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Review Article

Accelerated Starvation of Childhood in the Paediatric Emergency Department

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Abstract

Accelerated starvation of childhood (ASC) is a frequent, yet underrecognized condition in children presenting to the paediatric emergency department (PED). Typically, a prolonged fasting state resulting from an intercurrent illness or peri-operative fasting periods causes hyperketonaemia with or without hypoglycaemia (≤3.9 mmol/L) and/or metabolic acidosis with distinctive clinical signs and symptoms including lethargy, nausea, abdominal pain, vomiting, or seizures and should prompt correction of ketosis with oral, nasogastric (NG) or intravenous (IV) glucose solution. We describe a case of ASC and discuss recognition and management of this condition in the PED based on a review of the literature.

Keywords: Accelerated Starvation of Childhood; Intravenous; Childhood; Starvation Ketosis; Children; Pediatric Emergency Departmen; Blood Ketone Bodies; Glucose Substitution

Abbreviations

ASC: Accelerated Starvation of Childhood; BES: Balanced Electrolyte Solutions; BHB: Beta-Hydroxybutyrate; BSL: Blood Sugar Level; DTR: Deep Tendon Reflex; IV: Intravenous; KH: Ketonaemic Hypoglycaemia; NG: Nasogastric; ORS: Oral Rehydration Solutions; PED: Paediatric Emergency Department; PEM: Paediatric Emergency Medicine; POCT: Point of Care Test

Introduction

Accelerated starvation of childhood (ASC) is a frequent, easily detectable, and treatable yet underrecognized condition in children presenting to the paediatric emergency department (PED) but for this very reason requires prompt recognition and treatment [1]. Typically, a prolonged fasting state causes hyperketonaemia with or without hypoglycaemia (≤3.9 mmol/L) and/or metabolic acidosis [1-3] with distinctive clinical signs and symptoms including lethargy, nausea, abdominal pain, vomiting, or seizures [1,4] and should prompt correction of ketosis with oral, nasogastric (NG) or intravenous (IV) glucose solution. There is a research gap regarding the prevalence of the accelerated version of starvation ketosis in children. Whereas the prevalence of ketotic hypoglycemia (KH) in non-diabetic children presenting to the PED has been outlined as 4 per 100 000 presentations [5], the incidence of ASC including eu-and hypoglycemic keto (acido) -sis is much higher from our own clinical experience. To raise awareness of ASC we present an illustrational case followed by a discussion of relevant up-to-date literature.

Case

A five-year-old girl presented to a tertiary PED, with a 24-hour history of reduced general condition, lethargy and weakness, nausea, and vomiting (x2), generalized limb myalgia and decreased ap-

petite. Her mother (herself a paediatrician) had noted absent patellar deep tendon reflexes (DTR). On clinical examination the girl was lethargic, not smiling, pale and nauseated, however, well hydrated. Apart from lethargy, her neurological examination was normal and all DTR were elicited (weaker left patellar DTR). Cardiopulmonary and abdominal status were unremarkable and vital signs were normal (HR 102/bpm, BP 105/62 mmHg, RR 24/min, oxygen saturation 98% in room air, 36.5°C temperature). Point of care test (POCT) ketones were sharply raised (5.4 mmHg) with mild hypoglycaemia (3.4 mmol/L), normal lactate and pH. The patient was diagnosed with ASC and admitted to the ED short stay unit. An IV rapid rehydration protocol was administered using 0.9% saline and 5% glucose at 10ml/kg/h. Four hours later, the girl was chatty, smiling, skin colour was normal and vomiting had ceased. The patient was discharged home and encouraged to ensure sufficient oral carbohydrate intake.

Discussion

How to recognize ASC in the ED

Typical clinical signs and symptoms that should suggest ASC and alert the paediatric emergency medicine (PEM) physician to testing POCT ketones and BSL include lethargy, nausea, abdominal pain, vomiting or seizures in children commonly aged 6 months to 6 years as described in the literature [1] but up to 10 years from our own unpublished clinical experience. Usually, there is a history of poor appetite and prolonged starvation >24h due to gastrointestinal symptoms, stomatitis, other intercurrent illness or perioperative fasting state. ASC most often occurs in the morning after the longest fasting period of the day. Lethargy and degree of ketosis frequently seem out of proportion to illness duration and an often relatively mild dehydration. Patients may be more unwell than a child with classic gastroenteritis [1]. Simple bedside blood ketone body and glucose tests are key to diagnosis [4]. Typically, hyperketosis (S-ketone bodies >0.6mmol/L) is found, with or without hypoglycaemia (≤3.9 mmol/L) and/or metabolic acidosis [1-3].

Management of ASC in the ED

Treatment of ASC consists in reversing ketosis with oral, NG or IV glucosaline solution to break the vicious cycle in which untreated hyperketosis may worsen the abdominal symptoms, further prevent oral intake, and prolong starvation, in turn leading to even higher blood ketone levels. The patient generally will not or only slowly improve with glucose-free fluids.

Since clinical practice guidelines for the management of ASC are scarce [1], we conducted an updated systematic literature search until June 2021 in Medline (OVID) and PubMed, performed with the support of a trained librarian at Karolinska University hospital. The most recent literature review dating from April 2019 [1], we only found scant additional data in our search (1 publication, 1 conference abstract) [6], thus, there is still only limited evidence for the treatment of ASC which we discuss below [1,6].

A beta-hydroxybutyrate (BHB) cut-off threshold ≥2.5 mmol/L has been suggested at which medical intervention, monitoring and admission should be considered until the ketonaemic state resolves, as otherwise clinical recovery might be unnecessarily prolonged [1]. Importantly, in contrast to classical gastroenteritis, children with ASC most often are only mildly dehydrated and should above all receive IV, NG or oral glucose rather than rehydration only. The appropriate choice of glucose administration route should be based on the child's age and clinical findings. Ongoing vomiting, nausea and inability to tolerate oral fluids should be indications for IV glucosaline administration, uing fluids containing 5% glucose and given as continuous or rapid (e.g. 10ml/kg/h over 2-4 hours) rehydration, reversing ketosis more promptly than rehydration with low glucose or glucose-free fluids alone. Milder symptoms may be treated via oral or NG (continuous or rapid rehydration) route, likewise using fluids containing enough glucose to reversing ketosis (e.g., oral rehydration solutions (ORS), juice, breastmilk or formula, popsicles (45-100 g/L) [1]). Of note, ORS available in most EDs often contain a lower glucose amount (approx. 2.5-3%) than IV solutions. Exogenous insulin is only necessary in the most severe cases with profound acidosis and appears to provide more rapid resolution than bicarbonate infusion or renal replacement therapy in the critically unwell [7].

Acute ketosis is an important physiological response to ensure a continuous energy supply to the nervous system under fasting periods. The metabolic response towards decreasing blood sugar levels (BSL) includes gluconeogenesis and production of ketone bodies substituting glucose for energy supply. A subset of children is more vulnerable to accumulation of BHB and acetoacetate in the blood than others and may develop mild to severe ketosis or ketoacidosis [3]. This contrasts with diabetic ketoacidosis (DKA) where acidosis is typically combined with hyperglycaemia and glucosuria and non-diabetic ketoacidosis (NDKA), where ketosis is imperatively associated with metabolic acidosis and dehydration,

often requiring intensive care management, and having unfavourable clinical outcomes [6,7]. The milder end of ASC is again and again misdiagnosed as other gastrointestinal diagnoses while at its most extreme, it may present as NDKA with e.g., kidney failure, seizures or coma requiring critical care interventions and resuscitation. In a case series (n = 7) of ASC with bicarbonate levels as low as 3 mmol/L, only two cases were associated with hypoglycaemia, but all required insulin and glucose infusions as well as continuous renal replacement therapy [7]. In contrast to ASC, ketonaemic hypoglycaemia (KH) (defined as blood ketones >2.5 mmol/L and BSL <3.9 mmol/L) is a better understood condition and always associated with low BSL. KH has been described since the early 1900s and most of the current literature describing ketosis relates to KH [7]. Missed diagnosis and delayed appropriate treatment of ASC may lead to prolonged lethargy, abdominal symptoms, hypoglycaemia and ketoacidosis, and if untreated, to neurological sequelae.

Discharge from ED is generally possible when the child has clinically improved, i.e., normal skin color, alert, receding gastrointestinal symptoms and normal BSL (glucose ≥4 mmol/L) and ketonaemia <2.5 mmol/L are tested [1,2]. At discharge, caregivers should be instructed to prevent future episodes of ASC by providing frequent carbohydrate snacks or drinks during periods of illness or peri-operative state [1,8]. The intentional increase of calorie intake within the context of peri-operative fasting awaiting afternoon surgery has shown to prevent prolonged starvation ketosis in Japanese children [9].

Conclusion

ASC, especially its milder form of isolated ketosis, is an underrecognized condition and there is scant evidence for its treatment. We suggest that PEM physicians should measure POCT ketones and glucose in children presenting with reduced oral intake, vomiting, abdominal pain, lethargy or nausea due to illness-related or perioperative fasting state. Prompt glucose administration via oral, NG or IV route may prevent hypoglycaemia, ketoacidosis, and more severe neurological sequelae. Clinical practitioners should be mindful of keeping peri-operative fasting times as short as possible and substitute IV glucose for children undergoing elective surgery under prolonged fasting periods. Prospective studies into the prevalence of ASC and interventional studies into the optimal management of ASC are required to gain insight into the true incidence of ASC in the PED setting and the optimal treatment of ASC needed to restore sufficient carbohydrate sources, respectively.

Conflict of Interest

No financial, consultant, institutional and other relationships declared by the authors.

Subject Consent

Written consent for the publication of the case report was obtained from the patient's mother.

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