mucosa, and vagal irritation.^[16] This association between hiccups and the GIS may also be linked to the gender factor. Studies have reported that the development of hiccups in male gender is not associated with diseases involving the (CNS) and that hiccups derive from non-CNS causes. In women, the situation is different, and hiccups have been linked to such diseases of the CNS as neuromyelitis optica.^[9] Rey *et al.* focused on GERD, reporting that this condition caused hiccups in 7.9% of women and 10% of men.^[17] Several diseases previous linked to hiccups were present in our patients. These may include diseases of the CNS such as Parkinson's disease and cerebrovascular hemorrhage/stroke, oncological diseases with or without chemotherapy (cisplatin and dexamethasone), and psychiatric diseases such as anxiety disorder and depression. However, GIS diseases, and particularly gastritis and GERD, were present in a large proportion of cases. Discharged patients were also determined to subsequently present most frequently to the Gastroenterology Department. In addition, when we examined the relation between these causes of hiccups and gender and type of hiccups, we determined an association between GIS diseases and both male gender and protracted hiccups. Our findings are compatible with previous studies showing that hiccups in men derive from nonCNS causes, and are important in showing that they derive from the GIS.

Limitations

There are some limitations to this study. The first is the study's retrospective nature. Second, since hiccups are frequently overlooked as a symptom, these patients' ICD codes may have been entered with different diagnoses, and patients' reports may not have been entirely accurate. Third, no patients presenting to the emergency department due to hiccups subsequently underwent polyclinic follow-up (particularly those with complete resolution after transient attacks), and this may have

affected the case number, and thus the statistical analysis results.

CONCLUSION

Protracted hiccups are more common in men. This gender difference also applies to GIS-related hiccups. Further prospective studies are needed to confirm our findings.

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Conflicts of interest

There are no conflicts of interest.

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