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Iron, ketone bodies, and brain development

To the Editor:

Iron deficiency is deleterious in early life brain development and a risk for short- and long-term cognitive, motor, and socioemotional impairment.[1,2] Parkin et al recently reported that increasing serum ferritin values, up to a level of 17 μg/L, were correlated with higher cognitive function in infants of 1-3 years of age.[3] Here, we address another aspect of the role of iron deficiency in brain development in relation to ketone bodies as an energy source for brain metabolism.

In the starved state, ketone bodies are synthesized from free fatty acids produced by breakdown of body fat, and cross the blood-brain barrier for use in brain metabolism. Ketone bodies may have neuroprotective effects and a ketogenic diet is used in treatment of neurological diseases such as refractory epilepsy, Parkinson disease, Alzheimer disease, and traumatic brain injury.[4,5]

Kuzawa and Blair hypothesized that body fat is a critical brain energy source, especially during infancy and early childhood.[6] In this period, the brain consumes about 40% of daily energy expenditure (20% for adults). Glucose alone cannot supply this energy, and ketone bodies are used. Thus, brain energy expenditure is inversely related to body fat gain (increased body mass index) during early childhood, and thus, decreases the risk of obesity.[6,7]

In an iron-deficient state, ketogenesis is impaired, citrate synthase and succinate dehydrogenase activities are decreased, and production of free fatty acids and ketone bodies is limited.[8,9] Therefore, iron deficiency may not only have a direct effect on brain function and development, but may also decrease the availability of ketone bodies as an energy source.[3] This possibility that the brain is deprived of ketone bodies as an energy source in iron deficiency indicates a need for further research into how iron is involved in brain development during early childhood.

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Pediatric poison center exposures and outcomes in the context of grandparent supervision

To the Editor:

We read with interest the report by Agarwal et al.[1] Our clinical toxicology service quite frequently manages pediatric poisonings that result from exposures to medications that are not in their original containers. In addition, we regularly manage patients who present in the context of being under the care of a grandparent. We applaud the authors for their timely and consequential study and would like to complement their results with some of our data focusing on outcomes in this patient population.

We retrospectively queried hospitalized pediatric (aged ≤6 years) cases from a 2-year period (2016-2017) reported to our poison center. The patients were then divided into 2 groups for comparison (126 cases with grandparent involvement vs 482 cases without grandparent involvement). Demographic data, clinical effects, and outcomes were then compared. Similarities in the 2 groups included average age (2.1 years), length of stay (<1.5 days), rate of seizures (1%), and rate of intubation (3%). Respective differences between the groups included the following: medicinal product (96% vs 63%), antihypertensive agent (48% vs 15%), source of exposure (25% pill organizer vs 15% pill bottle), intensive care unit (ICU) admission (60% vs 47%), hypoglycemia (8% vs 3%), and death (1.6% vs 0.2%).

The presence of a grandparent is a known risk factor for unintentional pediatric exposure to pharmaceuticals.[2] Older adults are more commonly prescribed cardiovascular and diabetic medications, and these drugs may lead to higher rates of ICU admissions and severe effects, such as hypoglycemia and death. We agree with Agarwal et al that preventive messages should be targeted at intended recipients of medications. In addition, larger studies are needed to fully understand the risk of severe outcome in pediatric patients under the care of grandparents.

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