

How to Evaluate the Child Presenting with an Apparent Life-Threatening Event?

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ABSTRACT: **Background:** Infants who have experienced an apparent life-threatening event typically undergo an extensive evaluation to rule out serious underlying conditions.

Objectives: To evaluate the yield of different tests performed after an apparent life-threatening event and to identify high risk groups in which more extensive diagnostic tests are required.

Methods: A retrospective study was conducted in a children's hospital for a 4 year period and the charts of infants who were admitted with an apparent life-threatening event were reviewed. The yield for each diagnostic test was established according to the ratio of positive results contributing to the diagnosis of the apparent life-threatening event.

Results: The study included 69 infants between the ages of 1 week and 1 year. There were abnormal findings in 36% of the cases. Gastroesophageal reflux was the most common diagnosis (60%). In the remaining patients the diagnosis was either seizures (12%) or respiratory tract infections (28%). Tests used for the diagnosis of cardiac, metabolic and non-respiratory infections had no yield. A positive correlation was found between abnormal test results and abnormal physical examination ($P = 0.001$), an abnormal perinatal history ($P = 0.017$), and age older than 2 months ($P = 0.002$).

Conclusions: The yield of most of the tests performed after an apparent life-threatening event is low, especially in infants with a normal perinatal history and physical examination.

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been demonstrated that as many as 50–80% of ALTE cases can be attributed to a medical entity [2,3]. Because some cases may need significant medical interventions, the common practice is to admit patients after an ALTE for observation, although this approach has been questioned [4-6]. The appropriate evaluation either in the emergency department or after admission is also controversial. There is currently no standard minimal workup for evaluation of ALTE [3]. The purpose of this study was to determine retrospectively the yield of different tests performed after apparent life-threatening events, and to identify specific high risk groups of infants in whom the yield of diagnostic testing is higher.

PATIENTS AND METHODS

We conducted a retrospective study in the Dana Children's Hospital of the Tel Aviv Sourasky Medical Center. Infants who experience an ALTE and present to the emergency room are routinely admitted and undergo standard testing procedures, including a complete blood count, glucose, electrolytes, venous blood gases, electrocardiography, echocardiography, electroencephalography, brain ultrasonography, 24 hour pH monitoring and upper gastrointestinal series. If respiratory symptoms are also present, a chest X-ray is performed and a nasal swab is obtained for respiratory viruses, including respiratory syncytial virus. Further tests are ordered according to the clinical findings. Because of the retrospective nature of this study, not all the infants underwent the same combination of tests.

We reviewed the charts of all the infants who were admitted after an ALTE to Dana Children's Hospital during the years 2003–2006. The charts were retrieved from a computerized database using the key words "ALTE," "apparent life-threatening event," and "apnea." The inclusion criteria were age under 1 year with an apparent life-threatening event according to the definitions of the 1987 National Institutes of Health Consensus Panel on Infantile Apnea and Home Monitoring [1]. Data on the medical history, physical examination, diagnostic tests and hospitalization course, and the final diagnosis were retrieved from the charts. The yield for each diagnostic test was established according to the ratio of positive results contributing to the diagnosis of an ALTE in each testing modality (complete

The definition of apparent life-threatening event is "an episode that is frightening to the observer and is characterized by some combination of apnea, color change, marked change in muscle tone, choking or gagging" [1]. The differential diagnosis for such an event is extensive. The most frequent diagnoses reported are gastroesophageal reflux, respiratory tract infections and seizures, though many other medical conditions could present as an ALTE [2,3]. It has

ALTE = apparent life-threatening event

blood count, ECG, imaging, etc.). We evaluated the influence of certain risk factors (abnormal perinatal history, abnormal physical examination, recurrent events, young age) on the rate of abnormal test results. In addition, we divided the study cohort into two groups: high risk and low risk. The high risk group included patients with an abnormal perinatal history, recurrent episodes of such events, or a pathological physical examination on admission. The low risk group included patients with a normal perinatal history, no recurrent episodes of apparent life-threatening events, and a normal physical examination. We compared the yield of diagnostic tests between the two groups.

STATISTICAL ANALYSIS

The yield for each diagnostic test was established according to the ratio of positive results contributing to the diagnosis of ALTE in each testing modality. The influence of four risk factors (abnormal perinatal history, abnormal physical examination, recurrent events, young age) on the rate of abnormal test results was evaluated using a chi-square test and Fisher's exact test. Comparison of the yield of diagnostic tests performed in the two groups was performed using the chi-square test.

RESULTS

Table 1 summarizes the demographic profile and medical history of the study cohort. The 69 infants who fulfilled the study entry criteria included 36 boys and 33 girls between the ages of 1 week and 1 year (average 8 ± 8.25 weeks, median 6 weeks). The perinatal history was abnormal in 21 infants (30%): 18 were associated with prematurity with or without complications and 3 involved intrauterine growth retardation. There was a high prevalence of infants who were one of twins (27%). Twenty-three (33%) had a positive history of three or more similar events before admission. Fifteen (21%) infants had an abnormal finding on physical examination; for example, rales or wheezing on auscultation, or an abnormal neurological examination, such as hypotonia or increased muscle tone.

Table 1. Demographic characteristics and medical history of infants evaluated for ALTE

	n	%
M:F ratio	36:33	52:48
Age < 2 mos	44	64
One of twins	19	27
Medical history		
Prematurity	18	26
Apnea of prematurity	4	5
Respiratory distress syndrome	8	11
Intrauterine growth retardation	3	4
Recurrent events before admission	23	33

Table 2. The influence of different risk factors on the yield of diagnostic tests in the study cohort

	Test results				P value
	Negative		Positive		
	N	%	N	%	
Normal physical exam	40	90.9	14	56	0.001
Abnormal physical exam	4	9.1	11	44	
Normal perinatal history	35	79.5	13	52	0.017
Abnormal perinatal history	9	20.5	12	48	
Recurrent events	32	72.7	14	56	0.16
No recurrent events	12	27.3	11	44	

The diagnosis was reached in 25 cases (36%) according to a diagnostic test, and in 7 cases (10%) it was based on the history and physical examination. In 37 cases (53%) no definitive diagnosis was reached. Fifteen infants (21%) were diagnosed as having gastroesophageal reflux by an abnormal 24 hour pH monitoring result (i.e., pH < 4 for more than 10% of the time) or an upper gastrointestinal series demonstrating massive reflux. In 3 cases (4%) a seizure was diagnosed according to an EEG that demonstrated epileptic activity. In two cases (3%) the nasal swab was positive for respiratory syncytial virus while in 5 cases (7%) the diagnosis was non-respiratory syncytial virus bronchiolitis, according to clinical and radiological findings. Among the seven patients in whom a diagnosis was based on clinical findings, four were diagnosed as having gastroesophageal reflux because of significant regurgitation that responded to anti-reflux therapy, two were diagnosed with breath-holding spells and one with overfeeding. Tests with a positive yield were upper gastrointestinal series (two of three), 24 hr pH monitoring (14/32, 43%), chest X-ray (7/32, 21%), nasal aspirate for respiratory syncytial virus antigen (2/25, 8%), and EEG (3/63, 4.5%). By contrast, complete blood count, urinalysis, electrolytes, blood gases, blood and urine cultures, ECG, echocardiography and brain ultrasound were non-contributory. As mentioned earlier, not all the infants underwent the complete investigation.

Some of the tests had abnormal results that did not contribute to the diagnosis of an apparent life-threatening event and were therefore considered as incidental findings. For example, there were five cases of atrial septal defects with no hemodynamic significance. Brain ultrasonography demonstrated hyperechoic lines in the basal ganglia of two infants, both of whom were negative for toxoplasmosis, rubella, cytomegalovirus, herpes simplex and syphilis serology. Four of the 49 patients in whom venous blood gases were taken on admission had abnormal results (respiratory acidosis): the findings on repeated tests were normal and the ammonia and lactate levels that were measured were also normal.

EEG = electroencephalogram

There was a significant positive correlation between abnormal test results and abnormal findings on physical examination ($P = 0.001$) and an abnormal perinatal history ($P = 0.017$) [Table 2]. The 28 cases with a normal history and physical examination were classified as low risk. The other 41 infants were categorized as high risk because of an abnormal perinatal history, recurrent apparent life-threatening events, or an abnormal physical exam. The yield of diagnostic testing in the low risk group was 14% compared to 51% in the high risk group ($P = 0.003$),

DISCUSSION

This study indicates a low yield for most of the diagnostic tests performed after an ALTE. In general, the evaluation was abnormal in 36% of the cases, and in 14% of the infants without risk factors (low risk group). The tests with any yield were those used for diagnosing gastroesophageal reflux, respiratory tract infections, and seizures. Tests aimed at diagnosing cardiac, metabolic and non-respiratory infections had no yield.

The < 40% rate of abnormal results in the evaluation for gastroesophageal reflux could be attributed to the fact that there was a higher level of suspicion for the condition in the 35 infants who underwent this evaluation. Furthermore, the prevalence of gastroesophageal reflux in this age group is high and not necessarily the cause for the ALTE, as indicated in a few studies [6-8]. It is prudent to say that at least some of the cases positive for gastroesophageal reflux are incidental. Only the infants with respiratory symptoms were evaluated for possible respiratory tract infections. For them, the diagnostic yield of a chest X-ray was 21% and 8% for respiratory syncytial virus antigen. Brand et al. [9] showed a yield of 2% for chest X-ray and no yield for the respiratory syncytial virus antigen test when the history and physical examination were normal, but 36% and 38%, respectively, when the history and exam were abnormal. These findings support an investigation for respiratory etiologies when there is clinical suspicion. EEG was performed in 63 of the infants in our study group and was abnormal in 3 (a yield of 4.5%). Two of these three infants were found on follow-up to have a convulsive disorder, and both had an abnormal perinatal history and an abnormal physical examination. The third infant who was diagnosed as having undergone a seizure was in the low risk group and did not have any further neurological symptoms on follow-up.

Only a few studies have compared the yield of diagnostic tests performed after an apparent life-threatening event [9-12]. In their prospective study on 69 infants Davies and Gupta [10] used a standard testing protocol similar to ours. Their protocol included a radioisotope milk scan, complete blood count, blood chemistry, nasal swab for pertussis, chest X-ray, metabolic screening, urine toxicology and ECG. All the tests, except for the ECG, yielded positive results to some degree. For example, the radioisotope milk scan was abnor-

mal in 89% of the cases, the chest X-ray in 55%, the blood count in 33%, the urine culture in 13% and the ammonia level in 4%. The contribution of the various positive results specific to the diagnosis of apparent life-threatening event was not clearly delineated in that study. Their reported high rate of abnormal radioisotope milk scans is similar to our demonstration of a relatively high yield for tests used for the diagnosis of gastroesophageal reflux. The large retrospective study (243 patients) of Brand et al. [9] demonstrated that the number of tests that contributed to identifying the etiology of an apparent life-threatening event was considerably lower in patients with a normal history and physical exam. Their recommendation was to limit the screening of the latter cases to the tests that had a positive yield in their low risk group: complete blood count, pneumogram, brain imaging, urinalysis, and screening for gastroesophageal reflux.

Although our study indicated no yield for urinalysis, complete blood count and blood culture, the fact that these tests did contribute to the diagnosis of apparent life-threatening events in other studies [9-11], and the relative simplicity of performing these tests favor them as a first-line screening test. Brain imaging is an important diagnostic tool that could reveal congenital malformations, tumors, hydrocephalus and other central nervous system abnormalities capable of causing an apparent life-threatening event. Brain ultrasonography had no yield in the 45 infants in our study group. Our review of the literature failed to come up with other studies in which brain ultrasonography was used as a screening test. Taking into consideration the risks of performing a computed tomography scan or magnetic resonance imaging in an infant, we believe that brain imaging should be reserved for cases with a strong clinical suspicion for neurological pathologies. Our findings of a low yield for venous blood gases as a screening test for metabolic disease are compatible with those of other investigators [9,11]. Nevertheless, the identification of respiratory acidosis in blood gases could help to evaluate the severity of the event in the emergency department setting. The limitations of the study are the small sample group and its retrospective nature, as well as the fact that not all the infants underwent the whole evaluation.

In conclusion, the yield of most of the diagnostic tests routinely performed after an ALTE is low, especially in low risk infants with a normal perinatal history and physical examination. Screening tests for gastroesophageal reflux, respiratory infections and seizures have the highest yield and should be considered in any high risk child.

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