SPECIAL REPORT

Investigations for infants admitted with apparent life-threatening event (ALTE): Necessity or liability? Assessment at a tertiary care hospital

Reem Alfattouh,[1] Nedaa Aldairi,[2] Nazish Masud,[3] Asma Awadalla[4]

Abstract

The retrospective study was planned to assess the outcome of extensive investigations done for infants admitted with apparent life-threatening event (ALTE), and comprised chart review of 275 infants admitted to King Abdul-Aziz Medical City (KAMC), Riyadh, Saudi Arabia, between 2012 and 2015. The outcome of each investigation was compared in terms of whether the test was performed or not performed, and, if performed, whether the test report was normal or abnormal. Also, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) was assessed for each test. All culture tests, including those of blood, urine and cerebrospinal fluid (CSF), were of little help in contributing to the final diagnosis. Nasopharyngeal aspiration (NPA), chest X-ray and upper gastrointestinal (GI) study were more relevant in terms of finding an underlying cause for ALTE ($p=0.01$, $p=0.04$ and $p<0.001$ respectively). Of the total, 87(32%) subjects did not have a final diagnosis and were considered normal. Gastro-oesophageal reflux 59(22%) and bronchiolitis 58(21%) were the most common diagnoses; both can be diagnosed clinically without any invasive investigations.

Keywords: Gastroesophageal reflux, GER, Cyanosis, Infant, Bronchiolitis, Investigations, Apnoea.

Introduction

Apparent life-threatening event (ALTE), as defined by National Institutes of Health (NIH), is "an episode that is frightening to the observer and that is characterised by some combination of apnoea (central or occasionally obstructive), colour change (usually cyanotic or pallid but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking, or gagging. In some cases, the observer fears that the infant has died."[1] No better definition was formed until recently.

[1,2]King Abdullah Specialist Children Hospital, [3]Research Unit, Medical Education Department, College of Medicine, King Saud bin Abdulaziz University for Health Sciences, [4]Department of Pediatrics, King Abdullah Specialist Children Hospital, Riyadh, Saudi Arabia, and King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia.

Correspondence: Nazish Masud. Email: nazishmsd@yahoo.co.uk

ALTE represents 0.6-0.8% of emergency department (ED) visits, and occurs in 0.6 to 2.46 per 1000 live-born infants worldwide.[2,3] This presentation has been a diagnostic challenge for many decades. Previously, experts all over the world were linking the event to sudden infant death syndrome (SIDS), but studies showed no association between the two conditions.[4]

Management varies depending on the clinical judgment and decision of the physician treating the patient. Parents' anxiety following the event contributes to an extent to this decision and causes a burden on treating physicians.[5] Various investigations are performed while planning the care of ALTE infants due to the absence of evidence-based practice.[5] Many studies have been conducted to optimise the clinical practice to pursue minimal investigations. The American Academy of Paediatrics re-defined ALTE as brief resolved unexplained events (BRUE) in its recent clinical practice guidelines to reduce the extent of investigations done for low-risk infants. In contrast to ALTE, the presence of a provisional diagnosis after detailed history and physical examination excludes the infant from BRUE.[6] The current study was planned to assess the outcome of extensive investigations in reaching the final diagnosis among infants admitted with ALTE.

Methods

The retrospective study was conducted from January to December 2016 at King Abdul-Aziz Medical City (KAMC), Riyadh, Saudi Arabia, and comprised chart review of infants admitted between 2012 and 2015 to the paediatric ward through ED with a clinical presentation of cyanosis, apnoea, choking, changes in muscle tone and/or abnormal movement. Ethical approval was obtained from the King Abdullah International Medical Research Centre, Riyadh. With 95% confidence level and 5% margin of error, the sample size calculated was 377. Those with confirmed previous ALTE attack, gestational age <34 weeks at birth, congenital heart disease, neurological disorders, chronic lung disease or recurrent ALTE were excluded. Files were retrieved through the bed management and statistics divisions at the Department of Health Informatics.

The data was collected for results of all investigations ordered for these infants in terms of normal result versus abnormal, and final diagnosis at discharge. Information about a total of 16 different blood, urine, radiological and culture tests were analysed. The diagnostic efficacy of the test itself was out of the scope of this research and no comparison was done between standard tests. Analysis was done using IBM SPSS Statistics version 22. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve (AUC) were calculated. P<0.05 was considered significant for all the tests applied.

Results and Discussion

There were 275 infants with a mean age of 52 ± 56.3 days and mean weight of 4.4±1.0kg. Overall, 173(63%) of the affected infants were aged ≤ 30 days. Those who spent two days at hospital were 116(42%) and 246(90%) were discharged within the first week. The mean length of stay in hospital was 4.4± 6.1 days. Cyanosis 229 (83%), apnoea 110 (40%), and choking 63 (23%) were the most commonly reported symptoms. Of the total, 87(32%) subjects did not have a final diagnosis and were considered normal. The most common diagnosis was gastro-oesophageal reflux (GER) in 59(22%), followed by bronchiolitis in 58(21%) and multiple diagnoses among 32(12%). Respiratory and other infections accounted for 16(6%) cases (Table-1).

The average number of tests performed for each infant was 5.8 ±2.2 (range: 3-12). Complete blood count (CBC), serum electrolyte (SE) and renal profile, including blood urea nitrogen (BUN) and creatinine, was done for all infants irrespective of age and symptoms. Blood culture was done in 182 (66%) cases. The specificity of all the tests was higher compared to sensitivity except for chest X-ray (CXR) and milk scan with sensitivity and specificity of 62% vs 55% and 71% vs 0% respectively. Nasopharyngeal

Table-1: Profile of participants and final diagnosis (N=275).

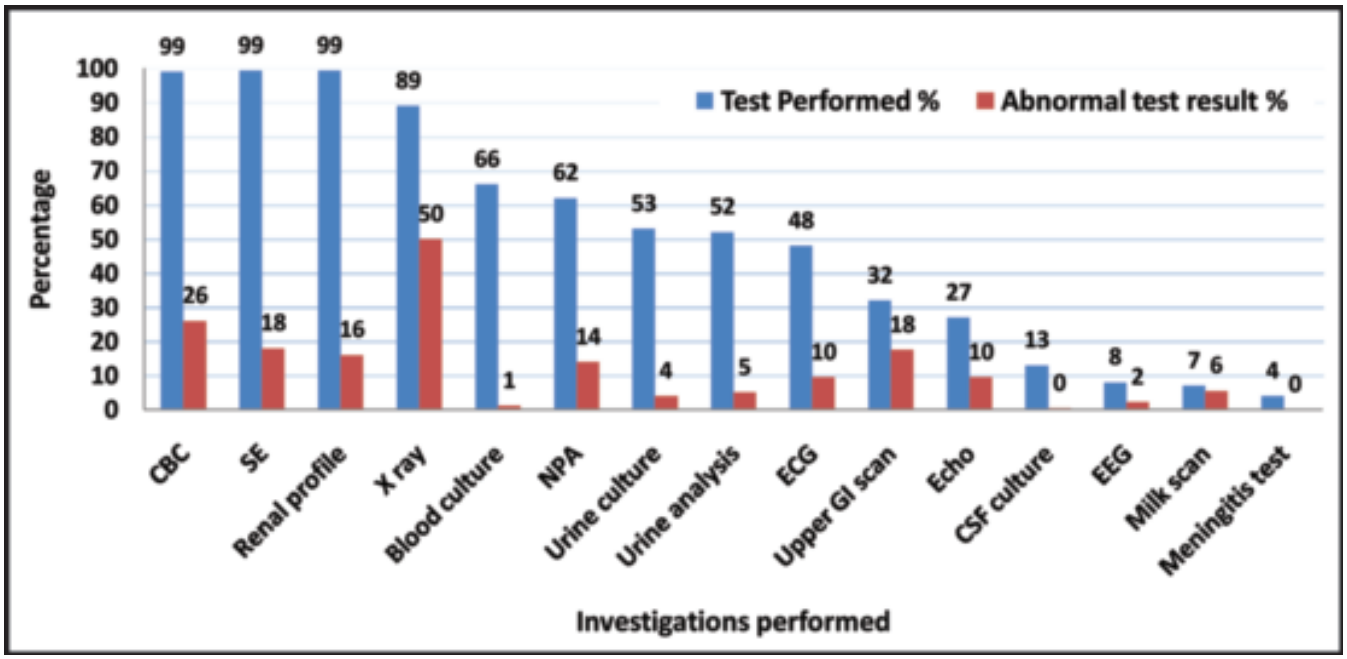
Variables	Frequency	Percentage
Mean age (standard deviation [SD])	52 ± 56.3 days	
Neonates (0-30 days)	173	63%
Infants (31-365 days)	102	37%
Gender		
Male	152	55%
Female	123	45%
Gestational age at birth		
Premature (<37 completed weeks of gestation)	42	15%
Full term (≥ 37 weeks of gestation)	233	85%
Mean weight	4.4±1.4 kg	
Mean length of stay	4.4± 6.1 days	
Final Diagnosis after investigations		
No definitive diagnosis	87	32%
Gastro-oesophageal reflux	59	22%
Bronchiolitis	58	21%
With multiple diagnosis	32	12%
Neurological problems	11	4%
Other respiratory infections	8	3%
Other infections	8	3%
Other co-morbidities	7	3%
Anatomical abnormalities	5	2%

Table-2: Diagnostic tests assessment.

Test performed	Sensitivity*	Specificity**	Positive predictive value***	Negative predictive value****	Area under the curve	p-value
Complete Blood Picture	32%	81%	79%	36%	0.57	0.07
Serum Electrolytes	19%	84%	72%	32%	0.52	0.69
Renal Profile	19%	88%	78%	33%	0.54	0.35
Blood Culture	2%	100%	100%	24%	0.51	0.83
Urine Analysis	11%	92%	79%	27%	0.51	0.81
Urine Culture	10%	100%	100%	26%	0.55	0.37
Cerebrospinal Fluid (CSF) cell count	31%	71%	80%	22%	0.51	0.93
CSF Culture	4%	100%	100%	21%	0.52	0.88
Meningitis test	0	100%	0	10%	0.50	1.00
Nasopharyngeal aspiration	28%	100%	100%	26%	0.64	0.01
Electroencephalogram	36%	88%	83%	44%	0.62	0.37
Electrocardiogram	18%	77%	62%	31%	0.47	0.62
Echocardiography Heart	43%	80%	81%	42%	0.61	0.11
X-ray Chest	62%	55%	75%	39%	0.58	0.04
Milk scan	71%	0	67%	0	0.36	0.35
Upper GI study	67%	89%	96%	43%	0.78	0.00

GI: Gastrointestinal

*Sensitivity: A/(A+C) × 100, **Specificity: D/(D+B) × 100,***Positive Predictive Value: A/(A+B) × 100, ****Negative Predictive Value: D/(D+C) × 100.p-value calculated through ROC test and significant at <0.05.



CBC: Complete blood count
NPA: Nasopharyngeal aspiration
ECG: Electrocardiogram
CSF: Cerebrospinal fluid
EEG: Electroencephalogram

Figure: Comparison of test performed with tests with abnormal results.

Aspiration (NPA), CXR and upper gastrointestinal (GI) study were more relevant in terms of ALTE diagnosis (p=0.01, p=0.04 and p<0.00) (Figure; Table-2).

The current study assessed the outcome of investigations among ALTE infants in a single-hospital setting. The causes or risk factors were beyond the scope of this research. The study found that specificity was always higher than sensitivity for most of the tests performed. These findings are similar to previous studies.[7] Important to note is that 32% of the cases had no definitive diagnosis even after investigations. They were discharged within 24 hours of observation without any confirmed aetiology. Cultures of blood, urine and CSF were done in a good number of cases. However, only 1% showed positive findings. This highlights that most culture tests were of no help in reaching a diagnosis and should be ordered after thorough clinical examination. The most common diagnosis among infants was GER, as shown by upper GI study and milk scan. Nevertheless, none of these investigations is the gold standard for diagnosis of GER because negative upper GI result does not rule out pathologic reflux. On the other hand, the high frequency of non-pathologic reflux in this age group can lead to a false positive diagnosis.[8] Milk scan had a better sensitivity than specificity amongst the investigations. Nonetheless, the deficiency of age-related values and precise technique limits its significance as a diagnostic test among infants with GER.[8] Therefore, history and physical examination were found sufficient to obtain a diagnosis in uncomplicated cases of GER and treatment modalities should be started on that basis.[8]

The study showed that 21% infants were discharged with the diagnosis of bronchiolitis as presenting symptoms are usually cough, tachypnoea, wheezing and difficulty in breathing. This could be the reason why majority of infants had CXR done. Although the test showed high sensitivity and significant results in reaching a diagnosis, as per the American Academy of Paediatrics (AAP) guidelines, use of CXR for establishing diagnosis of bronchiolitis is discouraged.[9] Unnecessary radiation exposure affects patient safety which should be considered in all circumstances. Benefits versus risks of such exposure should be weighed for each case. NPA is a highly sensitive and specific test for the detection of viral nucleic acids in respiratory secretions. In the current study, the test was significant, but it should be interpreted cautiously given that it may detect prolonged viral shedding from unrelated previous illness.[10] The AAP

dismisses the need for NPA testing except in an infant on palivizumab prophylactic injections to decide whether to continue or stop treatment.[9] CBC, SE and renal profile, irrespective of presentation, age and symptoms, were obtained for all infants as a routine. Their results were inconclusive. In the government-run hospitals of Saudi Arabia, eligible patients are treated free of cost. Thus, accessibility of labs and ordered tests without the need of approval from insurance companies may have contributed to the liberal investigations for patients in our study. Generalisability at large might not be applicable as this study is based on assessment of one hospital only.

The question of which diagnostic test should be done depends upon the individual case. Therefore, we recommend that doctors focus on the history and physical examination and then order investigations as deemed necessary. Future prospective multicenter studies are needed to see the applicability of the results in larger population.

Conclusion

CXR, NPA and upper GI were considerably better compared to other routine investigations, like CBC, SE, renal profile and cultures which contributed minimally in establishing an underlying cause for ALTE. Extensive investigations should be avoided.

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Conflict of Interest: None.

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