

Bleeding Risk in Children with Preoperative Prolonged Coagulation Tests

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What is known on this subject?

Repeated tests and controls are performed in mildly prolonged coagulation tests, and very essential surgical interventions are delayed.

What this study adds?

Repeated tests and checks are unnecessary in mildly prolonged coagulation tests.

ABSTRACT

Objective: Prolonged coagulation test is a common finding before surgery. This study determined the prolonged prothrombin time (PT) and/or activated partial thromboplastin time (aPTT) during the surgical preparation of pediatric patients.

Material and Methods: As a cross-sectional study, 74 children aged 0.25-17 years, who had prolonged preoperative coagulation tests, were included in the Eskişehir State Hospital Pediatric Hematology and Oncology Clinic between September 3, 2013, and September 16, 2014.

Results: The mean age of the children was 5.6 ± 3.4 years, wherein 60 (81%) cases were male. Adenoid-tonsillar operations were planned in 46%, circumcision in 43%, abdominal operations in 5%, and other operations in 6%. A history of bleeding was found in 7 (10%) of the families and 3 (4%) of the cases. Previous surgery or injury was found in 24 (32%) of the children and did not develop more bleeding than expected. The coagulation tests revealed 22 (30%) patients with prolonged PT (value range: 14-35.1 s), 47 (63%) with prolonged aPTT (value range: 37.1-129.6 s), and 5 (7%) with both prolonged PT and aPTT. A necessary operation was performed in 47 patients who did not have a history of bleeding diathesis in the patient or family, with a normal mixed test and factor levels, and PT of <20 s and aPTT of <63.3 s. No bleeding complications were observed during or after the operation in any of these cases.

Conclusion: Our results revealed that in case of prolonged PT or aPTT values before surgery, no risk of bleeding is encountered during the surgery if a history of bleeding diathesis is not present in the patient or family and factor levels are normal.

Keywords: Child, blood coagulation tests, bleeding diathesis, perioperative period

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Introduction

The cost and the effectiveness of coagulation tests that are performed before surgical intervention is a long-debated issue (1,2,3,4). Contrarily, existing habits and efforts are done to prevent possible complications, and problems arise from the delay of the planned surgery together with unnecessary time and financial loss.

Prothrombin time (PT) and activated partial thromboplastin time (aPTT) are used as hemostasis screening tests and are requested in preoperative "routine" analyzes (4,5). The clinical significance of prolonged PT and/or aPTT values that have been reported, especially in patients without anticoagulant therapy and significant liver pathology, is very limited and without bleeding symptoms before and after (6,7).

A limited number of articles have been published in our country on preoperative coagulation tests and evaluations that should be performed in case of prolonged results, and most of them are compiled (8,9,10,11,12,13). This study compiled the cross-sectional data of cases that are referred to Eskişehir State Hospital Pediatric Hematology and Oncology Outpatient Clinic because PT and/or aPTT measurements were longer than normal and discussed these results.

Material and Methods

In this cross-sectional study, 74 pediatric patients aged 0.25-17 years, who were found with prolonged preoperative PT and/or aPTT tests, were admitted to the Eskişehir State Hospital Pediatric Hematology and Oncology Outpatient Clinic between September 3, 2013, and September 16, 2014. PT was 13.5 s and aPTT was 37 s were given as the upper limits of the coagulation laboratory of the hospital where our study was conducted, thus these values were taken as basis in the study. All results included in the study were obtained from the same coagulation laboratory. For interventional procedures, PT and aPTT that is >1.5 times the upper normal limit (PT of >19 s and aPTT of >55 s) was determined as significant elevation and further investigations were planned (14). Age, gender, place of origin of cases, complaint upon arrival, easy bruising, delayed bleeding, nosebleeds, bleeding in other parts of the body, excessive menstrual bleeding during menstruation (the number of pads used in the first 2 days, the need to put a diaper when the bleeding increases, and total duration of menstruation), accompanying symptoms, and drug use was asked. PT and aPTT tests were performed with Greiner Vacuette® 9NC sodium citrate of 3.2%, IL-ACL TOP 500 CTS (USA) device on the samples taken into 3 mL coagulation tubes. Cases with prolonged results that persisted

in at least two measurements, those with a family history of bleeding diathesis, and those with prolonged results of >50% of the upper limit in the tests were subjected to, further coagulation factors and mixture tests. The mixture test is an easy and inexpensive test that guides the involvement of factor deficiency or the presence of inhibitors with prolonged coagulation test results. Coagulation tests are based on the principle of re-running the coagulation test by mixing a sample that is within normal limits with a long sample in half. If factor deficiency is the cause, coagulation tests are normal as a result of the mixture but do not return to normal in the presence of an inhibitor. In cases where tests were significantly longer but advanced coagulation studies were normal, the operation approval was given after the informed consent of the patient's parents. Ethical approval was obtained from the Chief Physician of Eskişehir State Hospital on 22.11.2013.

Statistical Analysis

The variables were checked for homogeneity of variance using the Levene statistic. Data were presented as number, ratio, and mean \pm standard deviation (SD). Chi-square was used to compare the ratios, and a dependent sample t-test was used to compare the means. Differences were considered to be statistically significant at a p value of <0.05. The Statistical Package for the Social Sciences version 16 for Windows (SPSS® Inc, Chicago, IL) was used for the statistical analysis program.

Results

A total of 60 (81%) male patients, with a mean age of 5.6 ± 3.4 years, were planned for adenoid-tonsillar operation in 46%, circumcision in 43%, abdominal in 5%, and other operations 6%. Even when circumcision operations were removed, prolonged coagulation tests were found to be significantly higher in boys than in girls ($p < 0.001$). Epistaxis was the only bleeding diathesis in the anamnesis that accounts for 3%. The anamnesis for bleeding diathesis in first or second-degree relatives was 7%, but none were diagnosed with bleeding disorders. Surgical intervention was previously undergone by 32% of patients and had no bleeding complications.

In cases with prolonged coagulation tests, 22 (30%) had prolonged PT (range; 14-35.1 s), 47 (63%) had prolonged aPTT (range; of 37.1-129.6 s), 5 (7%) had both prolonged PT and aPTT. Tests were repeated in the same week in all of these cases. The comparison of the mean values of both parameters and international normalized ratio (INR) values before and after surgery revealed no significant difference ($p > 0.05$, Table 1), and both were prolonged after the repetition. PT or aPTT was significantly longer in 5 of all cases. One patient had a

Table 1. The first and second measurement results of patients who were approved for the operation*

	PT (second)		INR		aPTT (second)	
	First	Repeat	First	Repeat	First	Repeat
Mean (\pm SD)	13.5 \pm 3.7	12.9 \pm 2.6	1.17 \pm 0.34	1.11 \pm 0.18	40.1 \pm 7.9	41.1 \pm 7.0
Shortest	10.6	10	0.92	0.86	20.9	26.1
Longest	35.1	20.2	3.03	1.74	62.3	62

*No significant difference was found between the means of the two measurements for PT, INR, and aPTT ($p>0.258$). PT: Prothrombin time, INR: International normalized ratio, aPTT: Activated partial thromboplastin time, SD: Standard deviation

history of suspicious bleeding diathesis (more than 1.5 times the normal value), although aPTT was 40 s, and 3 cases had a family history of bleeding diathesis with epistaxis (1 prolonged PT, 2 prolonged aPTT) examinations were made.

Mixture test in prolonged APTT, factor VIII, vWF, vWF R: C, and factor IX; factor VII levels were studied in patients with a prolonged PT, and factor X levels in those with prolonged PT. Factor VIII level was 44% in one case and factor VII level was 40% in one case. The levels of other cases were found to be within normal limits. Normal values were found in patients who underwent the mixture test, and no case had a significant length in aPTT value after 2 h of incubation.

A total of 65 cases had prolonged coagulation tests with normal factor level, suspected bleeding diathesis in their family, previous surgery but had no bleeding and had normal mixed tests and normal factor level with PT of ≤ 20.2 s or aPTT of < 63.3 s (normal for PT and aPTT was 1.7 times the upper limit) were approved for operation. Of these, 47 cases underwent the necessary surgical intervention, and none had bleeding complications during or after the operation.

Tests were repeated after an average of 80 days in 20 cases with significantly elevated coagulation tests and/or bleeding diathesis, and after an average of 150 days in 10, without significant difference in the mean PT and aPTT values compared to the baseline levels ($p>0.121$).

Discussion

Prolonged coagulation tests are a common finding in centers where pre-surgical screening is performed. In this case, the planned operation is postponed and the analyzes are repeated, as well as consultations from relevant branches, and new and advanced examinations are started. Surgery for a condition, such as adenoid vegetation, may cause treatment delays and additional complications in the patient, whereas an operation, such as circumcision, that is performed without medical necessity may cause an anxious process for the family. Contrarily, the obtained prolonged coagulation test may be the only finding of bleeding diathesis that was not diagnosed

until that time, since tests, such as complete blood count, is uncommon.

The basic hemostatic system is known in detail and quickly analyzed, but the main issue is the result interpretation and follow-up in these cases (15). The benefit of routine basic coagulation tests in surgical procedures or other medical conditions is controversial (6,16). These tests, which have limited sensitivity and specificity, were reported to have high false positivity, low accurate prediction and prediction levels, and high false negativity (4,15). However, prolonged coagulation test results in patients with a history of bleeding before surgery were emphasized to guide the diagnosis of bleeding diathesis (16,17,18). Preoperative coagulation studies in children have been investigated in adenoidectomy and/or tonsillectomy operations, as they are the most frequently performed operations worldwide (4,18,19,20,21).

Various values are accepted as limits in the literature; however, PT of >13 s and aPTT of >36 s are generally accepted as prolonged (6). Our study considered the normal limits of our laboratory, which are PT of 13.5 s, aPTT of 37 s as the upper normal limit. In case of significant increased PT and aPTT values, the tests were repeated, and further coagulation studies were performed with values that are 1.5 times and above the upper normal limit, but no abnormal results were found. Patients and their close relatives without bleeding in cases of previous surgical intervention, circumcision, and injury, and the absence of a diagnosed bleeding disease were supportive factors in the decision to approve the operation. Our study is different from other studies as it consisted of cases that were operated on despite the prolonged coagulation test results (7,17,21,22,23). A study reported that PT and/or aPTT were prolonged and surgical intervention was performed only with pro-coagulants and/or antifibrinolytics in mild factor deficiencies, and none required specific treatment due to bleeding complications (24). Since no specific factor deficiency was detected in our study, procoagulant or antifibrinolytic treatments were planned to be given in case of bleeding.

Cases with more than five nosebleeds annually are considered recurrent nosebleeds (25). In addition, if PT and

aPTT values are determined to be prolonged, studying the FVII, FVIII, FIX, vWF: Ag, and vWF-ristocetin cofactor activity as second-line tests is recommended. Our study found no coagulation factor deficiency in any patients with epistaxis.

Karaca et al. (12) reported that 21 of 100 children who underwent preoperative coagulation screening tests (PT, INR, and aPTT) for adenotonsillectomy operation were found to have longer than normal tests, wherein 2 (2%) had coagulation disorder; therefore, regardless of the cost, preoperative coagulation screening tests (PT, INR, and aPTT) were emphasized as necessary examination. However, in this study, the diagnosis of coagulation disorder was made with a value of 44.8% for factor VIII and 52% for vWF. These levels stand as a compelling and unnecessary situation, both for making a diagnosis and for leaving patients and their owners along with the diagnosis of hemorrhagic disease. In addition, with the obtained results, concluding that these tests are necessary before the operation seems impossible.

Bhasin and Parker (4) reported that results were found to be normal in repeated tests in approximately 50% of cases. Samková et al. (24) found a similar rate when the tests were repeated in the hematology laboratory. Since those who were normal in repeated tests in our study were excluded from the study, it is impossible to present the coagulation test results in the second test within the same week. However, patients with significantly prolonged tests and/or findings in bleeding diathesis had no significant changes in the coagulation tests that were performed in the same laboratory after approximately 3 and 5 months, which suggests no significant benefit for tests before 6 months, especially in cases without bleeding symptoms.

Manning et al. (19) determined that preoperative PT and aPTT screening were not associated with surgical bleeding in 994 patients who underwent adenotonsillectomy. A 12-year retrospective study published by Wei et al. (22) found that 90 (1.93%) of 4,662 patients who underwent tonsillectomy had bleeding, of which only 1 case was primary and the remaining 89 had secondary bleeding. Primary bleeding occurs in the

first 24 h after tonsillectomy, which usually accompanies coagulation disorder, whereas secondary bleeding was most common on days 5-6 postoperative. The mean bleeding risk after tonsillectomy has been reported to be between 0.1% and 9.3% (22,23). The absence of bleeding observed in any of our cases shows that the risk of bleeding is not different from the others in cases of a certain prolonged level in coagulation tests in patients without bleeding diathesis findings in the anamnesis and examination. A study supporting our finding reported that a higher probability of bleeding after surgery was associated with the standard medical questionnaire, not with abnormal coagulation tests (26).

Conclusion

Prolonged PT and aPTT values before surgery of up to 1.5 times, no diagnosis of bleeding diathesis in the child or family, and result returns to normal with mixed tests, then bleeding will not occur during and after the operation. We concluded that repeated tests and to test renewed before 3 months is not necessary to check for normalization. However, larger studies are needed on this subject.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Chief Physician of Eskişehir State Hospital on 22.11.2013.

Informed Consent: Patient consent was obtained.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: A.A., Design: A.A., Data Collection or Processing: A.A., A.S., Analysis or Interpretation: A.A., Literature Search: A.A., Writing: A.A.

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