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Abdominal and Thoracic Radiographic Findings in Elevated Intra-Abdominal Pressure Rats

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Abstract

The aim of the study was to establish the influence of the increased intra-abdominal pressure (IAP ≥ 20 mmHg) on the location and some functions of abdominal and thoracic organs in adult Wistar rats, as well as to determine a set of specific characteristics of the radiographic image of the condition studied that would facilitate its definition. Notable changes in gastro-intestinal motility of IAP-rats were observed radiographically during experiments: alterations in the location of the organs in the thoracic and abdominal region; lack of gut peristaltic activity due to intestinal paresis and impaired passage of contrast medium along the entire gastro-intestinal tract; reliable increase of frequency of respiratory movements and retardation of the frequency of heart rate of rats. It can be concluded that elevated IAP causes significant dysfunction of abdominal and thoracic organs. These functional changes are radiographically observable and can be used as an indication of elevated IAP.

1. Background

Intra-abdominal hypertension (IAH) is defined [1] as a condition characterized by abnormal intra-abdominal pressure (IAP) exceeding 12 mmHg and obtained from two consecutive measurements taken within 1-6 hours.

Intra-abdominal hypertension does not necessarily result in abdominal compartment syndrome (ACS) [2], but IAP elevation above a certain value is considered as an element of compartment syndrome development [3]. That is why the two conditions are viewed upon as different stages of a progressing pathologic process [4].

ACS developing at IAP > 20mmHg results in dysfunction of one or several organs and generally requires urgent surgical decompression [5].

The timely taking of measures for ACS management requires its rapid recognition prior to the development of fatal multi-organ deficiency. At the same time the complexity of the specific processes occurring at different body areas in elevated IAP and ACS, as well as the presence of a number of interrelations between these processes, lead to the manifestation of diverse symptoms, as a result of which a definitive diagnosis is difficult to make [6]. For the purposes of making a precise diagnosis the patients are transferred from one clinic to another, which almost always is accompanied by a diagnostic imaging investigation. This is valid for patients with trauma, peritonitis, intra-abdominal abscess, ileus, ruptured aneurysm of the abdominal aorta, acute pancreatitis and other conditions capable of provoking acute abdomen and possibly an ACS [6].

Inclusion of diagnostic imaging methods can shorten the diagnostic process of the above-mentioned conditions and can optimize their investigation. The information available on the radiographic characteristics of elevated IAH and ACS is scarce [7] This requires determining a set of objective, easily recognizable specific features of the radiographic image in investigating IAP and ACS, which would guarantee taking all appropriate measures. Such a set would aid the relatively complex manipulations requiring specific instruments, which are used in clinics to detect IAH [8, 9, 10, 11].

In an attempt to solve problems resulting from certain pathologic conditions, experimental models have been frequently used enabling researchers to study the role of a number of factors in the development of the respective condition. Apart from that, laboratory models have been utilized to elucidate the mechanisms underlying the pathology. The present study used a rat experimental model of increased IAP developed by us [*].

The aim of the study was to establish the influence of the increased IAP ($\geq$ 20 mmHg) on the location and some functions of abdominal and thoracic organs in rats, as well as to determine a set of specific characteristics of the radiographic image of the condition studied that would facilitate its definition.

2. Materials and Methods

2.1. Experimental Animals

The study involved 43 adult male Wistar rats with a weight of 0.250– 0.280kg, under conditions of adequate laboratory dietary regimen. For the duration of the experiment the animals were kept under identical conditions of dietary regimen, access to water, temperature, light/dark cycle. During the experiments the requirements of article 291 of Regulation № 15 on Humane Treatment of Laboratory Animals were strictly adhered to.

The rats were divided into three groups:

Control group consisting of 18 animals (contrast radiographic investigation of stomach and intestinal passage);

Model group including 25 animals (contrast radiographic investigation of stomach and intestinal passage) under conditions of artificially elevated IAP, divided into two subgroups:

I-st subgroup (n=12) treated as follows: elevation of IAP up to 25mmHg

by means of insufflating air (room temperature) into the abdominal cavity→waiting for 60 min→contrast medium (CM) probing→maintaining the IAP for 120 min following the CM introduction → contrast radiographic investigation following CM administration;

II-nd subgroup (n=13) treated as follows: CM probing →immediate contrast radiographic investigation → elevation of IAP up to 25mmHg 50 min following the CM introduction → contrast radiographic investigation.

2.2. Preliminary Preparation of the Experimental Animals

The preliminary preparation of the rats from all groups was performed as follows:

- Anaesthetizing (Xylazine 2% - 10 mg/kg + Ketamine (Calipsol) 5% - 100 mg/kg).
- Fixing the animal on a polystyrol table;
- Creating a pneumoperitoneum using a cannula and fixing the latter onto the skin.
- The elevation of IAP of the experimental group of rats was achieved by means of a pump and included the following stages:
- Coupling an elevated pressure system to the cannula and gradually (10 min) elevating IAP up to 25/30 mm/Hg.
- Maintaining the elevated IAP for more than 120 min for the purposes of simulating an acute ACS.
- The individual procedures were performed under conditions of continuous monitoring of anaesthesia depth, temperature, pulse and respiration.

3. Radiographic Investigations

Opera T-90 X-ray apparatus was used for the contrast investigations of rats, both radiographies and radioscopies. The latter were antero-posterior, with the rat in the supine position and were performed during/along 2-hours period following air insufflation into the abdominal cavity of the treated animals and 2.5 hours following fixation of the control animals.

Barium suspension was used as the contrast medium (120 ml + 200 ml), stirred up with a mixer at a temperature of 37°C. An amount of 2.0 to 2.5 ml of the contrast medium (CM) was introduced into the stomach by means of a metal probe, depending on the weight of the individual rat.

The radiographic investigations involving contrast medium in all groups were performed immediately following, as well as at the 15-th, 30-th, 45-th, 60-th, 120-th and 150-th minute following CM administration.

The investigation was performed with the apparatus set at the following technical parameters: 46 kV, 300 mA, 0.12 s, 320 mAS, 640 mS and focal distance of 70 cm.

4. Statistical Analysis

The mean and standard error mean were calculated for measurements of heart and respiratory rate. Student’s t-test

(95% confidence interval, $p<0.05$) for the data was made by using STATISTICA software (StatSoft).

5. Results

5.1. Characteristics of the Radiographic Image of Thoracic and Abdominal Region of Control Rats

The panoramic anteroposterior radiographies of all control rats (n=18) showed the typical size, form and location of thoracic and abdominal internal organs, identical to already observed in our previous investigations [12, 13].

The pulmonary parenchyma was of normal transparency and did not undergo any alteration throughout the radiographic investigation.

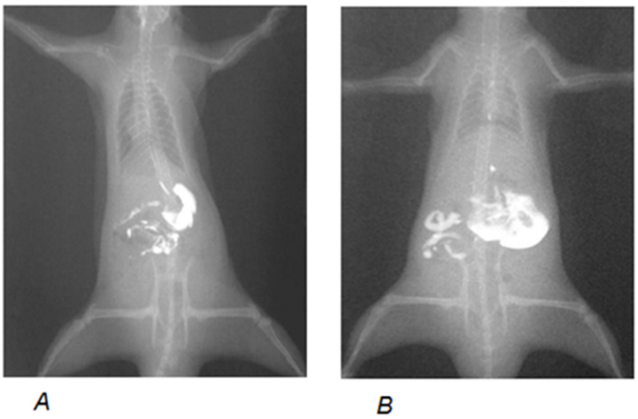

Fig. 1. Rats from the control group. Panoramic radiographies of thoracic and abdominal region immediately following CM administration (A) and 30 min later (B).

In the focus or our attention were the condition of the GI tract and the dynamics of CM passage through it.

Immediately following CM introduction the stomach and duodenum were visualized, with the initial segment of the small bowels only partially visualized. The stomach was of normal location and form, its anatomical parts – fornical and antral - being well discernible. Simultaneous occurrence of several peristaltic waves was observed along the gastric wall. The intestinal loops visualized were of normal location and standard lumen (fig. 1A).

Fifteen minutes following CM administration, no significant alteration was observed as compared to the baseline radiographic image. At the 30-th minute following its administration, CM passage along the course of the intestinal loops was observed. The stomach was completely filled with CM. Peristaltic waves could be discerned (Fig. 1B).

At the 45-th min normal passage of CM into the small bowels was observed. The latter were of normal location, with alternating segments of constricted and dilated lumen along their course. Peristaltic waves were registered in the stomach and small intestines (Fig. 2A).

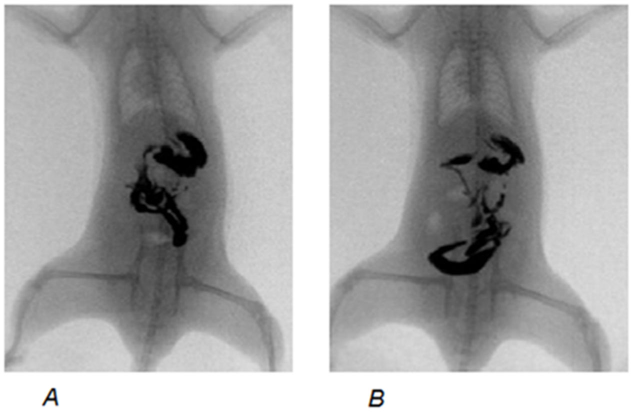

Fig. 2. Panoramic radiography of thoracic and abdominal region of control rats taken 45 min (A) and 120 min (B) following CM administration.

The period from the 45-th to the 120-th min was characterized by uniform CM passage along the course of the duodenum and the small bowel loops, accompanied by reduction of the contrast agent volume in the stomach and dilatation of bulbus duodeni. Consecutive segments of dilated and constricted lumen were formed, alternating uniformly over time on the subsequent radiographies and illustrating an even CM passage.

Towards the 120-th min CM was partially evacuated from the stomach and duodenum. The small bowel loops, normal in location and revealing presence of peristaltic activity, were completely filled with it. Passage of barium sulphate to the caecum was observed (Fig. 2B).

5.2. Characteristics of the Radiographic Image of Thoracic and Abdominal Region of Rats with Elevated IAP

I-st model subgroup

The panoramic anteroposterior radiographies and radioscopies of rats from the first model subgroup (n=12), performed 1 hour following elevation of IAP up to 25mmHg (immediately after CM introduction), showed specific alterations in the size, form and location of part of the internal organs. In all animals the diaphragm was in an elevated position. The intercostal spaces were constricted and the pulmonary fields were reduced. The transparency of pulmonary parenchyma was decreased on both sides. Cardiac silhouette was either non-traceable, or difficult to trace. The abdominal cavity was severely distended. A mild shadow of insufflated air was registered on both sides.

The liver was clearly visible, although located at a higher level than normal. Orientation of the location of internal organs toward the midline was frequently registered (n=9).

CM filled only the oesophagus immediately following its administration. In some of the animals an insignificant part of it partially entered the fornical segment of the stomach (fig. 3A).

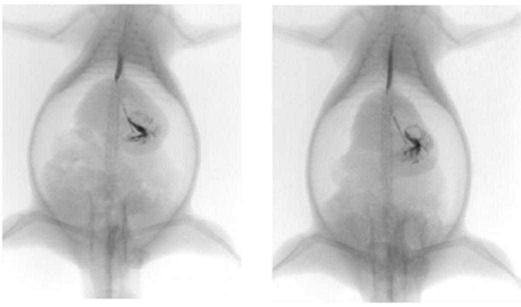

Fig. 3. *Rats from the I-st subgroup of the model group - elevated IAP (25 mmHg). Panoramic radiography of abdominal and thoracic region taken immediately following CM administration (A) and 60 min later (B).*

The subsequent radiographies did not show any alterations in the thoracic area or $BaSO_4$ passage along the GI tract. This finding was observed in each animal, no changes being registered on the radiographies at the 60-th and 120-th min (fig. 3B).

Some of the alterations observed in certain indices of the radiographic image, resulting from the elevation of IAP, are presented in Table 1.

II-nd model subgroup

The panoramic anteroposterior radiographs of each rat from this subgroup (n=13), were taken under conditions of normal and elevated IAP (25mmHg).

The radiographic images obtained up to the 45-th min (in normal IAP) were to a great extent identical with those of the control animals (fig. 1A and B and fig. 2A). The thoracic region was normal in size and radiographic density. CM passed along the course of the GI tract, and 45 min following its administration it filled an area of the GI tract including the stomach and a considerable part of the small bowels. Most rats demonstrated marked peristaltic activity.

Following IAP elevation through insufflation of atmospheric air around the 50-th min, drastic alterations occurred in the abdominal and thoracic region of the treated rats (fig. 4).

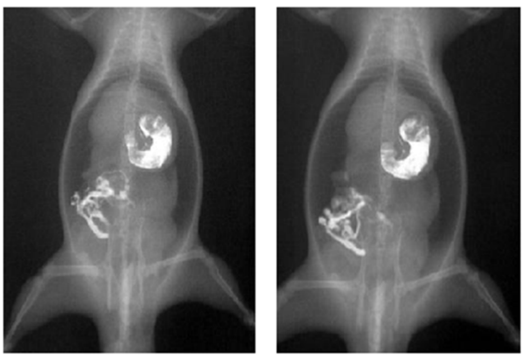

Fig. 4. *Panoramic radiographies of thoracic and abdominal region of rats from the II-nd subgroup of the model group immediately after IAP elevation (25 mmHg, 60 min following CM administration) (A) and 100 min following IAP elevation (160 min following CM administration) (B).*

The abdominal cavity was distended and a mild shadow of insufflated air was observed on both sides. The internal organs were oriented toward the midline.

The diaphragm was in an elevated position. Lung volume was considerably reduced and its radiographic image was severely shadowed. Respiratory movements were shallow and accelerated. No difference was observed in the radiographic density of the images of heart and lung. Some of the animals demonstrated gastroesophageal reflux.

On the subsequent radiographies (90-th, 120-th, 150-th min following CM administration) the image of the stomach and small bowel loops, which were already filled with CM, remained unaltered – no CM passage was registered along the GI tract.

Some of the changes observed in the radiographic image, caused by IAP elevation in the rats from the model group, are systematized in Table 1.

Table 1. *Indices of the radiographic images of rats with elevated IAP (25mmHg).*

№	Indices	Frequency of observation (% of total number of rats with elevated IAO)
1	Distension of abdominal cavity	100%
2	Stripe-like mild shadow along the sides of the abdominal cavity	100%
3	Lack of peristaltic activity	100%
4	Lack of CM passage along GI tract	100%
5	Gastroesophageal reflux	30%
6	Elevated position of diaphragm	100%
7	Narrow intercostal spaces	100%
8	Reduced pulmonary fields	100%
9	Bilateral shadowing of pulmonary fields	100%
10	Non-observable /non-discernible/ cardiac silhouette	100%

5.3. Alterations in the Frequency of Respiratory Movements and Cardiac Contractions Under Conditions of Elevated IAP

Elevation of IAP to the value mentioned above influenced the nature and frequency of respiration in the rats. The measurements were made prior to compression and 40 min following it. A reliable increase of frequency of respiratory movements was registered, as compared to the values obtained during the first stage of the experiment when the animal were under normal conditions (table 2, referred to 1-st model subgroup only). A reliable retardation of the frequency of heart rate was observed in the same period (table 2).

Table 2. *Changes in respiratory movements frequency and heart rate of IAP-rats.*

Index	Frequency, min $^{-1}$ (initial/after 40 min)	
	Respiratory movements	Heart rate
Controls, n = 18	38±10 / 51±11	165±23 / 153±31
IAP/p=25mmHg, n = 12	54±2 / 66±3 *	203±25 / 153±15 *

* Indicates significant differences – $p < 0.05$. Comparison is made separately in two groups.

6. Discussion

Insufflation of atmospheric air in the abdominal cavity of rats increases the pressure, which is equally transmitted according to Pascal's law and exerts equal influence on the tissues anatomically determining the abdominal region, as well as on the organs located in it.

The elevated IAP pushes the diaphragm upwards, resulting in raised position of the latter and reduced respiratory mobility of its domes. The diaphragm elevated position leads to reduced and bilaterally shadowed pulmonary fields, as well as narrow horizontal intercostal spaces. The reduced volume of the thoracic region results in increase in the intra-thoracic pressure and direct compression of the pulmonary tissue. From a functional point of view this means reduction in the static and dynamic pulmonary compliance, the total pulmonary capacity, the residual volume and functional residual capacity, as well as increase in intra alveolar pressure. Work in respiration is increased and respiratory movements become superficial. These alterations in pulmonary mechanics result in impaired lung function registered in our experiments as a compensatory increase in respiratory rate.

On the other hand, the high intra-thoracic and intra-abdominal pressures impede the lymphatic drainage from the lungs and create conditions for increased filtration flow to the extravascular space and risk of pulmonary edema.

Above mentioned observations occur in all experimental animals from the model group and in none from the control group. This finding gives us grounds to associate the radiographic alterations observed in the thoracic region with the elevation of IAP. This set of indications may include the finding "non-observable (non-discernible) cardiac silhouette", the latter being manifested because of the increased density of pulmonary tissue resulting from the reduced volume of the thoracic region.

A number of factors in the model used contribute to the decrease in the cardiac stroke volume. Leading among them is the reduced flow to the heart from the venous drainage because of the direct compression of the large veins - the inferior vena cava and the portal vein. Therefore the compensatory mechanism resulting from an impaired peripheral haemodynamics aiming at increase in the stroke volume is likely to have participation in reduced cardiac rate.

Radiographies and radioscopies of the control rat group revealed the GI tract as normal in size and location of the abdominal organs [14].

Until the end of the experiment continuous CM passage along the intestinal loops was observed. At the 45-th minute following its administration it filled parts of the small bowel, a considerable amount of its volume remaining in the stomach as well. Towards the end of the experiment (120-th minute), CM was partially evacuated from the stomach and duodenum, completely filled the small bowel loops and partially filled the caecum in most rats.

The animals showed good peristalsis throughout the experiment. No oesophageal reflux was observed.

The radiographic images of the rats from the model group were considerably different. On the background of a severely distended abdominal region with elevated IAP (subgroup A), CM filled the oesophagus and only some of the animals revealed passage of an insignificant part of CM into the gastric fornix. This results from the impaired CM passage through the gastro-oesophageal area due to the high pressure in the abdominal cavity acting upon the stomach. In the subsequent two hours and until the end of the experiment no dynamics was registered in the radiographic images, which means lack of CM movement along the GI tract. Intestinal paresis was observed – complete lack of peristaltic activity.

Similar was the effect of IAP elevated around the 50-th minute following CM administration on the dynamics of its passage (subgroup B). Up to this moment the GI tract radiographies were to a great extent analogous to those of the control animals – CM filled parts of the small bowel, the rats showed good peristalsis in the sections of the GI tract studied, no gastro-oesophageal reflux was observed.

Immediately following air insufflation into the abdominal cavity, the radiographies changed – CM passage was discontinued, peristaltic activity was either lacking or sluggish and shallow. Some of the rats showed gastro-oesophageal reflux.

These alterations, combined with the presence of a stripe-like mild shadowing on the sides of the abdominal cavity may be viewed as specific characteristics of the radiographic image resulting from the increased IAP. Pressure amounting to 25 mmHg (corresponding approximately to 45 mN/cm^2) can be supposed to simply physically block the movements characteristic of the GI tract, having in mind the fact that the strength of spontaneous contractions of circular smooth muscles from rat stomach and small intestines, which underlie propelling movement and peristaltic activity [15], are within the range of several mN. The lack of typical movements of the intestinal wall satisfactorily explains the lack of CM passage along the GI tract of the compressed animals. It may have been provoked by the influence of the mechanical pressure of the insufflated air on structures of the enteral nervous system. This pressure probably drives the irritation threshold of nervous receptors located in the submucosa, which trigger a signal for motility discontinuation because of an extreme body situation, and as a result a condition of paralytic ileus of the GI tract is caused.

Another specific characteristic of the elevated IAP reaction registered in our experiments was the occurrence of gastro-oesophageal reflux. The increased intra-abdominal pressure is considered to be the basic factor in the pathogenesis of this phenomenon [16]. The lower oesophageal sphincter in rats is a segment of 3 - 4 mm tonic contracting smooth muscles in the distal end of the oesophagus. The maximum force corresponding to pressure created by these muscles is approximately 10 mmHg [17]. An additional factor capable to reduce the value of the pressure in the sphincter is the gastric deformity which is a fact in IAP elevated to 25 mmHg. All this, as well as the possibility of discoordination of the mechanism of the sphincter muscle function [18], are likely to cause CM passage from the stomach into the oesophagus (i.e. a gastro-oesophageal reflux).

Not all structural and especially functional alterations result from the direct action of elevated IAP. Their occurrence is likely to be due to causes associated with its elevation - impaired abdominal and thoracic haemodynamics [19] accompanied by decline in perfusion pressure [20], release of proinflammatory cytokines [21] capable of damaging the endothelium and increasing vascular permeability [22], and release of prostaglandins [23].

7. Conclusions

1. Elevated IAP (25 mmHg) in rats causes radiographically observable alterations in the location and functions of the organs in the thoracic and abdominal region.

2.The alterations registered in the radiographic image of the abdominal and thoracic regions of the rats from the experimental group are identical, doubtlessly resulting from the IAP elevation and can be used as an indication of elevated IAP.

3. The significant functional changes caused by the elevated IAP support the idea that it is a major factor in the development of the multi-organ deficiency observed in abdominal compartment syndrome.

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