Analysis of pre-operative aspartate aminotransferase and alanine aminotransferase in 14,185 pediatric patients

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INTRODUCTION

Laboratory tests have long been regarded as the basic element of pre-anesthetic evaluation to determine the patient’s suitability for general anesthesia. However, unlike diagnostic testing ordered in symptomatic patients, most perioperative laboratory tests are habitual and screening tests, which are administered to asymptomatic patients [1]. Although aspartate aminotransferase (AST) and alanine aminotransferase (ALT) tests are indicators of hepatic cell injury, rather than reflecting hepatic function, they are considered core components of liver function test and are performed as a common pre-anesthetic laboratory test [2]. In a previous cohort study of 73,596 patients undergoing elective, low-risk ambulatory surgery, abnormal pre-anesthetic laboratory findings were not predictive of postoperative outcomes when compared with normal results [3]. Several studies have investigated the usefulness of preoperative routine AST and ALT testing in pediatric patients [4-6], however, there are scarce data for evaluation of routine pre-anesthetic AST and ALT testing in pediatric patients. Thus, the aim of this study was to evaluate routine pre-anesthetic AST and ALT screening tests for detection of hepatic abnormalities and their usefulness in perioperative management.

MATERIALS AND METHODS

The Institutional Review Board approved this study. We conducted a retrospective review of the medical charts of all patients, aged 18 years or younger, who underwent non-hepatic surgery under general anesthesia performed at Gachon University Gil Medical Center from October 2004 to December 2010. All charts were reviewed by one investigator (LSJ). The following data were collected: gender, age, preoperative history and physical examination, AST and ALT results, the type of surgery,
and perioperative complications.

Normal values of AST were defined as $35-140$ U/L in 0-5 days of age, $15-55$ U/L in 5 days to 9 years of age, and $5-45$ U/L in 10-18 years of age. Normal values of ALT were defined as $6-50$ U/L in 0-5 days of age and $5-45$ U/L in the 5 days to 18 years of age group. Due to non-specificity of ASD to liver disease, a single episode of ASD elevation could not be related to liver disease. Therefore, elevations of both AST and ALT were investigated. In patients with elevation of both preoperative AST and ALT, we sought repeated examination of AST and ALT preoperatively. Persistent elevation of AST and ALT over one week was defined as suspicious hepatic disease. Whether or not the patient had consultation to a pediatrician, the possible etiology of AST and ALT elevations, the diagnosis on additional ultrasonographic examination, and postponement of surgery or persistent abnormal AST and ALT over one week were investigated. The Excel program (Microsoft Corp, Redmond, WA, USA) was used for data processing. Values are expressed as a number of patients (%) or mean ± SD.

**RESULTS**

Over a period of 75 months, 14,185 patients underwent general anesthesia. The male/female ratio was 1.74:1, 9,015 males and 5,170 females. The mean ± SD of age was $9.1 ± 5.4$ years (range 3 month–18 years).

The mean ± SD of AST and ALT was $31.2 ± 30$ U/L and $21.9 ± 24.5$ U/L. A list of the surgical procedures performed and the prevalence of abnormal AST and ALT is shown in Table 1. Among 14,185 patients, a single episode of AST elevation was observed in 505 patients (3.6%) and that of ALT elevation was observed in 258 patients (1.8%); 221 patients (1.6%) had elevations of both AST and ALT. The mean ± SD of AST and ALT in patients with elevations of both AST and ALT was $92.1 ± 71.1$ U/L and $90.3 ± 45.0$ U/L. The highest AST and ALT was $345$ U/L and $231$ U/L in a patient (17-year-old girl) who underwent orthopedic surgery for clavicle fracture.

Among 221 patients with elevation of AST and ALT, 21 patients were classified as having suspicious hepatic disease for persistent elevation of both AST and ALT over one week preoperatively. Four patients postponed elective surgery due to elevation of both AST and ALT values. The causes of persistent elevation of AST and ALT are shown in Table 2. Among the 221 patients with elevation of both AST and ALT, 20 patients were examined by additional abdominal ultrasound.

### Table 1. Type of Surgery Performed and Results of Preoperative AST and ALT

| Department of surgery         | No. of patients (n = 14,185) | Elevations of both AST and ALT (n = 221) |
|------------------------------|------------------------------|----------------------------------------|
| Otolaryngology               | 4,172 (29.4)                 | 19 (8.6)                               |
| Orthopedics                  | 3,012 (21.2)                 | 92 (41.6)                              |
| General surgery              | 2,624 (18.5)                 | 58 (26.2)                              |
| Ophthalmology                | 1,637 (11.5)                 | 8 (3.6)                                |
| Plastic surgery              | 772 (5.4)                    | 6 (2.7)                                |
| Cardio-thoracic surgery      | 733 (5.2)                    | 14 (6.3)                               |
| Urology                      | 624 (4.4)                    | 2 (0.9)                                |
| Dental surgery               | 253 (1.8)                    | 6 (2.7)                                |
| Neurosurgery                 | 177 (1.2)                    | 14 (6.3)                               |
| Obstetrics and gynecology    | 169 (1.2)                    | 0 (0.0)                                |
| Others                       | 12 (0.0)                     | 2 (0.9)                                |

Values indicate number of patients (%). AST: aspartate aminotransferase, ALT: alanine aminotransferase.

### Table 2. Etiology and Diagnosis in Patients with Persistent Elevation of AST and ALT

| No. of patients (n = 21) |
|--------------------------|
| Surgery proceeded        | 17 (81) |
| Fatty liver              | 12 (57) |
| Hepatitis of unknown origin | 3 (14.1) |
| Dog-bite                 | 1 (4.7) |
| Persistent Ductus Arteriosus | 1 (4.7) |
| Surgery delayed          | 4 (19)  |
| Fatty liver              | 1 (4.7) |
| Hepatitis of unknown origin | 1 (4.7) |
| Trauma                   | 2 (9.5) |

Values indicate number of patients (%). AST: aspartate aminotransferase, ALT: alanine aminotransferase.
Table 3. Overall Etiology and Diagnosis in Patients with Elevation of both AST and ALT

| Etiology / Diagnosis                          | No. of patients (n = 221) |
|-----------------------------------------------|---------------------------|
| Consultation to the department of pediatrics or internal medicine | 40 (18)                   |
| Fatty liver                                   | 12 (5.4)                  |
| Hepatitis of unknown origin                   | 1 (0.5)                   |
| Trauma                                        | 23 (10.4)                 |
| Non-specific findings                         | 4 (2.8)                   |
| Others without consultation                   | 181 (82)                  |
| Trauma                                        | 82 (37.1)                 |
| Cardiac problems                              | 6 (2.7)                   |
| Epstein-Barr virus infection                  | 1 (0.5)                   |
| Down syndrome                                 | 1 (0.5)                   |
| Unknown etiology                              | 14 (6.3)                  |
| Non-specific findings                         | 77 (34.8)                 |

Values indicate number of patients (%). AST: aspartate aminotransferase, ALT: alanine aminotransferase.

in this retrospective study, only 21 cases of suspicious hepatic disease were found by routine pre-anesthetic AST and ALT screening tests and there were discrepancies between the preoperative AST and ALT value and the rate of consultation at surgeons’ discretion. The incidence of real hepatic abnormality confirmed by additional ultrasonogram consultation was less than that of suspicious hepatic disease.

AST and ALT have been regarded as a marker of necrosis or damage of hepatocytes. AST and ALT are found in the liver and leak into the bloodstream in case of hepatic cellular damage, such as acute hepatitis, toxic injury, or ischemic injury. However, considering that AST is also found in the heart, skeletal muscle, brain, kidney, pancreas, lungs, leukocytes, and red blood cells, a single episode of AST elevation is non-specific for detection of hepatic disease. ALT is found predominantly in the cytoplasm of hepatic parenchymal cells and considered to be more specific to the liver, thus, accompanied by ALT, AST is more valuable for detection of hepatic abnormalities [7]. However, the serum ALT level may correlate less with hepatic injury in patients with chronic hepatitis or cirrhosis. Hepatocytes dying by apoptosis, rather than necrosis, presumably synthesize less AST and ALT as they wither away during the progression of hepatitis C. Actually, a considerable number of patients with chronic hepatic disease have normal ALT level [8,9]. Therefore, the usefulness of AST and ALT as a pre-anesthetic screening test for evaluation of hepatic function should be closely evaluated.

In a previous report by Turnbull and Buck [10], who performed 5,003 screening tests on 1,010 patients, 226 abnormal findings were detected (4.5% of prevalence). They suggested that, compared with their results and information obtained from history taking and physical examination, routine preoperative screening tests provided little additional information that might alter the perioperative management in otherwise healthy surgical patients undergoing surgery [10]. In our investigation, the prevalence of abnormal serum AST and/or ALT value was approximately 7% (984/14,185). Prevalence of elevation of both AST and ALT was only 1.6% (221/14,185), which is far lower than that reported in a previous retrospective study in adults (3.7%; 73/1,968) [11].

Considering the low predictive value of preoperative routine laboratory testing and slight effect on perioperative management, routine preoperative screening tests might be clinically

sonography at surgeons’ discretion without consultation; hepatic abnormalities were detected in 13 of these 20 patients (65%); nine patients were diagnosed as fatty liver, two patients as choledochal cysts, one patient as hepatic hemangioma, and one patient as cirrhotic liver change. The other seven patients showed non-specific findings. Among the 13 patients with detected hepatic abnormalities, only 9 cases of fatty liver were consulted to the department of pediatrics preoperatively and 4 other patients were followed up by the department of general surgery postoperatively.

Overall causes of AST and ALT elevations are shown in Table 3. Among the 221 patients with elevation of both AST and ALT, 40 patients (including 15 cases of suspicious hepatic disease) were consulted to the department of pediatrics or gastrointestinal internal medicine, 12 of whom were diagnosed as fatty liver on abdominal ultrasonogram, 23 as trauma origin, one as hepatitis of unknown etiology, and four had no specific abnormal findings. Among the other 181 patients without consultations, 82 were diagnosed as trauma origin (including 1 dog bite and 2 trauma, shown in Table 2), six as cardiac problem origin (including 1 persistent ductus arteriosus, shown in Table 2), one as Epstein-Barr virus infection, one as Down syndrome, and 14 as unknown etiology (including 3 hepatitis of unknown origin and 1 fatty liver suspected by history taking, shown in Table 2), and 77 had no specific abnormal findings. No patient was consulted as aggravated hepatic lesion after surgery.
insignificant [12,13]. In our study of 221 patients with elevations of both AST and ALT, 20 patients were examined by additional abdominal ultrasonography and hepatic abnormalities were detected in 65% of them. Even after addition of patients with hepatic abnormalities detected by consultation, the detection of a real hepatic lesion (28.3%) was lower than that of preoperative AST and ALT testing.

There are limitations of this study. Because this study was conducted retrospectively, patients with normal preoperative AST and ALT results were not followed properly; therefore, the negative predictive value, sensitivity, and specificity of the AST and ALT screening tests could not be estimated. In addition, we could not exclude the loss of chronic liver diseases, which could have a normal range of values for AST and ALT.

In conclusion, in this single-center, retrograde study, the usefulness of preoperative routine AST and ALT testing was shown to be limited for detection of hepatic abnormalities in pediatric patients undergoing general anesthesia. Further multicenter, large-scale investigation would be required.

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