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Research Article

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Preoperative Fibrinogen as a Predictor for Development of Postoperative Hyperamylasemia and Postoperative Pancreatitis

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Abstract

Introduction: Postoperative pancreatitis complications can be separated into two main groups based on literature reviews and clinical and experimental trials. Some authors suggest that postoperative pancreatitis is a severe complication that should be treated conservatively and operatively if needed. Other authors defend an opposite opinion that only postoperative hyperamylasemia exists, which is a transitory condition with no risk of complications.

Keywords: Postoperative Pancreatitis; Hyperamylasemia; Preoperative Fibrinogen

Methods

At the University Hospital for Active Treatment Alexandrovska, Clinic of General and Liver-Pancreatic Surgery, a cohort of patients with increased amylase concentrations in the postoperative period between January 2017 and December 2018 were studied and followed with retrospective analysis of preoperative fibrinogen. Regardless of the type of surgery to which they were subjected, all patients who presented with an elevated amylase concentration in the postoperative period were selected. The working hypotheses were the following: i) preoperative fibrinogen levels are directly relevant in the development of postoperative pancreatitis; ii) the concentration of fibrinogen preoperatively is a prognostic factor in the early postoperative period and mark the boundary at which patients will develop postoperative pancreatitis and its various clinical manifestations and iii) the postoperative period is accompanied by transient postoperative hyperamylasemia and absence of complications when preoperative fibrinogen is under a specific level. To test these hypotheses, the values of preoperative fibrinogen and all patients who developed postoperative pancreatitis and transient postoperative hyperamylasemia were statistically analyzed using SPSS v23 software.

Results

The results show that, with an 80% confidence interval (CI), a statistically significant difference is found in the concentration of preoperative fibrinogen in patients who developed postoperative pancreatitis versus those with transient hyperamylasemia.

Discussion/Conclusion: The present study shows a direct link between preoperative fibrinogen levels, and the course of both postoperative pancreatitis and transient hyperamylasemia, making this marker valuable in elucidating the differences in the development of postoperative pancreatitis and transient hyperamylasemia in the early postoperative period. Thus, preoperative fibrinogen can be used to inform the correct diagnosis and decide effective treatment.

Introduction

Postoperative pancreatitis is a severe complication in the postoperative period. Although postoperative pancreatitis develops in a pathway quite similar to acute pancreatitis, there are a number of specifics in its etiology and evolution, making postoperative pancreatitis a matter of clinical interest and providing it with individual characteristics. The cases of postoperative inflammation of the

pancreatic gland constitute 10% of all cases of acute pancreatitis. Different aspects dependent on immunological cell diversity of the pancreas, pro- and anti-inflammatory cytokines, and biochemical reactions may cause postoperative inflammation of the pancreatic gland [1]. In the early postoperative period, another clinical event can be observed-postoperative hyperamylasemia. This is a transitory condition, associated with higher levels of serum amylase, which develops with no risk of complications [2]. This versatile picture of clinical conditions, which can appear in the early postoperative period, is directly associated with the great diversity of immune cells in the pancreas and the vast majority of reactions between them and secretion of cytokines and their interaction with some normal blood plasma proteins.

The effort was to distinguish whether there is an acute postoperative pancreatitis or there is just a case of a transitory hyperamylasemia in the early postoperative period. In the search for an accurate preoperative marker predicting which of these two conditions will appear, a five-year retrospective study has been done, electing all patient cases with elevated amylase levels postoperatively. As a result, a blood serum marker has been found to be directly relevant for development of pancreatitis – fibrinogen.

Fibrinogen is a glycoprotein complex normally secreted by the liver [3]. Nevertheless, of its major role in blood coagulation and formation of blood cloth during tissue and vascular injury, fibrinogen is also an acute phase protein and it levels rise in response of systemic inflammation [4, 5]. In the early postoperative period in an event of pancreatitis, there is a great level of tissue damage and a huge inflammatory systemic response. As an early marker of that life-threatening condition are used the rising levels of serum amylase and lipase. However, in most of the cases, the pathologic chain reaction once triggered cannot be stopped and the postoperative pancreatitis develops with versatile picture of complications. Fibrinogen as a preoperative marker can elucidate the risk of development of pancreatitis and predict whether pancreatitis or hyperamylasemia will appear in the early postoperative period [6-8]. Thus, this marker can aid correct diagnosis and effective treatment.

Aim

The aim of the study was to determine a specific interval, in the levels of preoperative fibrinogen, above which there is a high risk of development of pancreatitis in the early postoperative period. The study also aimed to determine the accuracy of fibrinogen as a marker to differentiate postoperative hyperamylasemia from postoperative pancreatitis.

Materials and Methods

At the University Hospital for Active Treatment Alexandrovska, Clinic of General and Liver-Pancreatic Surgery, a cohort of patients with increased amylase concentrations in the postoperative period between January 2013 and December 2018, were studied retrospectively as the preoperative levels of the fibrinogen were examined and follow up prospective study was done with description of all versatile complications which have appeared during evolution of postoperative pancreatitis. A second cohort group was separated in the postoperative follow-up, including all cases of transitory hyperamylasemia. In both cohort groups the levels of the albumin were normal, so the fibrinogen – albumin ratio was normal. Regardless of the type of abdominal surgery to which the patients were subjected, all of them who presented with an elevated amylase concentration in the postoperative period were selected. The study protocol and ethics approval were postulated by a clinical council of the Department of General and Operative Surgery, Medical University Sofia, which serves as a scientific-ethical committee for the Clinic of General and Liver-Pancreatic Surgery at the University Hospital for Active Treatment Alexandrovska. The clinical council stated that biochemical tests for fibrinogen, albumin, etc. are standard procedures in the diagnostic and treatment process at the Clinic of General and Liver-Pancreatic Surgery and do not need a specific ethics approval.

One standard tube of peripheral venous blood was taken from each patient at the day before operation. The tubes were of the BD Vacutainer Plus Coagulation Citrate Tubes with a volume of 2.7 mL and dimensions of 13 x 75 mm and contain 3.2% sodium citrate in them.

Results

A retrospective correlation analysis was done associating the levels of preoperative fibrinogen and the appearance of postoperative pancreatitis. The cohort consisted of 412 cases of patient who underwent an abdominal surgery and all of the patients had elevated levels of blood serum amylase in the early postoperative period. In 70% of all the cases in the studied cohort preoperative levels of the fibrinogen were elevated above normal and all these patients developed pancreatitis in the early postoperative period. These findings gave the conclusion that there is a direct connection between preoperative levels of the fibrinogen and the development of pancreatitis postoperatively. In the other 30% of the patients in the studied cohort some developed pancreatitis and other had just a transitory hyperamylasemia postoperatively. By applying retrospective correlation analysis was found that if preoperative levels of fibrinogen are above 3.4 g/l there is a statistically confirmed with 80% confidence interval -development of postoperative pancreatitis. This result showed a direct statistically proved connection, between preoperative levels of fibrinogen and development of pancreatitis. Pearson ‘s correlation coefficient for use with Eta coefficient was = 0,829 which shows a verry strong statistical correlation between these two factors. This concluded that preoperative levels of the fibrinogen are accurate marker for development of postoperative pancreatitis.

Table 1 and Figure 1 present distribution of patients’ preoperative fibrinogen separated in different groups by the factors: 1/ type of operated abdominal organ 2/ levels of fibrinogen above and below the boundary of 3.4g/l.

Figure 1 and Table 1 show the superior number of patient cases with elevated level of preoperative fibrinogen above0 3.4g/l.

Number of patients in each group	Preoperative level of fibrinogen up to 3,4 g/l	Preoperative level of fibrinogen above 3,4 g/l
Gallbladder and bile ducts	31	161
Stomach	20	109
Pancreas	17	82
Liver	10	55
Colon and intestine	17	114
Spleen	25	82
Other organs	4	27

Table 1 Preoperative levels of fibrinogen in different groups elected by the type of operation

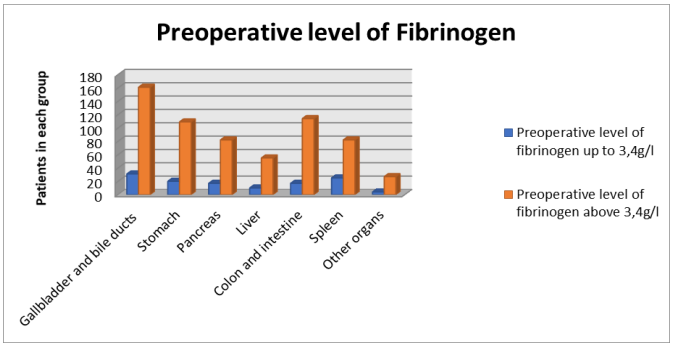

Figure 1 Preoperative levels of fibrinogen in different groups elected by the type of operation

Discussion

The present study shows a direct association between the preoperative fibrinogen levels, and the pathway of development of postoperative pancreatitis. Statistically proven fibrinogen levels predict postoperative pancreatitis progression as an acute inflammation and development of various clinical manifestations, or progression into a transient postoperative hyperamylasemia with absence of complications. Results show that, with a very high CI, levels of preoperative fibrinogen above 3.4g/l is a predictor of the inflammatory process in the pancreas and is associated with the severity of inflammation. Lower preoperative levels of fibrinogen -under 3.4g/l, exhibits with a very high CI, evolution of pancreatitis into a transient postoperative hyperamylasemia. The results from that specific clinical trial confirm the results obtained by other authors and also elucidate the direct connection between clinical evolution of postoperative pancreatitis and preoperative levels of fibrinogen. Postoperative pancreatitis is a complex process with many factors involved in its regulation. The results obtained will elucidate a better understanding of postoperative pancreatitis evolution and also help in optimizing treatment process by early prediction of development of various clinical manifestations and complications.

Conclusion

The present study shows a direct link between the preoperative fibrinogen levels, and the evolution of postoperative pancreatitis and transient hyperamylasemia. With a 80% confidence interval, a statistically significant difference was found between patients who developed postoperative pancreatitis and those with transient hyperamylasemia in the preoperative period. These results show that preoperative fibrinogen levels can be used to clinically elucidate differences in the development of postoperative pancreatitis and transient hyperamylasemia in the early postoperative period, thus this marker can aid correct diagnosis and effective treatment.

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