

BRUE guidelines

Brief resolved unexplained events in infants (BRUE) are every pediatrician's nightmare. Earlier termed as apparently life-threatening events (ALTE), in 2016 the American Academy of Pediatrics tried to make the criteria more specific and renamed it BRUE. This was done to evaluate clinical interventions such as hospital admission or diagnostic testing. It includes all events in well looking infants associated with a change in color (cyanosis/pallor), change in tone (increased/decreased), change in sensorium or change in breathing pattern (cessation/ irregularity/ decreased) and lasting less than 1 minute.

The previous term 'apparently life-threatening event' was coined in 1987 for episodes which were "frightening to the observer and had some combination of color change, tone change usually marked limpness, choking or gagging." ALTE differs from BRUE in several ways. BRUE is a disorder of exclusion in an apparently healthy infant, while ALTE may occur with underlying illnesses and at any age not just infancy. Choking or gagging is not included in BRUE and color change is restricted to cyanosis or pallor while ALTE may include redness / erythema / plethora.

BRUE is further classified as high risk if any of the following are associated-age <60 days, born preterm with a corrected gestational age <45 weeks, CPR provided by a trained provider, duration >1 minute, more than one event or high risk concerns based on history or physical examination.

How seriously should one take these episodes? A meta-analysis suggested that the risk of death 4 months after a BRUE episode is 1:800. A retrospective cohort study including around 2000 infants found a serious diagnosis in 4%. They included seizures in 1%, airway abnormalities in <1% and abusive head trauma in <1%. Stratifying it as low risk and high risk had a negative predictive value of 90% and positive predictive value of 23%.

Clinical practice guidelines by the AAP suggest that these children may be observed for 1-4 hours with oximetry. One may obtain an ECG, evaluate for pertussis and abusive head trauma. They do not recommend routine hospital admission, neuroimaging, CSF, detailed blood biochemistry or work up for inborn errors of metabolism.

Though BRUE has received acceptance in the US, Europeans are still reluctant to separate it from ALTE. One of the chief advantages documented is a lower hospital admission rate in the US with a reduction of detailed investigations in view of the low risk of mortality. (*Eur J Pediatr* 28 Aug 2021)

COVID-19 vaccination in children

The CDC has approved COVID vaccination using the pediatric Pfizer mRNA vaccine in children. Vaccinations in children between 5-11 years have begun in the US. The dose is 10µg, one third of that of adults. The booster follows in 3 weeks. Vaccination of children is purported to slow down transmission, reduce risks of multisystem inflammatory syndrome and increase parental confidence in sending children to school.

The vaccine can be co-administered with other vaccines albeit at a different site. Children who have had COVID-19 infection earlier may also be vaccinated. Children with MIS-C may be vaccinated 90 days after the diagnosis, if they have recovered clinically and are at increased risk of viral exposure.

Clinical trials in about 3000 children reported a vaccine efficacy of 90.7% in preventing symptomatic infections. Adverse effects were mild to moderate and included headache, fatigue and pain. Myocarditis was not observed in these small trials though it was possibly underpowered to detect that. (*AAP News*, 3 November 2021)

Oral anti-virals for COVID-19

Two new oral drugs effective against COVID-19 have recently been announced. Molnupiravir was developed by Merck and has been approved in some countries such as the UK and Sri Lanka for mild to moderate infections with associated comorbidities. It must be given within 5 days of symptom onset in patients with comorbidities such as obesity, age > 60 years, diabetes or heart disease. It has an unusual mechanism of action. This nucleoside analog (chemical formula is N-hydroxycytidine) is mistaken for both cytidine triphosphate and uridine triphosphate during RNA replication by the SARS COV-2. This results in multiple RNA mutations resulting quickly in the death of the virus. Clinical trials have shown that it may reduce of death or hospitalization by 50%.

The second drug from Pfizer is a protease inhibitor which has shown a reduction of hospitalizations by 89% when used within 3 days of symptom onset. The drug PF-07321332 was given with ritonavir twice a day for 5 days. Ritonavir is used to reduce the drug's break down. Besides reducing severity it also has been shown to reduce transmission. The data as of 8th November, 2021 is yet to be published or peer reviewed. (*Science* 8 November 2021)

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