Disorders of Hemostasis in the Course and After Laparoscopic Cholecystectomy

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SUMMARY
Introduction: Hemostasis is a very important mechanism, whose changes can cause different complications. In the course of surgical interventions some changes in the system of coagulation happen. Laparoscopic cholecystectomy is a method of choice in the treatment of gallbladder calculosis. In the course of the procedure, parameters of hemostasis change, which stimulates a possible appearance of thromboembolic complications. The objective of our research was to reveal the changes in the system of coagulation in patients treated by laparoscopic cholecystectomy. Examinees and methods: Total sample involved 60 patients, divided into two groups, who were treated either by classical or laparoscopic method. Parameters of primary and secondary hemostasis were determined for the patients of both groups in Polyclinic for Transfusiology UKC Tuzla, before the operation, in the course, and 24 hours after the operation, and on the 5th day after the surgery. Results: Patients from both groups showed changes in the process of coagulation. The changes were more expressed in the group of patients treated by laparoscopic cholecystectomy. Very important result was the increased value of D-dimer measured on the 5th day after the operation in the patients operated by laparoscopic cholecystectomy, where value was 2.5 times higher in the relation to preoperative value (263.5 µg/l, so it was out of referential value). Increase of fibrinogen in both groups were an important result of this study. Discussion and conclusion: Results of the study showed changes in the process of coagulation in both groups, and increased fibrinolytic activity of the organism after laparoscopic cholecystectomy (requires a discussion on longer and thorough prophylaxis of tromboembolism).

Keywords: hemostasis, laparoscopic cholecystectomy, D-dimer, prevention of tromboembolism

1. INTRODUCTION

Hemostasis means very important mechanism with two primary functions: to provide liquid state of blood in circulation and prevent bleeding (hemorrhage) at the site of damaged blood vessels (1). Hemostasis disorders are a result of a deficit or a changed function of one of more factors of hemostasis. Clinical manifestations of hemostasis disorders are bleeding (hemoragic syndrome) and thrombosis. Hemorrhagic syndromes are the result of blood vessels disorders, and changes in the flow and composition of blood (2).

An organism responds to every surgical intervention, as well as to any other trauma. Systemic and local response of an organism is coordinated on the metabolic, immunological and neurovegetative level. Surgical trauma causes a high degree–defence of an organism and leads to its reaction to damage, which results in hemodynamic and biochemical disorders, that can be proved by objective methods (3, 4).

Thrombosis as a multifactorial disease is a huge – serious health problem, particularly if it occurred in the course or immediately after the surgical treatment, and one of the first parameters indicating to that complication, are changes in the coagulation system.

Laparoscopic cholecystectomy (LCH) as a minimal invasive method has been more and more applied in surgical practice. Because of its evidenced advantages, it is currently considered as a method of choice in treatment of gallbladder calculosis (5).

Physiologic changes occurring in an organism in the course of laparoscopic procedures are an outcome of pneumoperitoneum influence, and they depend on more factors. The technique itself means a controlled application of insufflation pressure inside abdominal cavity. Pneumoperitoneum occurred in this way has two important effects. The first effect of increased intraabdominal pressure, is a mechanical effect on all intraabdominal organs. The second negative effect of pneumoperitoneum is resulted by CO₂ resorption into the surrounding tissues and blood, what causes biochemical changes and development of acidosis in an organism (6, 7). The increased vein stasis in the region of lower extremities and abdomen, that occurs in the course of LCH, is a good base for thromboembolism occurrence. Debates on thromboembolism incidence in the course of LCH have been constantly present, and it is evidenced that thromboembolism incidence in the course of LCH is very low.

The objective of the study was to establish changes in the system of coagulation in the course and after the operation in patients treated either by laparoscopic or classical methods, and then to compare the results.

The results of most studies pointed to decreased risks of thromboembolism in the course of LCH, regardless to the increased vein stasis and increased intraabdominal pressure.

2. PATIENTS AND METHODS

Prospective study involved 60 patients divided into two groups, who were operated either by laparoscopic or classical cholecystectomy, because of the gallbladder calculosis. The research was carried out in the period from February to July, 2008 year. The patients were of both sexes, from 18 to 80 years old. Before the operation, patients were administered enoxaparin (Clexan) as prophylactic therapy for thromboembolism. The study excluded the patients suffering from acute, malignant and autoimmunologic diseases, and the patients favourable for hemorrhages, with coagulopathies and previously verified thromboembolitic states. The following parameters were determined for all the patients: activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT), fibrinogen, factor VII, antithrombin III, D-dimer and the number of thrombocytes before operation, in the course of operation, 24 hours after the operation, and between 5th and 10th day (most frequently on the 7th day).

Venin blood with no signs of hemolysis and lipemia was used for all the tests. Testing was made out of citrate plasma, and analyzed by device BCT-Behring.

Statistical analysis was done in programme SPSS 15.0 (Chicago, IL, USA). Basic tests of descriptive statistics were done, with survey of measures of central tendency and dispersion.

Tests for each variable for belonging to the normal distribution, were done
by means of Kolmogorov-Smirnoff-test, and histogram graph–survey, as well. Quantitative variables were compared by t-test with correction for unequal variances where they were shedulled according to the normal distribution. For the quantitative variables that were not shedulled according to the normal distribution, we used Mann-Whitney U-test.

3. RESULTS

In the total sample, average age of examinees (±SD) was 50 ± 11 years, with minimum from 23 and maximum 80 years. Appropriate distribution of examinees is given in the Fig. 1.

In the total sample 45/60 (75%) females, and 15/60 (25%) males were present. There was not significant difference (p = 0,55) in sex participation between these two groups. In the examined group, females dominated percentually, what confirms the fact that women are more frequently affected by gallbladder disease (11). The length of hospitalization after LCH was 2 – 3 days, but after OH 4 – 6 days.

Statistically significant difference between these two groups was confirmed (p = 0,001). According to the important results of most studies, patients stayed in hospital after the LCH operation from 0,89 to 1,6 dana (12). Our results indicate a little longer hospitalization.

Median duration of hospitalization in the total sample was 3 days (25-75 percentile:2-5 days). Median duration of hospitalization in the group of the patients operated by laparoscopic method was 2 days (25-75 percentile:2-3 days), while in those operated by classical method it was 5 days (25-75 percentile: 4-6 days). This difference was statistically significant (p < 0,001), shown in Figure 2.

Dynamics of D-dimer value changes is given in the Figure 3. D-dimer values were significantly higher in the examinees experienced laparoscopic cholecystectomy, than in those operated by classical method (p < 0,001). In every next measuring those values were increasing, particularly seen in the laparoscopic group of patients in the measurements made after the 5th day from the operation.

Dynamics of fibrinogen values change is given in the Figure 4. Significantly higher value of fibrinogen was found in the classical cholecystectomy examinees in measurements at the end of the operation (p = 0,02), while in measurements after 24 hours (p = 0,16) and several days after the operation (p = 0,44) there was a significant difference in values.

4. DISCUSSION AND CONCLUSION

In the course of the operation and particularly after it, very significant changes occurred in the process of coagulation. By surgical trauma or some other event, once initiated process of coagulation could cause hemostasis as a consequence, because of the uncontrolled spreading. One of the most applied operations in modern surgery is cholecystectomy, a method of choice in the treatment of gallbladder calculus. In relation to the classical method, LCH has a decreased systemic response, shorter hospitalization, faster functional recovery and aesthetic effect, and significantly lower chances for intraoperative complications (8, 9, 10).

The examinees’ age and sex were in agreement in the tested groups, while within each group females dominated percentually, what confirms the fact that women are more frequently affected by gallbladder disease (11). The length of hospitalization after LCH was 2 – 3 days, but after OH 4 – 6 days.

Statistically significant difference between these two groups was confirmed (p = 0,001). According to the important results of most studies, patients stayed in hospital after the LCH operation from 0,89 to 1,6 dana (12). Our results indicate a little longer hospitalization.
Analysis of the routine test, as APTT, TT, PT and thrombocyte number, did not show significant changes in the values obtained between the groups, nor in the targeted periods of investigation. Almost similar results were published by Vodnik et al. (2). Either factor VII as an activator did not show any difference within the targeted measurements. Milić et al. (13) gave more significantly lower values of F VII in 24 and 72 hours after laparoscopic cholecystectomy and considered it important predictor of risk from thromboembolism. Increased values of fibrinogen in both groups in every next measurements can be explained by the fact that fibrinogen is a protein in acute phase, that organism is in state of inflammation and the state of acute phase respond. Similar results were published by Martinez-Ramos, et al. (14); Prisco, et al. (15), and Vodnik, et al. (2) whose values were a little bit higher in patients operated by the classical method. Fibrinolysis as the strongest physiological mechanism for fibrinogen dissolution, enables recanalization of a blood vessel with a blood clot in it, whether it is a hemostatic clot at the site of a blood vessel damage, or pathologic thrombosis. D-dimer occurs as a result of leasing of stabilized fibrin under plasmin influence, and that is a certain sign of fibrin layer presence, i.e. a clot present somewhere in circulation. This test is a marker of hypercoagulable state of blood, as an essential factor in the thrombosis occurrence (2).

In our research D-dimer values increased going from the initial measuring, and between 5th and 10th days after the operation in the group of LCH patients those values were 2.5 times higher than the preoperative values, i.e. they were out of limits of referent values. Either in the group of OH patients slight increase of D-dimer values occurs in the course and 24 hours after the operation, and in the last measurements that increase was in referent limits. Similar results were published by Prisco et al. (15) and Dexter et al. (16), where D-dimer values in the course of the operation, then 6 and 24 hours after it, had increasing characteristics. In relation to the laparoscopic method, the values in the patients operated by classical method, were significantly higher. Martínez–Ramos et al. (14) in their studies found increasing D-dimer values immediately after the operation, after 24 hours, on the 7th day after the operation, what dominated in the group of LCH patients. Results published by Milić et al. (13) showed increased D-dimer values in both groups in the course of the operation, 24 and hours after it, that so higher increase was found in the group operated by classical method. This research was done with no prophylaxis of thromboembolism. Regardless of this kind of data, final conclusion was that laparoscopy either with smaller changes in coagulation represents a risk of thromboembolism occurrence, and that prophylaxis should be a routine part of the procedure itself. The studies carried out in Serbia, Vodnik et al. (2) showed increased D-dimer values in both groups, with higher values in the group of the patients operated by classical method, immediately after the operation and 24 hours after it, but these values got normal still in three days in the LCH patients.

So, many studies, as well as ours, point to the increased fibrinolytic activity, even if prophylaxis of thromboembolism was included. Probably because of shorter hospitalization, and different attitudes to the question of thromboembolism prevention length, the tested groups were not treated equally.

Laparoscopic patients stayed shorter in hospital, and in relation to this, they experienced most two-day prophylaxis. On the other hand, the patients operated by the classical method, stayed significantly longer in the hospital, approximately around five days, and were continually receiving prophylactic therapy. Increase of D-dimer values in the LCH patients were far more expressive after the operation in the period after the 5th day, when no prophylaxis, while in the course and 24 hours after the operation, in the period of active prevention, this incres was insignificant.

An opened question still remains whether these changes would be reduced or completely prevented by means of a long prophylaxis, or be present because of the negative effects of laparoscopy (pneumoperitoneum, reverse Trendelburg’s position). As D-dimer is a parameter of hypercoagulable state and an indicator of fibrinolytic activity of an organism, it would be good to consider the implementation of longer and more complete prophylaxis in laparoscopy.

REFERENCES

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