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Post-Tonsillectomy Bleeding: A Meta-Analysis

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Objective/Hypothesis: **To reconcile conflicting reports and opinions of the value of preoperative coagulation studies for patients undergoing tonsillectomy.** ***Study Design:*** **Meta-analysis: Articles were identified by MEDLINE search, references from review articles, textbook chapter, and retrieved reports. Independent observers selected prospective trials of patients undergoing tonsillectomy or adenoidectomy and tonsillectomy. Retrospective studies meeting other inclusion and exclusion criteria were included for sensitivity analyses of results.** ***Methods:*** **Data were abstracted from studies for an end point of bleeding with normal and abnormal coagulation tests. Four prospective studies met all inclusion and exclusion criteria. These four studies were used in the data synthesis. An additional eight retrospective studies met all other criteria and were used in the sensitivity analysis.** ***Results:*** **Pooled analysis of 3384 patients revealed a rate of 3.3% (95% confidence interval [CI], 2.5%–4.1%) for post-tonsillectomy bleeding in patients with normal coagulation studies. A rate of 8.7% (95% CI, 1.5%–15.9%) was obtained for bleeding in patients with abnormal coagulation studies. No significant rate difference in post-tonsillectomy bleeding was demonstrated.** ***Conclusion:*** **There is no difference in the rate of post-tonsillectomy bleeding in patients with abnormal coagulation studies as compared with patients with normal coagulation studies obtained preoperatively.** ***Key Words:*** **Tonsillectomy, bleeding, coagulations studies, meta-analysis.**

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INTRODUCTION

The first tonsillectomy was described by Celsus in 30 A.D.[1] Tonsillectomy continues to be one of the most commonly performed surgical procedures. Although most patients who have tonsillectomies are healthy, there remains a small risk of postoperative bleeding in all patients. More recent studies have found a 2% to 4% risk of bleeding[2] with a mortality rate of 1 death in 20,000 procedures.[3] Coagulation studies have been used as screening tests to predict postoperative hemorrhage. There are conflicting reports concerning the usefulness of preoperative coagulation studies in predicting postoperative hemorrhage. The efficacy of the prothrombin time (PT) and activated partial thromboplastin time (aPTT) in predicting postoperative hemorrhage is unknown.

We performed a systematic review of published studies to reconcile the conflicting reports of the value of routine preoperative coagulation studies for patients undergoing tonsillectomy and adenoidectomy. Our hypothesis is that preoperative coagulation studies have minimal predictive value in detecting patients at risk for postoperative bleeding.

MATERIALS AND METHODS

Study Identification

Articles were identified by use of an English language MEDLINE search (MeSH, i.e., Medical Subject Headings) from January 1966 to October 2000. Initial subject terms were "tonsillectomy" and "bleeding." Search results were limited to human subjects and supplemented with review articles and source articles, as well as textbook bibliographies. Independent observers selected prospective trials of patients undergoing tonsillectomy or tonsillectomy and adenoidectomy (inclusion set). No search for unpublished data or trials was made. Retrospective studies meeting all other inclusion and exclusion criteria were included for a sensitivity analysis of the results. This combined list of references was designated as the initial data set. We did not consider it necessary to use computer databases other than MEDLINE and the Cochrane library because of extensive manual review.

We reviewed the titles and abstracts of the initial data set for studies of preoperative coagulation tests, postoperative bleeding, and tonsillectomies and adenoidectomies. Articles were excluded if they were review articles or retrospective studies, letters, and surveys of clinical management. Articles were also excluded for containing an animal model or patients with concomitant illnesses or patients undergoing procedures other than tonsillectomy and/or adenoidectomy. A spreadsheet was used for the remaining articles to identify controlled trials with suitable comparison groups. An effort to choose more articles than would qualify was made. We determined independently the studies to include according to reviews of the "Methods" sections of identified clinical trials. We chose articles that used human subjects, had tonsillectomy and/or adenoidectomy as the sole procedure, that were prospective, and had groups without concomitant ill-

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nesses. Data were abstracted from the studies for an end point of bleeding with normal and abnormal coagulation tests. The inclusion and exclusion criteria were distinct and separate from criteria used to judge the quality of the articles found in the final data set.

Two reviewers independently rated each study in the final data set. The study was given a score from 0 to 2 for six items: description of the patient sample, diagnostic criteria for bleeding, randomization protocol, statistical analysis, results presentation, and compliance check. The measures used to calculate the quality score are not inclusion or exclusion criteria. These measures were used to assess quality of the selected articles. An overall quality score from 0 to 1 was calculated by dividing points accrued by the maximum attainable points. This value was used to assign relative weights to each study for the sensitivity analysis. A total of four studies met all the criteria for the meta-analysis and are included in the current study.[4–7]

Statistical Methods and Sensitivity Analysis

Four prospective studies met all inclusion and exclusion criteria and are included in the data synthesis. Data evaluated included sample size, definition of bleeding, type of study, total number of postoperative bleeds, total number of abnormal coagulation studies, number of patients with normal coagulation tests and bleeding, and number of patients with abnormal coagulation tests and bleeding. The rate of bleeding was assessed by computation of the rate difference (RD) with exact 95% confidence interval (CI). If the RD with the 95% CI contains zero, then the results of the study are not statistically significant.

Sensitivity analysis was conducted by including the retrospective studies that met all the other criteria and by examining whether this changed the combined results. In addition, we calculated the number of studies finding the opposite results needed to refute our findings.

RESULTS

Literature Search

The initial data set contained 549 articles. Two hundred eight foreign language articles were then excluded. From the remaining 341 articles, 337 were excluded for various reasons as shown in Table I. Age was not an exclusion criteria as many studies contained patients of all ages. Only four articles met all the criteria and are included in the analysis. Eight additional articles met all inclusion criteria except for retrospective design. These articles were used for sensitivity analysis. Characteristics of each individual study are listed in Table II. Five of the eight retrospective articles are represented in Table II.

TABLE I.
Selection of Final Dataset for Meta-Analysis.

Total		Remaining	Excluded
English	549	341	208
Review/opinion			54
Letters/case reports			57
Animal			1
Concomitant illness			28
Procedure other than T&A			
Retrospective			42/8*
Outcome of interest			45
Inclusion criteria:			
Human			see above
Pt/Ptt screening and defined outcome of bleeding			109
Prospective/clinical trials meeting above			
Inclusion criteria	4	1	
Final dataset	4		

* Eight from 42 articles were used for sensitivity analysis, meeting all inclusion criteria except for prospectivity.

T & A = tonsillectomy and adenoidectomy; PT/PTT = prothrombin time/partial thromboplastin time.

Quality of Reporting

The average quality score was 0.56 with a range between 0.33 to 0.75 (maximum attainable score of 1.00). Most trials received credit for description of the patient sample (75%), diagnostic criteria for bleeding (100%), and clear results presentation (100%). Randomization (0%) and compliance checks (50%) occurred less frequently.

Outcomes of Individual Trials

The rates of bleeding between the prospective articles ranged between 2.3% and 11.2%. The sensitivity of the trials ranged from 0.00 to 0.16 (Table III). The specificity range was 0.93 to 1.00. Positive predictive value varied between 0.00 and 0.14. Negative predictive value ranged from 0.83 to 0.98. Both sensitivity and positive predictive value were markedly low and specificity and negative predictive value was, in contrast, high.

Sensitivity Analysis and Rate Difference

Pooled analysis of 3384 patients in the prospective trials revealed nine patients with an abnormal coagulation profile and perioperative bleeding and 107 patients with normal coagulation profiles and perioperative bleeding. This produced a sensitivity of 0.08, specificity of 0.97, positive predictive value of 0.10, and negative predictive value of 0.97. Sensitivity analysis of 8988 additional patients in retrospective studies that met the inclusion and exclusion criteria showed a sensitivity of 0.02, specificity of 0.98, positive predictive value of 0.01, and negative predictive value of 0.98. The rate difference for patients with abnormal tests and postoperative bleeding was 8.7% (95% CI, 1.5%–15.9%) and for patients with normal tests and postoperative bleeding it was 3.3% (95% CI, 2.5%–4.1%). Because the confidence intervals overlap, this implies no rate difference between the two groups of patients.

DISCUSSION

A recent article quoted that approximately 300,000 tonsillectomies with and without adenoidectomies are performed every year in the United States[8] at a cost of nearly half a billion dollars. Based on the number of surgeries, the cost of routine preoperative coagulation tests is estimated at nearly $30 million. Clearly in an era of cost containment medicine, the value of preoperative coagulation testing has been questioned.

In this meta-analysis, the rate of postoperative bleeding remained constant between the studies ranging from

TABLE II.
Characteristics of Individual Studies.

Source	Sample Size	Age Range	No. of Bleeds	No. of Bleeds With Abnormal PT/PTT
Prospective				
Burk et al.[4]	1603	3–16 y/o	37/1603	1/37
Close et al.[5]	96	17 mos.–40 y/o	6/96	0/6
Gabriel et al.[6]	1479	9 mos–15 yr	50/1479	8/50
Thomas et al.[7]	206	NOS	23/206	0/23
Retrospective				
Howells et al.[2]	339	Under 12 y/o	10/339	1/10
Tami et al.[10]	775	All ages	21/775	5/21
Kang et al.[11]	1061	Children (age NOS)	64/1061	6/64 (5 reverted to nl)
Handler et al.[12]	1445	Children (age NOS)	38	0/38
Manning et al.[13]	994	Children (age NOS)	36	2/36
Zwack et al.[14]	4374	2 –17 y/o	38	1/38 (only 30 had lab tests done)

PT/PTT = prothrombin time/partial thromboplastin time; NOS ± not not otherwise specified; nl = normal.

2% to 7%.[4] In the two prospective studies, the sensitivity of the PT and PTT was very low. This figure is partly explained by the low overall number of post-tonsillectomy bleeds. The pooled RD with 95% CI did not reach statistical significance. This may be a result of too small a sample size or that there truly is no difference in the rates of bleeding. Because of the pooling of studies, the sample size was large. This implies a true lack of rate difference. Analysis revealed a low sensitivity and positive predictive value. For a routine screening test to be considered reliable, its sensitivity and positive predictive value should be high.

Clinical Significance

Immediate primary post-tonsillectomy bleeding is defined as bleeding within the first 24 hours after the procedure. Delayed bleeding occurs greater than 24 hours after the procedure, and usually between 5 and 10 days in the case of tonsillectomies.[2] The former is generally attributed to surgical technique and the reopening of small blood vessels. The latter is generally attributed to the sloughing of the primary eschar. Most bleeds reported in these studies were delayed, although this was not always specified.

The PT and aPTT are the most used preoperative coagulation tests. Both tests are elevated in the presence of deficiencies in coagulation factors or a circulating inhibitor of the clotting system.[9] Neither of these tests evaluate platelet function and neither is able to differentiate between mild and potentially serious coagulopathies. Both parameters are subject to transient influences such as viral illness or the presence of medications in the bloodstream, especially antibiotics. Native factors such as circulating anticoagulants or inhibitors (i.e., lupus anticoagulant) are increasingly being recognized as causing false elevations of the coagulation tests.

The argument for ordering PT and aPTT routinely stems from the fact that postoperative tonsil bleeds are potentially lethal. Serious disorders such as von Willebrand's disease can be discovered in an otherwise asymptomatic patient. Also, the postoperative tonsil bed is an open wound that heals through secondary intention, and even normal patients can experience significant bleeding. One study from the entire set of articles reviewed found a significant link between abnormal coagulation tests and postoperative bleeding.[10] Documentation of abnormal coagulation tests is important from the medicolegal perspective as well. Preoperative histories are also important in detecting familial predisposition to bleed. Many patients experience their first hemostatic challenge during and after surgery.

The arguments against ordering PT and PTT routinely cite the cost involved. Our meta-analysis confirms that these tests have poor sensitivity in detecting serious blood dyscrasias and that there are many false-positives. Surgeons should always be cognizant of potential bleeding

TABLE III.
Individual Outcomes of Trials Included in the Meta-Analysis.

Source	n = 3384	Sensitivity	Specificity	PPV	NPV
Burk et al.[4]	1603	0.03	0.98	0.03	0.98
Close et al.[5]	96	0.00	0.93	0.00	0.83
Gabriel et al.[6]	1479	0.16	0.97	0.14	0.97
Thomas et al.[7]	206	0.00	1.00	0.00	0.89

PPV = positive predictive value; NPV = negative predictive value.

TABLE IV.
Steps Used in Performing the Meta-Analysis.

1. State study hypothesis
2. Specify explicity inclusion and exclusion criteria
3. Search the literature
4. Document the search strategy
5. Apply the inclusion criteria and exclusion criteria to articles from the search, keep log of all rejected articles
6. Assess the quality of the articles
7. Extract data from articles
8. Statistically combine data to obtain estimate of overall effect
9. Perform a sensitivity analysis
10. Discuss clinical significance of findings

and be meticulous about securing hemostasis. Only four studies reviewed were prospective studies and in these four, only nine patients had abnormal tests and bleeding. The other studies indicated similar findings although retrospective, even demonstrating a reversion of abnormal tests to normal.[11]

The difficulty with performing a meta-analysis on this subject was that only four articles fulfilled all criteria. The studies spanned all ages and were not controlled for surgical technique. Also, in some studies, some subjects that had abnormal lab tests did not have surgery performed. The true incidence of postoperative bleeding in light of abnormal tests may be underreported.

The strengths of this study include a priori hypothesis testing, detailed documentation of a comprehensive literature search and strict study selection criteria, and sensitivity analysis of the results. The weaknesses of this study are possible bias of pooled results of nonrandomized and heterogeneous studies that could end in misleading conclusions. There also remains a possibility of publication bias.

Despite the weaknesses, sensitivity analyses for the included and excluded groups were similar. This is explained by the already low incidence of coagulopathies in the general population. It is therefore understandable that when an already insensitive test (PT/PTT) is used to detect a disorder with a low prevalence, that the predictive value of this test will be low. Given the pooled analyses results of the prospective and retrospective studies we reviewed, we recommend that routine PT and PTT tests not be ordered, but that patient and family histories should be noted carefully and depending on these individual cases, coagulation studies can then be ordered. The role of clinical histories in predicting postoperative bleeding has not been studied in a large series and so it remains to be clearly delineated.[12–15]

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