



## The Effect of Hyoscine on Pain, Tenderness, and Rebound Tenderness in Patients with Appendicitis: Quasi-Interventional Study

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### ABSTRACT

**Objective:** To evaluate the effect of hyoscine on pain and tenderness, rebound tenderness and appendicitis patients before surgery and this study can be considered as the first study investigated the efficacy of hyoscine on pain, tenderness, and rebound tenderness in patients with appendicitis.

**Methods:** In this single-group, prospective interventional study (before-after) according to inclusion and exclusion criteria, 70 patients with pain in the right lower abdomen and typical symptoms of appendicitis were evaluated and after surgery, diagnostic accuracy was examined by pathologic results. The pain was evaluated before and after administration of hyoscine by numerical and verbal examination. Tenderness and rebound tenderness were also determined.

**Results:** The mean age of patients was  $26.81 \pm 7.66$ . Totally, 42 patients (60%) had reduction in pain, 50 patients (71% percent) had reduction in tenderness, and 39 (55%) had reduction in rebound tenderness after treatment with the drug. A statistically significant reduction of pain and tenderness, rebound tenderness was observed in all of men after administration of hyoscine ( $p < 0.001$ ) but in women, the reduction of severity of tender results was only significant ( $p = 0.002$ ). Data analysis in women and men together showed the significant reduction of pain, tenderness, and rebound tenderness ( $p < 0.001$ ).

**Conclusion:** According to the results, hyoscine can reduce pain, tenderness, and rebound tenderness. So, it seems that hyoscine is a good candidate for patients with appendicitis.

**Trial registration number:** IRCT2015111825123N1

**Keywords:** Appendicitis; Scopolamine hydrobromide; Pain; Appendectomy; Surgery.

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## Introduction

Studies revealed that acute abdominal pain is one of the most common patients' complaints in different societies. Acute appendicitis is the most common cause of acute abdomen in the world which can be easily treated by emergency surgery. Appendicitis is caused by the obstruction of the inside (lumen) of the appendix due to various causes [1-3]. Once this obstruction occurs, the lumen becomes filled with mucus and swells. This continued production of mucus leads to increased pressure within the lumen and the walls of the appendix. The causative agents include fecalitis, lymphoid hyperplasia, infections, and tumors [1-3]. This problem affects so many people and is more common in male [2,3].

Classically, pain and tenderness as main symptom of the disease are mostly found in all cases. There is moderate and constant pain without stopping in periumbilical hernia and then after a few hours, pain transfers to lower and right area of the abdomen. The hypersensitivity of the pain is about 80%. The patients move very cautiously and bend their knees toward their chest to experience less pain. Alvarado is the most common criterion for evaluating appendicitis in the world. The other important criteria are pain, tenderness, and rebound tenderness. Although the clinical examinations and laboratory methods have contributed to diagnosis, there are problems in diagnosis and management of the disease and in many cases the misdiagnosis leads to negative appendectomy [3, 4]. One leading reason for misdiagnosis of the disease is using drugs which change the patient's main clinical manifestation. For example, using drugs such as morphine relieves pain; however, disrupts the process of scoring the severity of the appendicitis by the surgeon and even, in some cases, may lead to death of the patient. On the other hand, reducing pain is one of the most important physicians' tasks in the treatment of patient.

Hyoscine also known as scopolamine is an antispasmodic drug that blocks acetylcholine at parasympathetic sites and has antispasmodic effect on organs with smooth muscle. Therefore, it can be indicated to treat many diseases including colitis, diverticulitis, stomach cramps, biliary colic, invasive diagnostic procedures such as colonoscopy, dysmenorrhea, and colic. Hyoscine is extracted from *Duboisia* plants. It crosses the blood-brain barrier and doesn't have any effect on the level of consciousness [5-7].

The effectiveness of this drug for treating abdominal pain can be due to interaction of the drug with muscarinic receptors which caused antispasmodic effect and improved spasms or cramps, especially in the digestive track. Generally, nowadays the primary usage of this drug for treating abdominal pain is non-specific [8, 9]. Regarding high prevalence of acute appendicitis and lack of proper medicines to control the pain induced by this disease (without changing

the signs and symptoms), this study attempted to investigate the efficacy of hyoscine as a new agent on pain, tenderness, and rebound tenderness in patients with appendicitis.

## Materials and Methods

### *Design and Setting*

This single-group, prospective interventional study (before-after) was conducted on 70 patients 18- 60 years' old who were candidates for appendicitis surgery (according to Alvarado score) and referred to Shahid Sadoughi and Shahid Rahnemon hospitals, Yazd, Iran, 2016. The patients were selected in a nonrandom manner (convenience sampling). This research was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences. All patients were announced about the probable drug side effects and we did not perform any additional invasive procedures. A written consent form was obtained from all patients. The purpose of the study was explained to the patients. All patients' information remained confidential and ethical issues related to human studies (according to the Helsinki Statement) were considered. The trial was registered with the Iranian Clinical Trials Registry (IRCT registration number: IRCT2015111825123N1). No placebo group was considered as there was no expectation to reduce the pain without analgesics. Exclusion criteria of the current study were as follows: taking any psychiatric medicine, lesions on the abdominal surface such as cellulite, scars, taking analgesic drugs before entering the emergency room, any type of hernia related to abdomen, history of kidney stones, current urinary infection, history of trauma on the area during last two weeks, menstrual bleeding, drug addiction, and sensitivity to hyoscine.

### *Procedure and Data Collection*

First, demographic information including age and sex was obtained. To establish appendicitis diagnosis of surgery candidates, patients' pain, tenderness (pressing over the tender spot), and rebound tenderness (pressing over the tender spot and then suddenly removing it) were evaluated using numeric rating scale by emergency medicine resident and the data was recorded. Then 0.3 mg/kg of hyoscine (OSVE-HYOSCINE-N-BUTYL BROMIDE, Ampoule, Manufactured in Iran by OSVAH Pharma. CO. Tehran) was administered slowly intravenously. After drug administration, all patients underwent the direct supervision of emergency medicine resident. Using the previous method, tenderness, rebound tenderness and pain were remeasured by emergency medicine resident fifteen minutes after drug administration and the data was recorded. Regarding the possibility of negative appendectomy or other diagnoses, we decided to investigate just the patients that were diagnosed with appendicitis by pathologist. Finally, appendicitis in 70 patients'

appendicitis was confirmed by pathologist.

**Statistical Analysis**

The sample volume was set at 59, considering type I error of 0.05 and type II error of %10 (power=0.9) which was increased to 70 to enhance the validity of the study results.

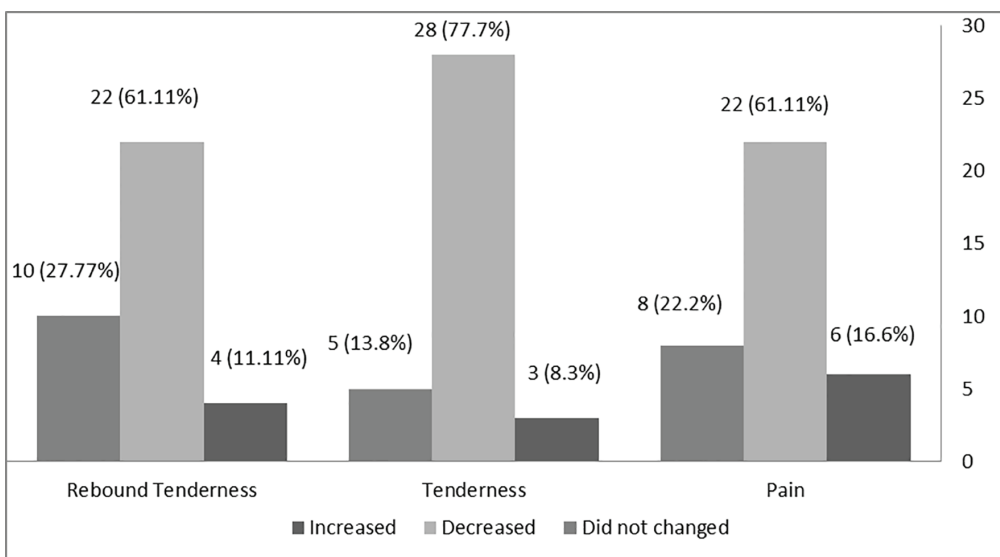
$$n = \frac{\left( z_{1-\frac{\alpha}{2}} + z_{1-\beta} \right)^2 \sigma_{\delta}^2}{\delta^2} + \frac{z_{1-\frac{\alpha}{2}}^2}{2}$$

Mean and standard deviation (SD) for quantitative variables and frequency (percentage) for qualitative variables were calculated. Statistical analysis was performed using SPSS version 16.0. (Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc.) and running independent T-test and paired T-tests. The level of significance was considered 0.05 in this study.

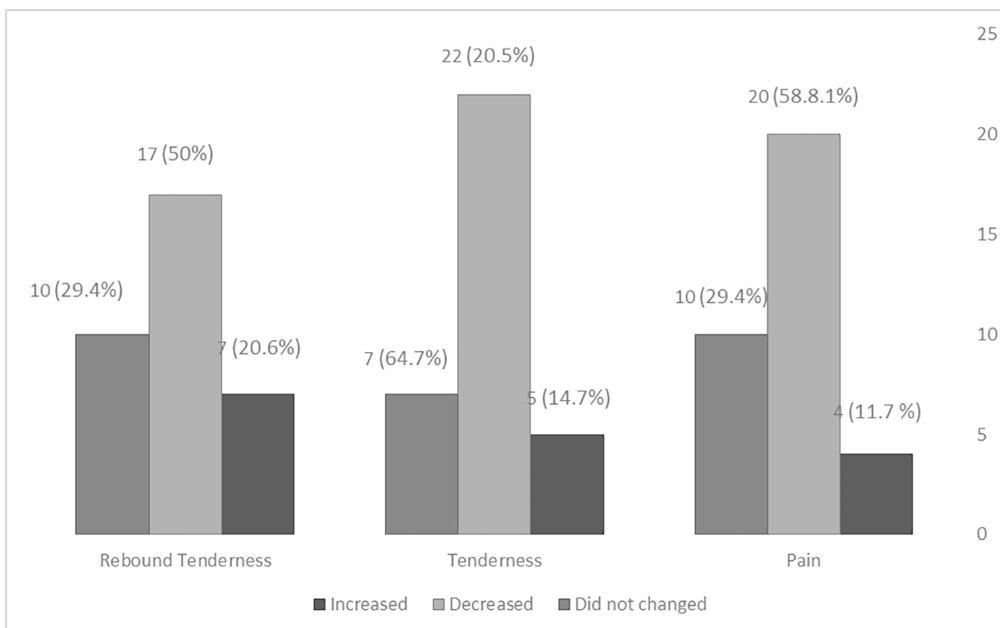
**Results**

Thirty-six patients (51.4 %) were male and 34 patients (48.6%) were female. The mean age of patients was 26.81±7.66. After hyoscine administration to males, pain in 22 patients (61.11%), tenderness in 28 patients (77.7%), and rebound tenderness in 22 patients (61.11%) decreased (Figure 1). After hyoscine administration to females, pain in 20 patients (58.11%), tenderness in 22 patients (64.7%), and rebound tenderness in 17 patients (50%) decreased (Figure 2). Totally, pain in 42 (60%) patients decreased and the reduction of these three variables was significant ( $p<0.001$ ) (Table 1).

The means of tenderness were significantly lower in males in comparison with males both before and after hyoscine administration ( $p<0.001$  and  $p=0.002$ , respectively) (Table 2). The difference between male (6.36±1.69) and female (7.47±1.65) group was



**Fig. 1.** Frequency of changes in pain, tenderness and rebound tenderness following administrating hyoscine to male patients with Appendicitis



**Fig. 2.** Frequency of changes in pain, tenderness and rebound tenderness following administrating hyoscine to female patients with Appendicitis

**Table 1.** The mean of pain, tenderness, and rebound tenderness before and after treatment in patients with appendicitis

	Number	Mean±SD <sup>a</sup>	p value
Tenderness (before)	70	7.11±1.72	<0.001
Tenderness (After)		6.48±1.64	
Pain (before)	70	7.84±1.69	<0.001
Pain (After)		6.90±1.75	
Rebound tenderness (before)	70	7.61±1.70	<0.001
Rebound tenderness (After)		6.68±1.89	

<sup>a</sup>Standard deviation**Table 2.** The mean of pain, tenderness, and rebound tenderness before and after treatment in term of sex in patients with appendicitis

		Number	Mean±SD <sup>a</sup>	Total	p value
Tenderness (before)	Male	36	6.61±1.67	70	<0.001
	Female	34	7.64 ±1.63		
Tenderness (After)	Male	36	5.88±1.50	70	0.002
	Female	34	7.08±1.58		
Pain (before)	Male	36	7.52±1.82	70	0.11
	Female	34	8.17±1.50		
Pain (After)	Male	36	6.36±1.69	70	0.007
	Female	34	7.47±1.65		
Rebound tenderness (before)	Male	36	7.38±1.72	70	0.225
	Female	34	7.85±1.68		
Rebound tenderness (After)	Male	36	6.11±1.62	70	0.06
	Female	34	7.29±2.19		

<sup>a</sup>Standard deviation**Table 3.** The mean of pain, tenderness, and rebound tenderness before and after treatment in patients with appendicitis

	Number	Mean±SD <sup>a</sup>	Total	p value
Male	Tenderness (before)	6.61±1.67	36	0.01
	Tenderness (After)	5.88±1.50		
	Pain (before)	7.52±1.82	36	<0.001
	Pain (After)	6.36±1.69		
	Rebound tenderness (before)	7.38±1.72	36	<0.001
	Rebound tenderness (After)	6.11±1.62		
Female	Tenderness (before)	7.65±1.63	34	0.02
	Tenderness (After)	7.08±1.58		
	Pain (before)	8.17±1.50	34	0.05
	Pain (After)	7.47±1.65		
	Rebound tenderness (before)	7.85±1.68	34	0.08
	Rebound tenderness (After)	7.29±2.16		

<sup>a</sup> Standard deviation

significant in terms of pain reduction after hyoscine administration ( $p=0.007$ ) (Table 2). Generally, the means of pain, tenderness, and rebound tenderness were significantly lower in males compared to females (Table 2).

The differences, among male patients, in terms of the pain, tenderness, and rebound tenderness reductions were statistically significant ( $p<0.001$ ) (Table 3). Also, the reduction of pain was more notable in male patients (1.16) in comparison with females (0.7) (Table 3). Before hyoscine administration, the mean of pain was more than 8 only in females; whereas, it was lower than 8 in all other groups.

## Discussion

This study can be considered as the first study

investigated the efficacy of hyoscine on pain, tenderness, and rebound tenderness in patients with appendicitis. This study showed that hyoscine can be a good choice for reducing pain, tenderness, and rebound tenderness in patients with appendicitis.

Many studies have evaluated the antispasmodic effect of hyoscine during parturition and revealed that 20 to 40 mg dose of hyoscine shorten the process of delivery in the first phase, reduce maternal pain, and caused better dilatation of the cervix [5, 10]. In another study, Kumar *et al.*, [11] compared the effects of diclofenac and hyoscine on colic pain and found that 69.4% of patients in hyoscine group experienced much less pain. They investigated the effect of hyoscine on biliary pain in dosage of 20, whereas, hyoscine was used in a dosage of 0.3 mg/kg in current study which can be considered as a



positive point.

In most studies investigated the efficacy of oral hyoscine on abdominal pain caused by spasm or cramping, hyoscine reduced pain in patients. For example, hyoscine administration led to less complains in patients suffered from biliary pain. Due to its antispasmodic property, it simplifies colonoscopy and endoscopy process. Tytgat *et al.*, in their review articles showed that 42% to 78% of cases experienced pain reduction [12, 13]. Ge *et al.*, evaluated the effect of hyoscine tablets and capsules on abdominal spasms of 302 patients, after about 30 minutes of taking pain medication, the pain was reduced about 20%. At the end of three days of treatment, about 46% pain reduction was observed in both groups [6]; whereas, in current study, 61.1% of males 58% of females experienced pain reduction.

Obvious differences in terms of pain reduction at the beginning of the medication may be due to kind of pain (appendicitis in this study) and administration. In the current study, intravenous administration had been used which its effect was much faster. In this study according to used scale, the pain, tenderness, and rebound tenderness significantly reduced after hyoscine administration in both groups. In this way, the pain mean of males, before and after the administration of the drug was 7.52 and 6.36, respectively. In addition, the mean pain of females, before and after administration of the drug was 8.17 and 7.47, respectively. This reduction in male patients was 1.16 and in females was 0.7. The tenderness and rebound tenderness reductions in male group was 0.73 and 1.27, respectively and this reduction in females was 0.57 and 0.56, respectively. In line with this study, Muller *et al.*, [14], during trial study evaluated 1637 patients with the abdominal cramping pain and supported anti-cramps and spasmodic property of hyoscine. According to considered scale, similar to the current

study, all the participants reported pain relief about 0.7 after hyoscine administration ( $p < 0.001$ ). Al-Waili also in similar study reported reduction of pain about 2.05 in patients treated with hyoscine [15]; however, current study reported less pain relief compared to aforementioned study. This difference can be due to pain assessment after 30 minutes' administration and the difference in kind and mechanism of pain. During this study, 3 patients faced with blurred vision and 1 patient with urinary retention. Muller *et al.*, [14] did similar study and reported hyoscine side effect about 16%. This difference may be due to long-term treatment (3weeks).

Current study had some limitations. We did not evaluate pain, tenderness and rebound tenderness for a long time after administration the hyoscine. Also, we did not consider control group. So, in future studies they can be considered. Clinical trials and double-blinded studies with a placebo control group or positive group, evaluating different doses of hyoscine, is recommended for further studies.

In conclusion, it seems that hyoscine can be a good choice for reducing pain, tenderness, and rebound tenderness in patients with appendicitis. However, the greatest effect was seen in males and tenderness, it can be concluded that hyoscine is clinically and statistically useful in reducing appendicitis complains. Along with results of previous studies, hyoscine is relatively safe, has few side effects, and can be a good option for reducing pain, tenderness and rebound tenderness in patients with appendicitis.

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**Conflicts of Interest:** None declared.

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