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Research Highlight

Diagnosis and treatment of syncope in pediatric patients: a new guideline

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Syncope is a common emergency of children and adolescents. The reoccurrence of syncope seriously affects children's physical and mental health. The pathogenesis, etiology, diagnosis and treatment of pediatric syncope differ from those in adults. Most pediatric syncope is relatively transient and benign in nature. But cardiac syncope, although the incidence is relatively low as compared with the neurally-mediated syncope (NMS), poses high risks of sudden death and needs to be quickly identified and managed. For the purpose of standardizing the diagnosis and management of pediatric syncope, Chinese Pediatric Cardiology Society (CPCS) of Chinese Pediatric Society, Chinese Medical Association (CMA), Committee on Pediatric Syncope of Pediatricians Branch, Chinese Medical Doctor Association (CMDA), Committee on Pediatric Cardiology of Chinese College of Cardiovascular Physicians, Chinese Medical Doctor Association (CMDA) and Pediatric Cardiology Society of Beijing Pediatric Society, Beijing Medical Association (BMA) jointly developed the guideline for diagnosis and treatment of syncope in children and adolescents, published in *Science Bulletin* [1].

In the guideline, the underlying diseases of syncope in children and adolescents are provided [1,2]. The diagnostic rate of syncope in children has been greatly improved on account of these efforts. The results of a single-center study in China showed that from 1985 to 1994, 89.3% of syncope children were with unclear reasons. While from 2005 to 2014, NMS became the main underlying disease of the syncope, accounting for 80.7%. The hemodynamic classification of NMS also gets refined. Meanwhile, unexplained syncope decreased from 89.3% of syncopal children to 13.9% [3]. Vasovagal syncope (VVS) and postural tachycardia syndrome (POTS) are associated with the syncope in children and adolescents. The manifestations of NMS are diverse, such as dizziness, headache, chest tightness, chest pain, pale complexion, fatigue, pre-syncope and even syncope. Although the clinical manifestations are similar, each subtype of NMS has its hemodynamic features and optimal treatment options [4,5]. The investigators first put forwarded a disease termed orthostatic hypertension in children, which increased the spectrum of underlying diseases of syncope in children [6].

In the past, the examinations including ambulatory electrocardiography (ECG), echocardiography, blood biochemistry, cranial CT or MRI and exercise testing were carried out for the majority of children with syncope, which further burdened the medical resources. In recent years, with the effort of Chinese pediatricians, an appropriate diagnostic flow chart for children with syncope has been established with a very good health-economic effectiveness [7]. In the guideline published, the diagnostic flow chart for children with syncope was introduced. The initial evaluation consists of history taking, physical examination, standing test and ECG. After the initial evaluation, some patients could be diagnosed definitely, such as POTS, OH, OHT and situational syncope (SS). Those with a suggestive diagnosis need further specific examinations. Patients for whom the causes of syncope remain undetermined need to undergo head-up tilt test (HUTT). In all of these diseases, cardiac syncope is the most life-threatening and needs to be quickly and accurately identified [7]. The modified Calgary score could be used to make an initial differential diagnosis between cardiac syncope and NMS in the clinic. When the score is less than −3, the diagnosis is suggestive of cardiac syncope [8,9]. In addition, abnormal ECG and history of post-exercise syncope are also high risk factors for the diagnosis of cardiac syncope [10].

The precise pathogenesis of NMS is not entirely clear. In recent years, studies have shown that NMS may be related to several factors including hypovolemia, high catecholamine status, abnormal local vascular tension, decreased skeletal muscle pump activity and abnormal neurohumoral factors. Currently based on the possible pathogenesis, the individualized treatment of NMS has been put forwarded in China [11].

As the guideline pointed out, generally, the management of NMS includes non-pharmacological and pharmacological interventions. Patient education is the fundamental part above all. NMS often has triggers, such as prolonged standing, quick position change from a long-term standing or a quick position change from standing or sitting to upright, a crowded or stuffy environment, and emotional stress. Therefore, avoiding the common triggers can help in reducing the occurrence of syncope. Besides, patients with NMS and their guardians are advised to recognize the presyncope symptoms. When presyncope occurs, patients should adjust their position, such as changing to a sitting position or lying down to rest if possible. Counter-pressure manoeuvres may avoid or delay the syncope by increasing peripheral venous return, such as bending the knees slightly, contracting abdominal muscles or limb muscles Most symptoms can be likely relieved in a short time.

Autonomic nervous function exercise is recommended for children with POTS, especially those with corrected QT interval

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dispersion (QTcd) >43 ms [12]. In addition to autonomic nervous function exercise, the first-line treatment mainly includes oral rehydration salts (ORS), beta adrenoreceptor blockers and alpha adrenoreceptor agonists. By analyzing the biomarkers of the patients before treatment, the efficacy of medication could be well predicted, which significant facilitates the progress of the therapeutics of pediatric syncope [11].

As mentioned earlier, NMS patients have low blood volume and shortage of water and salt intake. Thus, by means of increasing blood volume and serum sodium concentration, the baroreceptor could be stimulated and then reflectively decrease the sympathetic activity; finally the symptoms would be improved. The 24-hour sodium excretion of less than 124 mmol/24 h was an indicator for the effectiveness of ORS treatment in children and adolescents with POTS, with a sensitivity of 76.9% and specificity of 93% [13]. Besides, BMI is associated with the therapeutic response to ORS treatment in children with POTS. A cutoff value of the BMI of 18 kg/m^2 had high sensitivity (92%) and high specificity (82.8%), respectively, for the prediction of the ORS effectiveness [14].

Some of NMS patients have abnormal lower limb vascular tension. The vessels of lower limbs are excessively relaxed. Midodrine hydrochloride, an α-1 adrenpreceptor agonist, can act on the α-1 adrenergic receptor, constricting the vessels, so as to improve symptoms. Studies have shown that the measurement of plasma mid-regional pro-adrenomedullin (MR-proADM) could help in predicting the effectiveness of midodrine hydrochloride on POTS. Plasma MR-proADM concentration of higher than 61.5 pg/mL produced both high sensitivity (100%) and specificity (71.6%) in predicting the efficacy of midodrine hydrochloride therapy for treating POTS [15]. In addition, the erythrocytic H_2S production and the flow-mediated vasodilatation (FMD) could help in predicting the effectiveness of midodrine hydrochloride therapy on children with POTS [16,17].

Beta adrenoreceptor blockers mainly reduce the stimulation of cardiac pressure receptors and antagonize the high catecholamine action of children with NMS. Some case-control studies and meta analysis results showed that the efficacy of beta adrenoreceptor blockers is inconsistent.

All in all, the guideline for diagnosis and treatment of syncope in children and adolescents published in *Science Bulletin* is of reflective of the advance in the field of pediatric syncope. For instance, the disease spectrum of pediatric syncope in China has been constantly updated. The diagnostic procedure of pediatric syncope has been optimized as well. In the future, we need to explore the pathogenesis and the clinical diagnostic techniques of syncope and conduct large sample-sized and multi-center follow-up studies and randomized controlled trials to evaluate the efficacy of the treatment. It is believed that the diagnosis and treatment level of syncope in children will be further improved through the joint efforts of the multiple disciplines.

Conflict of interest

The authors delcare that they have no conflict of interest.

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