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Radiographic, Hematologic and Biochemical Alterations in Peritoneal Fluid after Intraperitoneal Injection of Barium Sulfate and Gastrografin in Rabbit

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Abstract

***Background*:** Evaluation of contrast-induced changes in the peritoneal area may reveal the effects of their permeation followed by gastrointestinal perforation. This study aims to compare the radiographic changes and hematological and biochemical parameters of peritoneal fluid and blood after intraperitoneal injection of barium sulfate and gastrografin to the rabbit.

***Materials and Methods*:** In this clinical trial, 15 healthy male rabbits were randomly divided into 3 groups. Respectively to each group 10 ml/kg barium sulfate 30%, 10 ml/kg gastrografin, and 10 ml/kg saline was intraperitoneally injected. Before injection and 24 hours after injection, blood samples and peritoneal fluid were collected to measure glucose, total protein, WBC count and pH. Lateral and dorsal-ventral radiography was provided 20 min and 24 hours after contrast injection.

***Results*:** After injection of barium sulfate, serum glucose decreased, cell count and blood neutrophil percentage increased, glucose and the percentage of peritoneal fluid lymphocytes decreased ($p<0.05$). The amount of total protein, cell count and peritoneal fluid neutrophil percentage increased ($p<0.05$). Gastrografin injection only increased peritoneal fluid total protein ($p=0.04$). Other blood factors and peritoneal fluid showed no significant changes. In radiographies, barium sulfate remained in abdominal area and rapid absorption of gastrografin was observed.

***Conclusion*:** The use of gastrografin has fewer side effects than barium sulfate and is recommended in patients suspected with gastrointestinal perforation.

Introduction

In many gastrointestinal tract diseases, radiography is necessary to be studied in cases which need for oral or enema administration of contrast, in which case the diagnosis will be more accurate and definitive [1, 2]. In some cases, there is a possibility of gastrointestinal perforation such as malignant lesions in the gut wall, intestinal diverticula inflammation, peptic ulcer in the anal area, fouling as well as any errors in contrast enema such as sharpness of enema catheter [3-6]. In some cases, gastrointestinal perforation was also diagnosed via contrast. Thus, these substances will also reach to the abdominal cavity [7]. Therefore, it is necessary for changes occurred in this regard to be clear for the radiologist to avoid mistakes in the diagnosis.

Considering that the value of a contrast is evaluated by its selected density in a specific organ in order to create a clear radiographic image of since the contrast is only as a tool to help diagnose, it is expected to have the least pharmacologic activity. Side effects of some contrasts in patients are expressed [4, 8, 9]. Peritoneal inflammation induced by the entry of barium sulfate to abdominal is lethal [8, 10]. In addition, the entry of barium sulfate due to the gastrointestinal tract perforation into the abdominal cavity enhanced the harmful effects of entry of feces to the peritoneal cavity of the rabbit [11]. Barium sulfate increases the activity of white blood cells and their phagocytosis [7]. While it is shown that barium sulfate has had no substantial effect on healing of surgical wounds in the gastrointestinal tract [6]. This study was performed to compare the effects of injection of barium sulfate and gastrografin (meglumine diatrizoate) into rabbit abdominal cavity on radiographic changes and hematological and biochemical parameters in blood and peritoneal fluid.

Materials and Methods

For this clinical trial, 15 healthy male New Zealand white rabbits with a mean age of 6 months, and weight 2500±400g were selected. After clinical examination and ensuring about health of rabbits, they were kept at a room with temperature 21±2^{o}C and humidity of 50±5% and 14 hours light/10 hours' dark (light from 7:00 to 21:00) for three weeks. They were freely provided with standard

rabbit food and water. The attempt was put to minimize the number of animals used. The research was conducted based on the instructions approved by the Shiraz University of Medical Sciences for the work with laboratory animals.

Before contrast injection, body temperature, heart rate and respiratory rate were measured. Five ml blood was collected from the jugular vein in tubes containing heparin and conventional tube and 2 ml of peritoneal fluid was collected using the catheter No. 18 and syringe. To collect peritoneal fluid samples, general anesthesia was intramuscularly performed using xylazine 2% (0/1 ml/kg; Bayer, Germany) and ketamine 10% (20 ml/kg; Park-Davis, America). Then, rabbits were laid to the flank and an area as large as 2×2 cm at the distance of one centimeter from navel and one centimeter to the right flank was shaved and prepared. Then, using a catheter and syringe, 2 ml of peritoneal fluid was collected.

Then, rabbits were randomly divided into 3 groups and each group was divided into 5 rabbits. The first group of rabbits was intraperitoneally injected with 10 ml/kg barium sulfate 30% (Daroupakhsh, Iran) dissolved in saline, the second group of rabbits was intraperitoneally injected with 10 ml/kg soluble Gastrografin (EG shrink, Berlin, Germany) and the third group of rabbits was intraperitoneally injected with 10 ml/kg saline.

Twenty minutes after contrast injection, both lateral and dorsal-abdominal radiography was provided. About 24 hours after contrast injection, body temperature, heart rate and respiratory rate were again measured in rabbits and both lateral and dorsal-abdominal radiography was provided. Also, the blood samples and peritoneal fluid were collected in rabbits through previous methods.

Then, rabbits were transferred to the recovery room and were kept in good condition. Immediately after coagulation, blood serum was separated by centrifugation with the round 3,000 times per minute and was stored in the freezer -20^{o}C. WBC count and determination of percentage of cells of neutrophils, lymphocytes, monocytes, basophilic and eosinophil were performed through the conventional method of blood cells count using hemocytometer lam. Glucose was measured according to reaction (Sigma, St. Louis, United States) and total protein was measured with Biuret method and blood pH and peritoneal fluid were measured with pH meter.

Hematological and biochemical parameters, and vital signals was statistically compared between the three groups using one-way ANOVA and Duncan's multiple range test. In addition, the indices express before and after contrast injection were compared through paired *t* test. $p<0.05$ was considered significant and software SPSS-11.5 was used for statistical analysis.

Results

Results of the evaluation of biochemical parameters of serum and hematology of rabbits before and after contrast injection are shown in tables 1 and 2. Comparing to the gastrografin group and normal saline group as well as before injection, blood glucose was reduced after barium sulfate injection and the number of white blood cells and the percentage of blood neutrophils increased ($p<0.05$). No significant difference was observed between different groups and different times in the percentage of other white blood cells and other serum biochemical parameters.

The results of biochemical and hematological parameters of rabbit peritoneal fluid are shown in table 3 and 4. Compared to the gastrografin group and normal saline group and before injection of barium sulfate, total protein, white blood cell number and neutrophil percentage were higher and serum glucose was lower after injection of barium sulfate ($p<0.05$). In addition, total protein after injection in Gastrografin group was higher than before injection, but it was lower than total protein after injection of barium sulfate ($p<0.05$). No significant difference was observed between different groups and different times in the percentage of other white blood cells, peritoneal fluid and other biochemical parameters. After intraperitoneal injection of barium sulfate, a significant increase was observed in body temperature, heart rate and breathing compared with gastrografin and normal saline group as well as before barium sulfate injection ($p<0.05$). Rabbits of this group were clinically depressed with low appetite. Peritoneal fluid color in all the rabbits was pale yellow before contrast injection and was significantly increased and turned to brick red color after injection of barium sulfate. In radiographic evaluation of the rabbits, 20 min after injection of barium sulfate, the substance got inclined to accumulation in an area (Fig. 2-A). However gastrografin had been uniformly distributed 20 min after the injection (Fig. 2-B). Barium sulfate particles remained in the peritoneal cavity 24 hours after contrast injection (Fig. 2-C), whereas no trace of gastrografin was observed (Fig. 2-D).

Table 1. Mean and standard error of alterations of blood cells before and 24 hours after injection of contrast media in rabbit (n=5)

Treatment groups	Sampling time	WBC 10^3/µl	Neutrophil %	Lymphocyte %	Monocyte %	Eosinophil %	Basophil %
Normal saline	Before	7.2±1.8 ^{a}	45±3 ^{a}	50±2 ^{a}	1±1 ^{a}	0 ^{a}	1±0 ^{a}
	After	7.5±3.0 ^{a}	51±3 ^{a}	45±2 ^{a}	0 ^{a}	0 ^{a}	1±0 ^{a}
Barium sulfate	Before	7.8±1.1 ^{a}	45±5 ^{a}	52±6 ^{a}	1±1 ^{a}	1±1 ^{a}	1±1 ^{a}
	After	11±2.5 ^{b}	61±8 ^{b}	45±7 ^{a}	0 ^{a}	0 ^{a}	0 ^{a}
Gastrografin	Before	7.8±1.1 ^{a}	46±2 ^{a}	49±5 ^{a}	1±1 ^{a}	0 ^{a}	1±1 ^{a}
	After	7.4±3.1 ^{a}	49±3 ^{a}	50±4 ^{a}	0 ^{a}	0 ^{a}	0 ^{a}

a, b Different superscript letters indicate significant differences in the same column ($p<0.05$).

Table 2. Mean and standard error of alterations of serum biochemical parameters before and 24 hours after injection of contrast media in rabbit (n=5)

Treatment groups	Sampling time	Glucose g/dl	Total protein g/dl	pH
Normal saline	Before	75±4.2 [a]	6.0±3.1 [a]	7.27±0.03 [a]
	After	79±5.1 [a]	5.7±2.0 [a]	7.28±0.02 [a]
Barium sulfate	Before	79±4.5 [a]	6.1±2.4 [a]	7.39±0.03 [a]
	After	60±8.8 [b]	8.6±3.1 [a]	7.30±0.03 [a]
Gastrografin	Before	78±4.2 [a]	5.9±2.5 [a]	7.32±0.02 [a]
	After	76±4.2 [a]	6.0±1.8 [a]	7.28±0.03 [a]

a, b Different superscript letters indicate significant differences in the same column ($p<0.05$).

Table 3. Mean and standard error of alterations of peritoneal cells parameters before and 24 hours after injection of contrast media in rabbit (n=5)

Treatment groups	Sampling time	WBC $10^3/\mu l$	Neutrophil %	Lymphocyte %	Monocyte %	Eosinophil %	Basophil %
Normal saline	Before	2.1±1.6 [a]	50±6 [a]	47±8 [a]	0 [a]	0 [a]	1±0 [a]
	After	2.5±3.0 [a]	51±4 [a]	49±4 [a]	0 [a]	0 [a]	1±0 [a]
Barium sulfate	Before	2.3±1.9 [a]	47±3 [a]	52±5 [a]	0 [a]	0 [a]	1±1 [a]
	After	3.8±1.9 [b]	61±7 [b]	38±4 [a]	0 [a]	0 [a]	0 [a]
Gastrografin	Before	2.5±1.6 [a]	42±4 [a]	55±5 [a]	0 [a]	0 [a]	0 [a]
	After	2.6±1.9 [a]	45±6 [a]	58±6 [a]	0 [a]	0 [a]	1±0 [a]

a, b Different superscript letters indicate significant differences in the same column ($p<0.05$).

Table 4. Mean and standard error of alterations of peritoneal biochemical parameters before and 24 hours after injection of contrast media in rabbit (n=5)

Treatment groups	Sampling time	Glucose g/dl	Total protein g/dl	pH
Normal saline	Before	88.1±7.5 [a]	2.8±1.7 [a]	7.37±0.04 [a]
	After	80±11.6 [a]	2.7±2.0 [a]	7.35±0.03 [a]
Barium sulfate	Before	85.2±6.2 [a]	2.4±1.8 [a]	7.40±0.03 [a]
	After	55±10.0 [b]	5.3±2.8 [b]	7.37±0.03 [a]
Gastrografin	Before	84.5±7.3 [a]	2.7±1.6 [a]	7.35±0.03 [a]
	After	80±6.5 [a]	3.4±0.7 [c]	7.34±0.04 [a]

a, b, c Different superscript letters indicate significant differences in the same column ($p<0.05$).

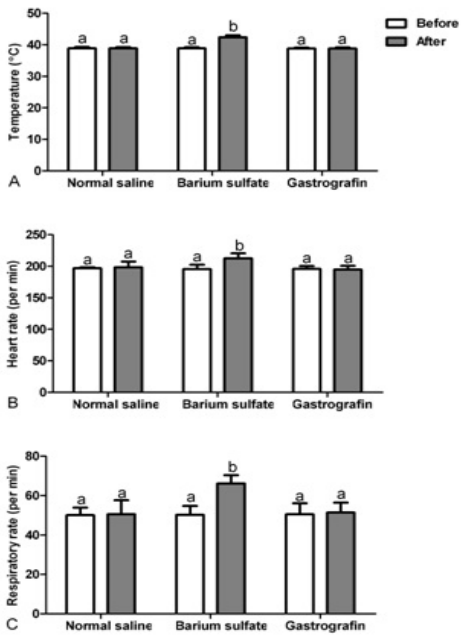

Figure 1. Mean and standard error of alterations of A) temperature, B) heart rate and C) respiratory rate before and 24 hours after injection of contrast media in rabbit (n=5). a, b Different superscript letters indicate significant differences between columns ($p<0.05$).

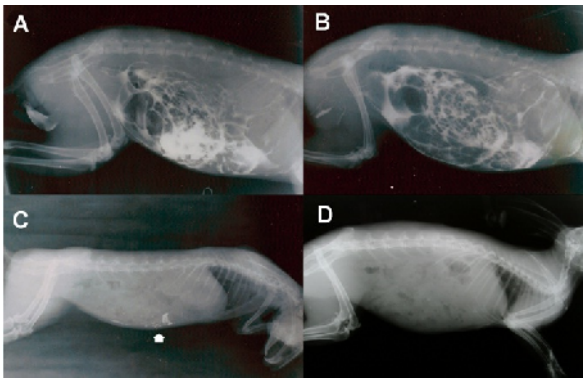

Figure 2. A) Lateral positioning of rabbit of group 1, 20 min after injection of barium sulfate which inclined to accumulation in an area. B) Dorsoventral positioning of rabbit of group 1, 20 min after injection of gastrografin which uniformly distributed. C) Lateral positioning of rabbit of group 1, 24 hours after injection of barium sulfate which barium sulfate particles remained in peritoneal cavity. D) Lateral positioning of rabbit of group 1, 24 hours after injection of gastrografin whereas no trace of gastrografin was observed.

Discussion

In barium sulfate group of rabbits, the increase of the number of white blood cells and total protein was observed. On the other hand, the radiographic images showed that barium sulfate remained in the peritoneum even up to 24 hours after the injection. In inflammation of the peritoneum, nucleated cells and peritoneal fluid

volume increase [7]. Remaining barium sulfate in the peritoneum and irritation of this eardrum and creation of peritonitis causes nucleated cells to migrate to the peritoneum and their number to increase [7]. The fluid volume obtained from the peritoneal significantly increased with red blood cells which indicated the peritoneal hemorrhaging inflammation [13, 14].Peritoneal liquid obtained from the injection of barium sulfate was slimy and sticky due to its containing blood and protein. Bacterial and red blood cells have been observed in patients with peritoneal inflammation and blood proteins and peritoneal fluid also increased in these patients [8].

White blood cells decrease due to their migration to the peritoneum and this occurs when several hours have been passed from the entry of barium sulfate [7]. In the present study, considering that peritoneal fluid sampling was performed from rabbits after 24 hours, white blood cells increased due to the more recall and production. Blood glucose levels and peritoneal fluid decreased in barium sulfate group, which can also be due to the blood glucose consumption by white blood cells accumulated in the inflammatory environment [7]. Albumin entered to the peritoneal cavity along with exudate and consequently, peritoneal fluid protein was increased [8]. Fluid leakages in the peritoneal cavity take place due to barium agglutination. Fibrin in the peritoneal fluid which is placed on barium is created by the activation of the clotting system [7]. Peritoneal damage interferes with fibrinolytic activity and thus, fibrin is not decomposed and remains [15]. Thereby, to wash peritoneum and remove barium, substances such as activated plasmin or urokinase, which are fibrinolytic are used to facilitate the access to the barium attached to the peritoneum [4]. According to the location of gastrointestinal perforation and the extent of the gastrointestinal contents entered into the abdominal cavity along with barium, intensity of inflammation of the peritoneum and losses caused by it increase [8, 11]. In addition, due to the inflammation, 24 hours after injection of barium sulfate, body temperature rose and respiration and heart rate increased.

In this case, dehydration and depression were also created. It has been suggested that the excretion of extracellular fluid is a secondary response to mechanical stimulation of abdominal viscera due to the particles in suspension barium [16].

Radiographs showed that in the gastrografin group of rabbits, this solvent contrast was distributed and absorbed in water due to the rapid absorption of gastrografin from peritoneum, and thus, no changes were observed in the number of white blood cells and serum total protein levels due to the lack of peritoneal inflammation. Solvent contrast did not cause inflammatory reaction in the peritoneum in other water with brand Conray (iothalamate meglumine) with concentration of 15% and 30%. [11] Only in the concentration 30%, due to fluid absorption from the peritoneum and decrease in osmolality contrast, losses were higher than the concentration 15% in guinea pigs after 24 hours [11]. In the blood and peritoneal parameters of gastrografin group rabbits, no change was observed except in peritoneal liquid protein.

According to the results of this study, using gastrografin had less hematological and biochemical changes compared with barium sulfate and gastrografin was well absorbed in the peritoneal cavity. Therefore, it is recommended to use gastrografin contrast instead of barium sulfate in the gastrointestinal tract radiography in patients suspected with gastrointestinal obstruction or perforation and in the study of the abdominal organs.

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Authors' Contributions

Dr. S. Varzandian participated in the project conception as his DVM thesis, carried out most of the experimental work. Dr. S. Jafari Shoorijeh and Dr. Tabatabai-Naini as project leaders, designed the study, and coordinated all manuscript preparation. Dr. A Tamadon drafted the first version of the manuscript and performed the statistical analysis.

Conflict of Interest

No conflict.

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