

CLINICAL RESEARCH

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Clinical Features, Risk Factors, and Endoscopic Treatment of Bezoars: A Retrospective Analysis from a Single Center in Northern China

[Stat Data nuscr Lit Fu	Study Design A Data Collection B istical Analysis C Interpretation D ipt Preparation E terature Search F ands Collection G	ABDF 2,3 BC 1 DF 1	Lei Wang* Shu-juan Jia Peng Wang	P.R. China 2 Department of Urology, Peking University Shougang Hospital, Beijing, P.R. China 3 Peking University Wujieping Urology Center, Peking University Health Science Center, Beijing, P.R. China
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	Back Material/A	kground: Aethods:	The aims of this study were to summa lyze the effectiveness and safety of the From January 2015 to February 2020, 7	ize the clinical characteristics and risk factors for bezoars and to ana- endoscopic treatment of bezoars. 5 of the 23 950 patients who underwent gastroscopic examination in
			our medical center were diagnosed wi collected retrospectively and analyzed.	h bezoars. Clinical and treatment information for these patients was
		Results:	The detection rate of bezoars was 0.31 th alcohol consumption, hypertension, dia thorn and persimmon. Abdominal pain zoars, while gastric mucosa erosion (90 scopic examination. Six patients with b rate for bezoars treated by gastroscopic apeutic effect of bezoars include patien than 9 cm were significantly more likely er than 9 cm (P <0.001).	6. Risk factors included the time of year (autumn and winter seasons), ibetes, and residing in the Mentougou district, which is rich in haw- (90.7%) and bloating (80.0%) were common clinical symptoms of be- .7%) and gastric ulcers (60%) were common manifestations on endo- ezoars were successfully discharged after drug treatment. The success i lithotripsy was 94.2% (65/69 patients). The factors affecting the ther- t age (<i>P</i> =0.025) and bezoar size (<i>P</i> =0.042). Patients with bezoars larger to have intestinal obstructions than were patients with bezoars small-
Conclusions:			Bezoars mainly occur in elderly patients most common in hawthorn and persimr zoars in general, but intestinal obstruct	with diseases such as gastrointestinal dyspraxia and diabetes, and are non producing areas. Endoscopic treatment is safe and effective for be- ion should be considered for bezoars larger than 9 cm.
	MeSH Ke	ywords:	Bezoars • Esophagitis, Peptic • Gastr	oscopes • Helicobacter pylori • Intestinal Obstruction
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Background

Bezoars are congregations or compact masses that are formed by the accumulation of matter, especially indigestible materials, including high-fiber vegetables, hair, and certain pharmaceutical agents [1]. The earliest report on bezoars was made by Tondreau and Kirklin in 1950 [2]. Phytobezoars are a seasonal disease, with a high incidence in autumn and winter. The prevalence of bezoars varies among ethnic groups and geographic locations. The occurrence rate of phytobezoars, the most common type of bezoars, are mostly reflective of food cultures. Many cases of persimmon phytobezoars have been reported in regions where residents frequently consume fresh and dried persimmons, such as South Korea, Japan, and Israel [3,4].

According to their composition, bezoars are divided into 4 categories: phytobezoars, trichobezoars, pharmacobezoars, and lactobezoars. Bezoars have important clinical value because they are associated with complications such as bloating, pain, nausea, and vomiting. Hawthorn, persimmon, and some other foods are rich in tannic acid and pectin. When tannic acid comes in contact with gastric acid, it forms an insoluble tannic acid protein, and pectin forms a gel with the gastric acid to bond the precipitated tannic acid protein and form a phytobezoar [5]. Trichobezoars contain hair, lactobezoars contain milk, and pharmacobezoars contain pharmaceutical products. Bezoars have a close relationship with abnormal gastric function, which could be caused by conditions including diabetes, indigestion, hypothyroidism, *Helicobacter pylori* infection, and high gastric acid [5,6].

The treatment of bezoars includes drug therapy, gastroscopic therapy, and surgical treatment. The primary drugs used for bezoar treatment are antacids, sodium bicarbonate, and Traditional Chinese Medicine (TCM). In recent years, with the continuous improvement of endoscopic techniques and instruments, reports of endoscopic lithotripsy have gradually increased, and it has become the mainstream treatment for bezoars. The principle behind this method is to perform the lithotripsy with a series of endoscopic instruments including biopsy forceps, toothed forceps, polyp traps, basket catheters, argon ion coagulation devices, and electrohydraulic lithotripsy equipment [7]. Smaller bezoars can be crushed so that they can be discharged. Larger bezoars require multiple trap cuttings. Surgical treatment is mainly applicable for patients with bleeding, perforation, and intestinal obstruction [8].

There are many studies on the types of bezoars and their complications, but few studies have focused on the endoscopic treatment, surgical treatment, and risk factors for bezoars. This study retrospectively analyzed the clinical data of patients with bezoars to explore possible risk factors and their relationship with *H. pylori* and reflux esophagitis. The study also analyzed the data of patients with bezoars who underwent surgical operations after gastroscopic therapy, to explore the possible risk factors for intestinal obstruction caused by bezoars.

Material and Methods

Patients who underwent gastroscopy in our gastroenterology center from January 2015 to February 2020 were enrolled in the study. Clinical information including symptoms, complications, gastroscopic data, treatment, and prognosis was retrospectively analyzed. All patients signed an informed consent form, and the study received ethical approval from the Peking University Shugang Hospital.

Experienced endoscopists used an Olympus CF-H260Ai gastroscope to make clear diagnoses of bezoars and perform endoscopic lithotriptic therapy. An amount of 10 mL of oral lidocaine slurry was given to the patients before gastroscopy.

After admission, the patients were first given 250 mL of 5% sodium bicarbonate orally 5 times, and the following day, the patients with bezoars were treated with endoscopic lithotripsy, including trap cutting, biopsy forceps crushing, and bicarbonate injection. Patients with intestinal obstruction after endoscopic lithotripsy were transferred to the surgical department for surgery.

Statistical analysis

SPSS 22.0 statistical software was used for the analysis. The t test was used to analyze measurement data, the chi-square test was used to analyze counting data, and one-way and multivariate analysis of variance were used for risk factor analysis. P<0.05 was considered to be statistically significant.

Results

Baseline characteristics

During the 5-year study period, gastroscopy was performed in a total of 23 950 patients, and bezoars were found in 75 patients (0.31%), of which 34 were men and 41 were women (male: female ratio,1: 1.2). Patients ranged between 21 and 84 years (53.4 \pm 16.7 years), and included 4 young patients (\leq 40 years), 15 middle-aged patients (40–60 years), and 56 elderly patients (\geq 60 years). Patients' average body mass index (BMI) was 24.2. Of the 75 patients with bezoars, 68 (90.7%) came to our center in either autumn or winter. Regarding geographical distribution, 42 of the 75 bezoar patients (56%) came from the Mentougou district, a mountainous suburban area of Beijing City, which is rich in hawthorns and persimmons. Based on the patients' habits of eating persimmon and hawthorn, and the typical appearance of phytobezoars under gastroscopy, we estimated that 75 bezoars were phytobezoars. Of the 75, there were 50 patients who consumed only hawthorns, 14 who consumed only persimmons, 6 who consumed both fruits, and 5 who consumed only date-plum persimmons.

Clinical manifestations

Many possible risk factors were analyzed, and the results showed that of all the patients who underwent gastroscopy examination, patients with bezoars had a higher rate of concomitant disease, such as hypertension (66.7% vs. 50%, P=0.004) and diabetes (61.3% vs. 32%, P<0.001), than patients without bezoars. Patients with bezoars also had a higher rate of alcohol consumption than did patients without bezoars (42.7% vs. 28.2%, P=0.005).

The clinical symptoms of patients with bezoars included abdominal pain (68/75, 90.7%), nausea (40/75, 53.3%), and vomiting (32/75, 42.7%), and were similar to those of patients without bezoars. Bloating was the only symptom that occurred more often in patients with bezoars (60/75, 80%) than in patients without bezoars (7879/23 875, 33%, P<0.001). Patient demographic characteristics and potential risk factors are shown in Table 1.

Gastroscopy results

Most bezoars were singular (66/75, 88%), 43 of 75 bezoars (57.3%) were between 5 and 9 cm; 6 of 75 bezoars (8%) were larger than 9 cm; and the largest bezoar measured $10 \times 8 \times 12$ cm. Thirty-five of the 75 bezoars (46.7%) were located in the mucus lake of the gastric body. The patients with bezoars had various complications, with gastric mucosa erosion being the most common (68/75, 90.7%). The details are shown in Table 2.

Bezoars and H. pylori

Since *H. pylori* infection and gastroesophageal reflux are often associated with bezoars, we calculated the differences of these 2 factors between the patients with bezoars and the patients without bezoars. The rate of positive *H. pylori* results in patients with bezoars was 56% (42/75), which was significantly higher than that in patients without bezoars (5672/23 875, 23.9%, *P*<0.001). Likewise, the prevalence of reflux esophagitis was 26.7% (20/75) in patients with bezoars, which was significantly higher than that of patients without bezoars (2 887/23 875, 12.1%, *P*<0.001). The prevalence of *H. pylori* and reflux esophagitis in women with bezoars was higher than that in men (*P*=0.002 and *P*=0.018, respectively). There was no significant difference in age or BMI between the 2 groups. The details are shown in Table 3.

Treatment measures

In this study, 75 patients were given sodium bicarbonate orally for 1 day and then underwent gastroscopy. Among them, 6 patients had no bezoar at the time of gastroscopy, and 65 patients successfully underwent gastroscopic lithotripsy. However, 4 patients of the 65 had an intestinal obstruction after gastroscopic lithotripsy and needed surgical treatment. An intestinal incision and removal of the foreign bodies were performed in the general surgical department. Postoperatively, the intestinal obstruction was relieved, and the patients were cured and discharged from the hospital. All 4 patients had bezoars larger than 9 cm. The mean diameter of the bezoars in patients who underwent surgery was greater than that of patients who underwent successful endoscopic lithotripsy (P=0.042). The patient age in the group with failed lithotripsy requiring surgery was higher than that of the successful lithotripsy group (P=0.025) (Table 4). Among all patients, 6 patients had bezoars larger than 9 cm, and 4 of the 6 patients had an intestinal obstruction after endoscopic lithotripsy. Bezoars ≥ 9 cm was a risk factor for intestinal obstruction (P<0.001). The clinical information of the 4 patients is shown in Tables 4 and 5.

Follow-up

Of the 75 patients in this study who were contacted for follow-up, 62 of them were reached. None of the 62 patients had eaten hawthorn or persimmon since bezoar removal, and upon follow-up examination with a gastroscope or abdominal computed tomography, no bezoars were found.

Discussion

The earliest surgical treatment of bezoars can be traced back to 1951. Kemeny et al. reported on the radiological and endoscopic diagnosis of bezoars as well as surgical treatment [9]. For a long period, surgery was the standard treatment for bezoars. In 1998, Ladas et al. reported the first stone extraction by laparoscopic gastrotomy [5], which initiated the stone extraction program of the minimally invasive era. In recent years, with the continuous improvement of endoscopic techniques and instruments, reports of endoscopic lithotripsy have increased, and it has gradually become the mainstream treatment for bezoars. The principle behind this method is to perform the lithotripsy with a series of endoscopic instruments, including biopsy forceps, toothed forceps, polyp traps, basket catheters, argon ion coagulation devices, and electrohydraulic lithotripsy equipment [4]. Because of the limitations of the equipment used in that approach, the main method Table 1. Patient demographic characteristics.

	Bezoar	n (%)	Non-bezoa	ur n (%)	Р
Age	53.4±2	16.7	54.2±1	16.5	0.42
≤40y	4	(5.3)			
40–60y	15	(20)			
≥60y	56	(74.7)			
Sex					0.70
Male	34	(45.3)	10 299	(43.1)	
Female	41	(54.7)	13 576	(56.9)	
Time					<0.001
January to June	7	(9.3)	12 415	(52)	
July to December	68	(90.7)	11 460	(48)	
Risk factors					
Smoking	21	(28)	9763	(40.9)	0.023
Alcohol	32	(42.7)	6725	(28.2)	0.0050
Hypertension	50	(66.7)	11 937	(50)	0.0040
Diabetes	46	(61.3)	7640	(32)	<0.001
Chronic heart disease	26	(34.7)	6775	(28.4)	0.23
Hyperlipidemia	40	(53.3)	10 446	(43.8)	0.10
Peptic ulcer	30	(40)	7500	(31.4)	0.11
Gastrectomy	8	(10.7)	1547	(6.5)	0.14
Depression	7	(9.3)	2100	(8.8)	0.87
Symptoms					
Abdominal pain	68	(90.7)	20 771	(87.0)	0.35
Nausea	40	(53.3)	16 240	(68.0)	0.0060
Vomiting	32	(42.7)	11 221	(47.0)	0.45
Acid reflux	23	(30.7)	10 743	(45.0)	0.01
Bloating	60	(80)	7879	(33.0)	<0.001
Heartburn	25	(33.3)	6923	(29.0)	0.41
Black stools	5	(6.7)	3231	(13.5)	0.082
District					0.033
Shijingshan	20	(26.7)	9550	(40)	
Mentougou	42	(56)	10 028	(42)	
Other	13	(17.3)	4297	(18.4)	

of the current study was the use of a trap gravel. One of the most important factors affecting the success rate of lithotripsy is the size of the bezoar. The success rate of lithotripsy in the current study was 94.2%, higher than the success rate of 89.7% reported by Park et al. [10]. For patients with bezoars <9 cm in the current study, sodium bicarbonate was used to soften the bezoar before gastroscopy, and the bezoar was made as small as possible during the lithotripsy process, which might have improved the success rate. In this study, 6 patients were treated with oral sodium bicarbonate to soften the gastroliths and promote the expulsion of bezoars before endoscopic treatment.

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Table 2. Clinical and endoscopic findings of the 75 bezoars.

	n	%
Number		
Single	66	88
Multiple	9	12
Size		
≤5 cm	26	34.7
5–9 cm	43	57.3
≥9 cm	6	8
Location		
Stomach body	35	46.7
Lower GI tract	26	34.7
Other	14	18.7
Complications		
Single ulcer	25	33.3
Multiple ulcer	20	26.7

	n	%	
Bleeding	7	9.3	
Obstruction	3	4	
Erosion	68	90.7	
Esophagitis	20	26.7	
Stage A	13	17.3	
Stage B	6	8	
Stage C	1	1.3	
Effect			
Success by GL	65	86.7	
Surgery after GL	4	5.3	
Success by drug	6	8	
H. pylori			
Positive	42	56	
Negative	33	44	

GI – gastrointestinal; GL – gastroscopic lithotripsy.

Table 3. Helicobacter pylori and reflux esophagitis in patients with bezoars.

	Bezoar	Non-bezoar	Р
Helicobacter pylori	56.0% (42/75)	23.9% (5672/23 875)	<0.001
Age	59.0±10.0	61.0±12.0	0.067
BMI	25.3±3.7	22.7±4.2	0.15
Male: Female	10: 32	2722: 2950	0.0020
Reflux esophagitis	26.7% (20/75)	12.1% (2887/23 875)	<0.001
Age	60.0±12.0	53.0±14.0	0.21
BMI	26.2±3.9	23.2±4.1	0.35
Male: Female	4: 16	1343: 1544	0.018

BMI - body mass index.

 Table 4. Bezoars treated by gastroscopic lithotripsy.

	Success	Fail	Р
Number	94.2% (65/69)	5.8% (4/69)	
Age	53.9±12.1	62.0 <u>±</u> 4.2	0.025
Size	5.4±1.5	9.5 <u>±</u> 0.6	0.042
Male: Female	29: 36	1: 3	0.442
Diabetes	66.2% (43/65)	75% (3/4)	0.72

No.	Diameter of bezoar (cm)	Gastroscope time (min)	Time to ileus (days)	Outcome
1	9	23	2	Good
2	9	24	3	Good
3	10	39	4	Good
4	10	29	3	Good

Table 5. Patients requiring surgery after gastroscopic lithotripsy.

Bezoar formation is a disorder of the digestive system with a relatively low morbidity rate of 0.07% to 0.4% [11]. Consuming too much hawthorn, date-plum persimmon, kelp, pomegranate, wheat shell, and other foods that contain tannic acid will cause phytobezoars [12]. In 1978, Kadian et al. reported a bezoar detection rate of 0.43% in 1400 patients [13]. We found a detection rate of 0.31% in patients who underwent gastroscopic examination, similar to the detection rate of 0.2% reported in the study by Zhang et al. [14]. Mihai et al. reported a detection rate of 0.068% [11]. Gokbulut et al. found that the detection rate of bezoars can reach as high as 0.9% [15]. As patients in these studies had different habits of consuming hawthorn and persimmon, and each study was a singlecenter trial, the detection rates of bezoars are also different. However, all of these studies warn that middle-aged and older people with lower gastrointestinal motility are susceptible to bezoars, and women who consume large amounts of hawthorn and persimmon have a higher rate. In this study, most of the patients with bezoars came from western Beijing, especially the Mentougou area, which is a hawthorn and persimmon producing area with local residents who are keen to eat these fruits. In terms of onset time, in the current study, the incidence rate during the second half of the year was significantly higher than that of the first half of the year (P < 0.001).

In this study, we found that alcohol consumption, hypertension, and diabetes can be risk factors for bezoars. One study showed that 61.3% of patients with bezoars had a history of diabetes, and the patients with diabetes had a 5% to 12% rate of gastroparesis complications [16]. Gastroparesis can reduce peristole and induce the formation of gastrocalculus. In addition, gastric acid secretion is decreased in patients with diabetes, which might also give rise to the formation of bezoars. Further, mental disorders, such as anxiety and depression, might lead to gastrointestinal dysfunction, thus promoting the formation of bezoars [17,18].

This study revealed that the most common clinical symptoms of patients with bezoars were abdominal pain and distension, which is in agreement with the study results of Ji et al. [12]. In the current study, the location of the bezoars was mostly in the gastric body (46.7%, 35/75). Iwamuro et al. reported that among 31 patients, 29 had bezoars in the stomach [19], and Park et al. revealed that 32 of 39 patients had bezoars in the gastric body [10]. Peptic ulcer is the most common complication induced by bezoars. In the current study, the incidence rate of peptic ulcers was 60%. In the study by Iwamuro et al., the incidence of ulcers was 52.9% [4]. In a study including 17 patients with bezoars, Lee et al. found that 41.2% of the patients had peptic ulcers [20]. In the study by Masaya et al., the incidence of bezoars with ulcers was 64.5% [19], which was similar to the results of the current study. Ulcer formation is related to the compression of gastric mucosa by bezoars and the long-term exposure of damaged gastric mucosa to gastric acid.

Other reports have suggested that bezoars are related to reflux esophagitis. The results of the current study showed that the proportion of patients with bezoars and reflux esophagitis was 26.7%. The prevalence of reflux esophagitis in patients with bezoars was higher than that in patients without bezoars, and the difference was statistically significant. The reason can be that the presence of bezoars destroys the integrity of the mucosal structure and increases the pressure in the stomach. The infection rate of H. pylori for patients with bezoars was 56% (42/75), which was higher than that of patients without bezoars, which was 23.9% (5672/23 875). According to the current study, this might have been because H. pylori infection affects the secretion of gastric acid and gastric mobility and then participates in the formation of bezoars, which agrees with the results of Zhang et al. [14]. H. pylori infection can cause chronic inflammation of the gastric mucosa, thus leading to stomach anomalies [21]. Corinaldesi et al. supposed that H. pylori is related to delayed gastric emptying [22]. However, Testoni et al. concluded that H. pylori infection does not affect gastric emptying [23], while other scholars have different opinions. For example, Liang reported that peptic ulcers followed by bezoars has no clear relationship to H. pylori infection, but H. pylori can affect the healing of ulcers and treatment in the late stage [24].

The reported success rate for endoscopic treatment of bezoars has improved in recent studies, increasing from 71.5% to 100% [25]. In the current study, 4 patients developed intestinal obstructions after endoscopic lithotripsy. Upon analyzing the specific causes of bezoar incarceration in the small intestine, it was found that 3 patients had a history of diabetes and constipation, and their gastrointestinal motility was slow, which may have led to intestinal obstruction. Therefore, endoscopic treatment of bezoars over 9 cm should be performed with caution, especially in patients with diabetes mellitus and gastrointestinal dyspnea.

This was a single-center, retrospective study with certain limitations. To further clarity the etiology and pathogenesis of bezoars, animal experiments should be conducted. For the treatment of bezoars larger than 9 cm, the cure rate of gastroscopy can be further enhanced by improving the gastroscopic equipment, among other measures.

In this retrospective study, we found that most of the patients with bezoars had consumed hawthorn and persimmon. Alcohol consumption, hypertension, and diabetes can be risk factors for bezoars. We also found a significant increase in the prevalence of *H. pylori* infection and reflux esophagitis in patients with bezoars. Generally, lithotripsy under gastroscopy yielded satisfactory results in treating bezoars, but the possibility of intestinal obstruction should be considered for patients with stones \geq 9 cm. This study is one of the most comprehensive

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summaries of clinical and gastroscopy research to date, and the first to study the relationship among bezoars, reflux esophagitis, and *H. pylori* infection.

Conclusions

The main cause of bezoars in the present study was the consumption of hawthorn and persimmon. The onset time was mostly in the seasons when hawthorn and persimmon were ripe, during the second half of the year. Possible risk factors for bezoars include alcohol consumption, hypertension, and diabetes. The main manifestations of bezoars were abdominal pain and bloating, and the main complications were gastric mucosa erosion and ulceration. In addition, the prevalence of *H. pylori* and reflux esophagitis was significantly increased in patients with bezoars. In terms of treatment, most patients can be successfully treated by gastroscopic lithotripsy, but for bezoars ≥ 9 cm, the difficulty of performing this procedure is increased, and the risk of intestinal obstruction is significantly increased.

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