EXPERIMENTAL STUDY

The preventive effects of atorvastatin and N-acetyl cysteine in experimentally induced ischemia-reperfusion injury in rats

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ABSTRACT

AIM: We investigated the effects of atorvastatin and N-acetyl cysteine in decreasing ischemia–reperfusion damage after detorsion of a volvulus of the cecum and ascending colon.

METHODS: Wistar albino rats (250–300 g) were divided into four groups. A cecal-ascending colon volvulus was created by the intestinal clockwise 720° rotation. At the end of one hour, the bowel was detorsioned. Group I (n = 7) was the sham (laparotomy) group, Group II (n = 7) the control (no treatment, volvulus or detorsion), Group III (n = 7) (N-acetyl cysteine administered ) , and Group IV (n = 7) (atorvastatin administered ) group. Blood samples were collected from each group via peripheral veins and centrifuged one hour after detorsion. The parameters of ischemia including malondialdehyde, glutathione peroxidase, catalase, and superoxide dismutase were then observed in the serous fluid.

RESULTS: Malondialdehyde and superoxide dismutase increased in the control group, whereas they were reduced in the Group III and Group IV (p = 0.005; p = 0.008, respectively). The glutathione peroxidase levels revealed no significant differences (p > 0.05), whereas the catalase levels of the group III was higher than in each of the other three groups (p < 0.001). Histopathological evaluation detected reduced lesioning of the organ in the groups which were given atorvastatin and N-acetyl cysteine.

CONCLUSION: Atorvastatin and of N-acetyl cysteine have a similar preventive effect in experimental ischemia–reperfusion injury (Tab. 8, Fig. 6, Ref. 24). Text in PDF www.elis.sk.

KEY WORDS: atorvastatin, N-acetyl cysteine, ischemia–reperfusion injury, volvulus.

Introduction

Colon volvulus is one of the causes of acute abdomen which requires urgent and specific diagnosis. Sigmoid colon volvulus is a very common disorder which responds to colonoscopic detorsion. In unresponsive cases, surgical resection, Hartman procedures and other surgical techniques are applied (1, 2).

Intestinal vascular ischemia also occurs due to the mechanical bowel obstruction in volvulus. Ischemia results when the organ or tissue perfused by insufficient blood flow develops reversible or irreversible cell and tissue damage (3). Following ischemia, the restoration of the blood flow in the region (reperfusion) takes place rapidly, along with the delivery of molecular oxygen into the cells together with reactive oxygen species (ROS) derivatives. In order to prevent irreversible cell damage, blood flow must be restored to the organs and tissues. However, reperfusion can cause more damage to the tissues and organs already damaged by ischemia (4).

N-acetyl cysteine (NAC) is an intracellular glutathione (GSH) precursor and markedly increases glutathione S-transferase activity in the liver. This activity is the foundation of the antioxidant, anticarcinogenic and antimutagenic effects of the agent. The antimutagenic effect of NAC on bacterial test systems as well as its mucolytic and antioxidant effects have long been known (5–7). Under hypoxic conditions, a decrease in blood and tissue GSH levels and an increase in lipid peroxidation products have been reported (8).

Atorvastatin is one of the HMG-CoA reductase inhibitor statins. Statins are known to be anti-inflammatory, to exhibit protective effects in atherosclerosis and to lower serum lipid levels. Additional effects, including the reduction of cytokines, the secretion of adhesion molecules and the proliferation of smooth muscle cells, have also been demonstrated (9–11). Moreover, statins have the pleiotropic effects of reducing vascular inflammation and improving endothelial function, the antithrombotic effects of regression and stabilization of atherosclerotic plaque, as well as onco-protective effects. They have also been found to decrease arterial compliance and improve insulin resistance.

In this study, it was thought that mortality could be reduced by preventing the tissue damage caused by the oxygen radicals generated in the process of reperfusion following detorsion of a volvulus. Atorvastatin and N-acetyl cysteine for reducing ischemia–reperfusion injury were used in experimental model.
Materials and methods

Experimental animals

For this experimental study, the necessary permits and approvals were obtained in accordance with the Animal Research Ethics Committee decision no. 2013/44, dated 12/02/2014. Our experimental animal trials were carried out in the Experimental Animal Center, while the other investigations were conducted in the biochemistry, pathology and pharmacology laboratories of our faculty.

For the study, 28 healthy, mixed male and female albino Wistar rats, 250–300 gm in weight, were selected and kept under appropriate temperature and feeding conditions. The rats were randomly divided into four groups of seven each. For ten days prior to the start of the experiment, the rats were given water and standard feed and housed in individual cages, allowing them to adapt to ambient conditions (Tab. 1).

Surgical procedures

Group I (Sham group): After proper cleaning and sterilization of the area with 10 % povidon iodine solution (Baticon®, Adeka, Turkey), the rats were anesthetized using Ketamine hydrochloride (Ketalar Eczacıbaşı, Istanbul, Turkey), 50 mg/kg i.p. and Xylazine (vial) (Rompun Bayer İlac, Turkey), 10 mg/kg. A midline laparotomy incision of about 3 cm was made and then closed with 3–0 silk. Peripheral venous blood samples (about 2 cc) were taken.

Group II (Control Group): After sterilization and anesthesia, laparotomy + volvulus + detorsion were performed (Fig. 1). One hour after reperfusion, a blood sample was taken and the laparotomy closed.

Group III (N-acetyl cysteine): After sterilization and anesthesia, laparotomy + volvulus + detorsion were performed + N-acetyl cysteine injectable (Asist ampoule, Hüsnü Arsan, Turkey), 300 mg/kg, i.p., was administered half an hour prior to detorsion. One hour after reperfusion, a blood sample was taken and the laparotomy closed with 4–0 silk.

Group IV (Atorvastatin): For this group, after sterilization and anesthesia, laparotomy + volvulus + detorsion were performed. Atorvastatin injectable (prepared in the pharmacology laboratory), 40 mg/kg, i.p., was administered half an hour prior to detorsion (Fig. 2). One hour after reperfusion, a blood sample was taken and the laparotomy was closed with 4–0 silk.

During the post-operative period, paracetamol injectable (Parol vial, Turkey) 100–300 mg/kg, s.c., was administered once every 4 h as an analgesic. Oral feeding was carried out.

One day later, after sterilization and under anesthesia, relaparotomy was performed on all groups, pathological specimens and control blood samples of arterial blood were taken and the animals were sacrificed.

In our experimental volvulus model, transmural occlusion was presented along with complete venous obstruction and partial arterial obstruction. Ischemia and perfusion times were equal and evaluated as one hour.

Biochemical analysis

Blood samples were centrifuged and transported while observing the blood cold chain. Ischemia parameters of the serum malondialdehyde (MDA), glutathione peroxidase (GSH-Px), catalase (CAT) and superoxide dismutase (SOD) were investigated and a statistical analysis was performed.
Measurement of the total (Cu-Zn and Mn) SOD activity was performed according to the method of Sun et al (12) as modified by Durak et al (13). In this method, the SOD activity is based on the reduction of the xanthine/xanthine oxidase system with the produced superoxitin nitroblue tetrazolium (NBT). Kits obtained from Cell Bioplastic and Usnc Life Science, Inc., and a Shimadzu spectrophotometer were used in the analyses.

**Histopathological examination**

For the histopathological examination, the cecum, ascending colon and distal ileum of all the sacrificed rats were removed, washed with physiological serum, placed in containers of formaldehyde and sent to the pathology laboratory. Antimesenteric cecal tissue samples were taken and fixed on paraffin blocks. The 4 μm-thick sections were stained with hemotoxilin–eosin and prepared for the light microscope by a single pathologist. A blind assessment was carried out using the Snyder scale for the classification of morphological changes. The semi quantitative histopathological changes, including hemorrhage, edema, degenerative changes and desquamation and presence or absence of necrosis, in every layer of the intestine were scored (Tabs 2 and 3, Figs 3–6).

### Tab. 2. Snyder’s semi quantitative histopathological evidence scale used to classify the morphological changes in the experimentally induced ascending colon volvulus in the rats.

1) Hemorrhage and edema in each separate layer of the intestine (mucosa, submucosa, muscularis) (Scored from 0–4)

| Group & Animal No. | Morphological Changes & Scores |
|-------------------|-------------------------------|
|                   | Edema | Hemorrhage | Degenerative changes and desquamation | Necrosis and gangrene |
| Group I (Sham)    | 1     | 0          | 0                                      | 0                    |
| 1                 | 0     | 0          | 0                                      | 0                    |
| 2                 | 0     | 0          | 0                                      | 0                    |
| 3                 | 0     | 0          | 0                                      | 0                    |
| 4                 | 0     | 0          | 0                                      | 0                    |
| 5                 | 0     | 0          | 0                                      | 0                    |
| 6                 | 0     | 0          | 0                                      | 0                    |
| 7                 | 0     | 0          | 0                                      | 0                    |

2) Degenerative changes and desquamation in the surface epithelium

| Group II (Control) | Morphological Changes & Scores |
|--------------------|-------------------------------|
|                    | Edema | Hemorrhage | Degenerative changes and desquamation | Necrosis and gangrene |
| 1                  | 4     | 3          | 3                                      | 3                    |
| 2                  | 2     | 2          | 1                                      | 0                    |
| 3                  | 4     | 3          | 3                                      | 3                    |
| 4                  | 4     | 3          | 3                                      | 3                    |
| 5                  | 1     | 1          | 1                                      | 0                    |
| 6                  | 1     | 0          | 1                                      | 0                    |
| 7                  | 3     | 2          | 3                                      | 3                    |

3) Necrosis and gangrene in the intestinal wall (Scored from 0–3)

| Group III (Positive Control) | Morphological Changes & Scores |
|------------------------------|-------------------------------|
|                              | Edema | Hemorrhage | Degenerative changes and desquamation | Necrosis and gangrene |
| 1                            | 1     | 1          | 2                                      | 2                    |
| 2                            | 1     | 0          | 0                                      | 0                    |
| 3                            | 2     | 2          | 3                                      | 2                    |
| 4                            | 3     | 1          | 3                                      | 2                    |
| 5                            | 1     | 0          | 0                                      | 0                    |
| 6                            | 3     | 2          | 3                                      | 2                    |
| 7                            | 2     | 3          | 2                                      | 2                    |

4) Absence of necrosis or gangrene

| Group IV (Treatment) | Morphological Changes & Scores |
|----------------------|-------------------------------|
| 1                    | Edema | Hemorrhage | Degenerative changes and desquamation | Necrosis and gangrene |
| 1                    | 1     | 1          | 0                                      | 0                    |
| 2                    | 1     | 2          | 0                                      | 0                    |
| 3                    | 1     | 2          | 0                                      | 0                    |
| 4                    | 1     | 3          | 2                                      | 2                    |
| 5                    | 1     | 2          | 2                                      | 2                    |
| 6                    | 1     | 0          | 0                                      | 0                    |
| 7                    | 1     | 1          | 0                                      | 0                    |
Statistical analysis

The quantitative variable identifier mean, standard deviation and median values are given in Table 4. The normality of the distribution of these variables was assessed using the Shapiro–Wilk test. The Kruskall–Wallis test was used to compare the groups in terms of edema, hemorrhage, desquamation, necrosis and gangrene variables. The investigation of variations in the group test results was aided by applying the Dunn test. A one-way analysis of variance (ANOVA) was used to examine the group variations in terms of the parameters measured on Day 1 and Day 2. The differences shown by the ANOVA results were evaluated by the Tukey test. The paired t-test was used to compare the groups separately in terms of the average parameters measured on days 1 and 2. The ANOVA was used to compare the averages of the groups in terms of the different values measured on days 1 and 2. The results of the statistical evaluations were found to be statistically significant (p ≤ 0.05). The PASW (ver. 18) program was used for the calculations.

Results

Table 4 shows a comparison of the resulting descriptive statistics and p values of the groups (sham, control, group III, and group IV) in terms of the variables of edema, hemorrhage, desquamation, necrosis and gangrene. Significant differences were determined among the study groups in terms of median values for edema, hemorrhage, desquamation, necrosis and gangrene, at p < 0.05 each. A detailed examination of the differences shows that the median edema value for the sham group was significantly lower than the values of the positive control group and the control group (p = 0.003; p < 0.001). The hemorrhage median for the sham group was significantly lower than the treatment group and control group (p = 0.048; p = 0.007). When desquamation differences are examined, the sham group median was determined as significantly lower than the positive control and control groups (p = 0.043; p = 0.005). When the medians groups are compared in terms of necrosis medians, only the sham group median was found to be significantly different from the control group (p = 0.05). No significant difference was observed among the other groups in terms of necrosis medians (p > 0.05 per comparison). After 24 h, one test subject each from the control and positive control groups died.

The descriptive statistics and p values obtained from the comparison of the groups in terms of MDA, GSHPX, CAT and SOD.
Tab. 4. Statistical comparison of histopathological results*.

| Group                      | Average | Median | Standard Deviation | Minimum | Maximum | p   |
|----------------------------|---------|--------|--------------------|---------|---------|-----|
| **Edema**                  |         |        |                    |         |         |     |
| Sham                       | 0.0000  | 0      | 0.00000            | 0.00    | 0.00    |     |
| Control                    | 2.7143  | 3      | 1.38013            | 1.00    | 4.00    | < 0.001 |
| Positive control           | 1.8571  | 2      | 0.89974            | 1.00    | 3.00    |     |
| Treatment                  | 1.0000  | 1      | 0.00000            | 1.00    | 1.00    |     |
| **Hemorrhage**             |         |        |                    |         |         |     |
| Sham                       | 0.0000  | 0      | 0.00000            | 0.00    | 0.00    |     |
| Control                    | 2.0000  | 2      | 1.15470            | 0.00    | 3.00    | 0.007 |
| Positive control           | 1.2857  | 1      | 1.11270            | 0.00    | 3.00    |     |
| Treatment                  | 1.5714  | 2      | 0.97590            | 0.00    | 3.00    |     |
| **Desquamation**           |         |        |                    |         |         |     |
| Sham                       | 0.0000  | 0      | 0.00000            | 0.00    | 0.00    |     |
| Control                    | 2.1429  | 3      | 1.06904            | 1.00    | 3.00    | 0.002 |
| Positive control           | 1.8571  | 2      | 1.34519            | 0.00    | 3.00    |     |
| Treatment                  | 0.5714  | 0      | 0.97590            | 0.00    | 2.00    |     |
| **Necrosis and Gangrene**  |         |        |                    |         |         |     |
| Sham                       | 0.0000  | 0      | 0.00000            | 0.00    | 0.00    |     |
| Control                    | 1.7143  | 3      | 1.60357            | 0.00    | 3.00    | 0.033 |
| Positive control           | 1.4286  | 2      | 0.97590            | 0.00    | 2.00    |     |
| Treatment                  | 0.5714  | 0      | 0.97590            | 0.00    | 2.00    |     |

* Kruskal–Wallis test

Tab. 5. Comparison of group biochemistry results for the first day (Day 1)*.

| Group | Average | Standard Deviation | Minimum | Maximum | p   |
|-------|---------|--------------------|---------|---------|-----|
| **MDA** |         |                    |         |         |     |
| Sham   | 1.09286 | 0.235319           | 0.672   | 1.310   |     |
| Control | 2.67386 | 0.997492           | 0.731   | 3.522   | 0.002 |
| Positive control | 1.18214 | 0.198211           | 0.945   | 1.511   |     |
| Treatment | 2.08343 | 1.174203           | 0.502   | 4.180   |     |
| **GSHPX** |         |                    |         |         |     |
| Sham   | 0.25243 | 0.060593           | 0.129   | 0.322   |     |
| Control | 0.26514 | 0.063154           | 0.155   | 0.349   | 0.751 |
| Positive control | 0.28671 | 0.080135           | 0.190   | 0.407   |     |
| Treatment | 0.28729 | 0.071542           | 0.200   | 0.386   |     |
| **CAT** |         |                    |         |         | <0.001 |
| Sham   | 0.13329 | 0.032113           | 0.080   | 0.173   |     |
| Control | 0.12671 | 0.018581           | 0.093   | 0.149   |     |
| Positive control | 0.37429 | 0.054503           | 0.291   | 0.449   |     |
| Treatment | 0.18114 | 0.070172           | 0.129   | 0.285   |     |
| **SOD** |         |                    |         |         | <0.001 |
| Sham   | 13.32629| 0.978441          | 11.981  | 14.437  |     |
| Control | 17.69029| 1.179833          | 16.006  | 19.134  |     |
| Positive control | 13.81571| 0.679664          | 13.006  | 15.112  |     |
| Treatment | 13.64586| 1.606397          | 11.036  | 15.700  |     |

* One-way ANOVA

Tab. 6. Comparison of group biochemistry results for the second day (Day 2)*.

| Group | Average | Standard Deviation | Minimum | Maximum | p   |
|-------|---------|--------------------|---------|---------|-----|
| **MDA_2** |         |                    |         |         |     |
| Sham   | 1.00714 | 0.257173           | 0.624   | 1.225   |     |
| Control | 2.56986 | 1.145517           | 0.512   | 3.722   | 0.008 |
| Positive control | 1.25686 | 0.248714           | 0.948   | 1.593   |     |
| Treatment | 2.02000 | 1.230621           | 0.420   | 3.752   |     |
| **GSHPX_2** |         |                    |         |         | 0.423 |
| Sham   | 0.32800 | 0.045607           | 0.248   | 0.395   |     |
| Control | 0.43257 | 0.200967           | 0.207   | 0.854   |     |
| Positive control | 0.37386 | 0.078334           | 0.276   | 0.534   |     |
| Treatment | 0.35917 | 0.070559           | 0.274   | 0.456   |     |
| **CAT_2** |         |                    |         |         | <0.001 |
| Sham   | 0.18971 | 0.054540           | 0.121   | 0.264   |     |
| Control | 0.20200 | 0.053460           | 0.129   | 0.278   |     |
| Positive control | 0.41814 | 0.096670           | 0.258   | 0.505   |     |
| Treatment | 0.23633 | 0.052914           | 0.177   | 0.304   |     |
| **SOD_2** |         |                    |         |         | <0.001 |
| Sham   | 14.13371| 0.777516           | 12.852  | 14.845  |     |
| Control | 18.14557| 1.771975           | 15.128  | 19.968  |     |
| Positive control | 14.44014| 0.639128           | 13.854  | 15.784  |     |
| Treatment | 14.20100| 0.621447           | 13.433  | 15.152  |     |

* One-way ANOVA
averages measured on the first day (Day 1) are given in Table 5. Upon examination of the table, no significant difference among the groups can be seen in the GSHPX averages (p > 0.05). However, significant differences can be observed among the group averages for MDA, CAT and SOD. Close examination of the differences shows that the MDA of the control group was significantly higher than the MDA averages of the sham and positive control groups (p = 0.005; p = 0.008). Similarly, the CAT average of the positive control group was significantly higher (p < 0.001 per comparison) than in the other three groups (sham, control and treatment). Although the SOD average for the control group was found to be significantly higher than the averages of the sham, positive control and treatment groups (p < 0.001 each), no significant difference was observed among the other groups in terms of SOD averages (p > 0.05).

The descriptive statistics and p values obtained from the comparison of the groups in terms of MDA, GSHPX, CAT and SOD averages measured on the second day (Day 2) are shown in Table 6. Upon examination of the table in terms of GSHPX averages, no significant difference was determined among the groups (p > 0.05). However, significant differences were seen among the group MDA, CAT and SOD averages. When the differences were examined, the control group MDA average was found to be significantly higher than the MDA averages of the sham and positive control groups (p = 0.010; p = 0.036). Similarly, the positive control group CAT average was significantly higher than the CAT averages (p < 0.001) per comparison of the other three groups (sham, control, treatment). Although the SOD average of the control group was found to be significantly higher than the SOD averages of the sham, positive control and treatment groups (p < 0.001 each), no significant difference was found among the other groups in terms of SOD averages (p > 0.05).

The p values are included in the examination of possible differences between the measurements for each group taken separately.
on days 1 and 2. As seen in Table 7, the sham group averages for CAT, GSHPX and SOD taken on Day 2 were significantly higher than those taken on Day 1 (p = 0.020; 0.008 and 0.008, respectively). However, no significant difference was seen between the MDA averages measured on days 1 and 2 (p = 0.120). No significant difference was found between the Day 1 and the Day 2 MDA, GSHPX and SOD averages for the control group (p > 0.05 each). In contrast, the Day 2 CAT average for the control group was significantly higher than that of Day 1 (p = 0.003). The Day 1 and Day 2 MDA and CAT averages for the positive control group were similar (p > 0.05); however, the GSHPX and SOD averages measured on Day 2 were significantly higher (p = 0.002 for both). The MDA, CAT and SOD averages for Days 1 and 2 were similar in the treatment group. However, the treatment group GSHPX average measured on Day 2 was significantly higher (p = 0.004).

The descriptive statistics and p values obtained from the comparison of the groups in terms of differences in the MDA, GSHPX, CAT and SOD averages for days 1 and 2 are given in Table 8. The table shows that the groups did not differ significantly in their variations of the averages between Day 1 and Day 2 (p > 0.05 for each).

**Discussion**

Colon volvulus was defined for the first time in 1836 by Rokitansky as “the anormal axial rotation of a segment of the large bowel around its mesentery causing an acute closed loop obstruction” (1). As a result of this obstruction, the endoluminal pressure increases, leading to the development of ischemia, gangrene and finally, perforation of the colon. Colon volvulus is life-threatening, and must be quickly and accurately diagnosed and treated in the most appropriate manner (1, 2). It is recognized that the most important predisposing pathological factors for volvulus are a narrow mesenteric base and a long and mobile colon segment structure. Other predisposing factors include chronic constipation, extended bed rest, colonic motility disorders, megacolon, advanced age, neuropsychiatric disorders, predisposing anatomical factors, previous abdominal surgery, pregnancy, living at high altitudes, Chagas’ disease, Hirschsprung disease and scleroderma (15, 16).

After the volvulus-induced ischemia, restoration of the blood flow to that region (reperfusion) and the reinduction of molecular oxygen along with reactive oxygen species (ROS) derivatives into the cells take place rapidly (3, 4).

It is known that the production of ROS derivatives resulting from intestinal ischemia–reperfusion (I–R) plays an important role in ischemic injury (17).

In this experimental study, the effect of atorvastatin was investigated in the rats exposed to I–R injury as a result of the volvulus. The structural features of NAC, used in the positive control group, were found to be similar to those of atorvastatin.

In addition to the mechanical intestinal obstruction of the volvulus, because of the vascular occlusions in question, many agents are available to prevent damage during reperfusion after torsion via colonoscopy or other procedures. One of these is atorvastatin. The effectiveness of atorvastatin in I–R injury has been observed clinically.

Time is important in dealing with I–R injury (18). Oxidants are formed in I–Rs lasting for as short a time as 2–5 min (18). In ischemia having a duration of up to 60 min, there is an increase in oxygen radicals, while in cases of ischemia that last more than 120 min, they are found to decrease (19). Because it is difficult to detect damage after the occurrence of reperfusion injury in ischemia cases of long duration, for this study, the ischemia duration was set as 60 min.

According to the histopathological results using the scores for edema, hemorrhage, degenerative changes, desquamation, necrosis and gangrene, the lesions in the control group increased, while a significant reduction was detected in the lesions in the positive control and treatment groups. Statistically, however, in the sham group, excepting the necrosis averages, no significant difference was found (p > 0.05 per comparison).

Following reperfusion, the oxygen radicals formed in the tissues lead to the peroxidation of phospholipid fat chains in the cell membrane, causing MDA to be produced (19).

Otamiri and Tagesson reported a 3–4-fold increase in the levels of mucosa and plasma MDA in rats after reperfusion of 5 min duration (20).

Naito et al. stated that the increased amount of MDA in the terminal ileum following I–R was significantly reduced with atorvastatin (21). Likewise, in this study, the MDA average in the control group was found to be significantly higher than the averages of the sham and positive control groups.

The effect of NAC on I–R injury was confirmed by several experiments carried out by Sun et al. Their study showed the effects of the NAC and indomethacin intestinal reperfusion model, and demonstrated that NAC ensured the integrity of the endothelial and epithelial barrier. Again, they determined that NAC was effective in preventing reperfusion injury (22). Another experimental study showed that NAC prevents reperfusion injury by impeding the adhesion molecules that inhibit peroxynitrite and that it provides for the reduction of neutrophils (23).

Demir et al. suggested that in I–R injury, there is an increase in the lipid peroxide levels in the liver, and that NAC application leads to a reduction in the lipid peroxide levels in the tissue (24).

In this study, the group given NAC (positive control group) exhibited less necrosis clinically, compared to the control group.

In the biochemical evaluation, the CAT average of the positive control group was significantly higher than the averages of the other three groups (sham, control and treatment).

MDA is the final product of lipid peroxidation, which is a marker of oxidative damage. Experimentally, in our study, a single dose of atorvastatin treatment given in the acute phase of the I–R injury created by the volvulus reduced the increased level of MDA.

The MDA average of the control group was found to be significantly higher than the MDA averages of the sham and the positive control group (p = 0.005, p = 0.008, respectively). However, no significant difference was seen between the MDA averages measured on days 1 and 2 (p > 0.05).

Although the SOD average of the control group was found to be significantly higher than the SOD averages of the sham, positive control and treatment groups (p < 0.001 each), in terms of the
SOD averages, no significant difference was seen among the other groups (p > 0.05). The SOD data, like those of MDA, presented high levels of I–R injury which dropped with the treatment of a single medical dose of NAC and atorvastatin.

Although no significant difference was detected in the GSH-Px and catalase values, the values were slightly high. Statistically, the CAT average of the positive control group was significantly higher than the averages of the other three groups (sham, control and treatment) (p < 0.001 per comparison). As for the GSHPX averages, among the groups, no significant difference was found (p > 0.05).

Conclusion

The effects of using atorvastatin were observed to be similar to those of N-acetyl cysteine in preventing experimentally induced ischemia–reperfusion injury after detorsion of the volvulus. Further comprehensive research needs to be carried out using other statins and materials.

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Received April 9, 2017. Accepted June 12, 2017.