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Review Article

A Clinical Approach to Altered Level of Consciousness in the Pediatric Patient

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Abstract

Altered level of consciousness in infants, children, and adolescents represents a spectrum of disease ranging from mild agitation to coma, and fluctuations in between. Early recognition and immediate management of airway, breathing and circulation are often required before a specific etiology has been identified. Common causes include toxic ingestions, systemic or central nervous system infection, metabolic derangements, and structural lesions. Consultation with pediatric subspecialists and referral to tertiary care facilities for intensive care is often required. Outcomes are typically good, with most patients experiencing full recovery, depending on severity of underlying disease. This review provides a clinical approach to the pediatric patient with altered level of consciousness, reviewing the initial management strategies required for stabilization, preliminary investigations that will aid in delineating cause for symptoms, and resources for specific situations.

Keywords: Coma; Consciousness disorders; Critical illness; Encephalopathy; Pediatrics

Abbreviations

ALC - Altered Level of Consciousness; CXR - Chest Radiograph; DKA: Diabetic Ketoacidosis; ECG - Electrocardiogram; EEG - Electroencephalogram; IV - Intravenous

Introduction

Altered level of consciousness (ALC) is a spectrum of disease that presents a diagnostic and therapeutic challenge to the practitioner caring for infants, children and adolescents. Clinical presentation can range from confusion, disorientation or agitation, to lethargy, obtundation and coma. History may be incomplete and patients may require stabilization of airway, breathing, and circulation prior to performing a more thorough physical examination and investigations to aid in diagnosis. Oftentimes, determination of the likely cause(s) and initiation of appropriate treatment(s) are required to stabilize the patient, and will need to occur in the community hospital setting prior to transfer to a regional referral centre offering pediatric intensive care. This article provides a brief synopsis of this disease, reviews the emergency management of the pediatric patient presenting with ALC, and outlines an approach to diagnosis and treatment of common underlying etiologies.

Epidemiology

Although no large population-based studies regarding the incidence of pediatric ALC are available in the published literature, the annual rate of hospital admission for significantly depressed level of consciousness secondary to non-traumatic causes has been documented at 30 per 100,000 children [1]. Estimated rates of severe traumatic brain injury from accidental and non-accidental causes are similar [2], with accidental injury remaining the leading cause of pediatric mortality in developed countries [3].

The outcome for infants, children and adolescents presenting with ALC varies depending on the etiology, with mortality rates ranging from 3 to 84% [1]. Whereas patients presenting with seizures or symptoms of delirium and agitation from intoxications tend to fully recover, those with more significant alterations in mental status, such as coma secondary to infection or severe traumatic brain injury, are less likely to survive or do so with permanent neurological sequelae [1].

Clinical Presentation

Infants, children and adolescents presenting with ALC may have a broad range of signs and symptoms. Fluctuating level of consciousness is not uncommon, and progression from confusion, disorientation, and agitation to lethargy and coma may occur quickly. Any change in level of responsiveness should prompt reassessment and consideration of the need for acute interventions that may be required to stabilize the patient.

Confusion and disorientation may be easily recognizable in older children and adolescents, but in the infant or young child, these symptoms may only manifest as inconsolability by parents or another familiar caregiver. By definition, the encephalopathic patient may have a non-specific presentation, whereas agitation secondary to ingestion may be accompanied by classic signs and symptoms suggesting intoxication with a particular substance.

The lethargic child presents with extreme drowsiness, drifting in and out of sleep states only when aroused by moderate stimuli. In severe cases, these patients will become unresponsive when left undisturbed and require vigorous and repeated simulation to arouse them again. Finally, in the worst case of altered level of consciousness, patients are completely unresponsive to stimulation, a state referred to as "coma".

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Impaired consciousness is almost always a feature of generalized seizure activity and is a distinguishing feature in the classification of focal seizures [4]. Status epilepticus may present as continuous clinical and / or electrographic seizure activity that lasts duration of 5 minutes or more, or as recurrent seizure activity without return to baseline between seizures [5]. Non-convulsive status epilepticus may be clinically indistinguishable from the post-ictal state in pediatric patients with decreased level of consciousness following the cessation of obvious seizure activity and the clinician should maintain a high index of suspicion.

Standard and pediatric versions of the Glasgow Coma Scale are available to describe level of responsiveness in infants, children and adolescents. However, the AVPU mnemonic (A: alert, V: responsive to verbal stimulation, P: responsive to painful stimulation, U: unresponsive) allows for rapid assessment using four simple categories that are easy for the clinician to remember and apply [6].

Differential Diagnosis

The pediatric patient with ALC presents a challenge to the clinician, as initial stabilization and ongoing management often must occur in the absence of a clear etiology. The mnemonic "DIMS" can be used to remember the common causes of ALC in the pediatric patient (Table 1). This can help guide the focused history and physical examination, as well as the laboratory and radiographic investigations that will aid in correctly identifying the underlying etiology. Accidental ingestions and intentional overdoses of potentially toxic substances can exert significant pharmacodynamic effects on the central nervous system and result in metabolic derangements that further contribute to alterations in mental status. Similarly, the omission of prescription medications, or altered pharmacokinetics due to impaired absorption or transiently abnormal metabolism of medication, can lead to similar effects. Both severe systemic infection and localized infections of the central nervous system (e.g., meningitis, encephalitis, and abscess) can lead to ALC, secondary to decreased cerebral perfusion or direct irritation of cerebral tissues, respectively. Metabolic abnormalities range from electrolyte disturbances that can be easily corrected, to more complex conditions such as uremic or hyperammonemic encephalopathy. Finally, structural causes of ALC include space-occupying lesions (e.g., tumor, blood) and obstructions to cerebral blood flow (e.g., thrombus, vasculitis). Determination of the cause for clinical presentation will guide many of the therapeutic decisions beyond initial stabilization, and the clinician must simultaneously initiate treatment and consider a broad differential diagnosis.

General Management

Initial management of the pediatric patient presenting with ALC should include simultaneous assessment and management of airway, breathing, and circulation, including the initiation of continuous cardio respiratory monitoring, provision of supplemental oxygen, and establishment of intravascular (IV) access.

Oxygenation and ventilation

Supplemental oxygen should be administered to all patients presenting with ALC secondary to seizures and those who have signs of shock (e.g. tachycardia, pallor / mottling, delayed capillary refill, weak pulses, oliguria), regardless of pulse oximetry saturations. These patients may have increased oxygen consumption or poor oxygen extraction and the administration of supplemental oxygen is a relatively simple strategy to optimize oxygen delivery in the pediatric patient with inadequate perfusion.

Patients who are unable to adequately protect their airway should be intubated using an appropriately-sized endotracheal tube. Almost all patients requiring intubation should receive premedication with a sedative agent and muscle relaxant. Atropine should be considered in all infants less than 12 months of age, and other high-risk children [7]. However, in the undifferentiated comatose patient, the practitioner may opt to delay administration of atropine unless absolutely necessary, as its antimuscarinic properties will result transient loss of the pupillary response to light. Immediate confirmation of endotracheal tube placement should be confirmed by capnography, chest rise, and auscultation, and once the patient is stable, a Chest Radiograph (CXR) should be obtained to assess position of the secured tube.

Assisted ventilation may be required in some patients, as many causes of ALC can suppress the respiratory drive. Hypercarbia must be avoided as it may further contribute to a depressed level of consciousness. Whether invasive (i.e., through the endotracheal tube) or non-invasive (e.g., bag-mask), $PaCO_2$ should be maintained within the normal range. Even in patients suspected to have increased intracranial pressure, prophylactic hyperventilation is not recommended [8].

Cardiac output

Several causes of ALC in the pediatric patient may compromise cardiac output, and management should include optimization of heart rate and rhythm, preload, contractility, and vascular resistance. Patients with signs of inadequate perfusion should receive an initial bolus of 20 cc/kg of isotonic fluid (i.e., 0.9% sodium chloride or lactated Ringer's) and be reassessed to determine adequacy of response and need for additional fluid administration. Further management, including initiation of inotropes or vasoactive medications, is dependent on underlying etiology.

Hypoglycemia

Measurement of bedside glucose should be performed as part of the primary assessment. Hypoglycemia should be corrected immediately with 10% dextrose 5 cc/kg IV as this is an easily reversible cause associated with poor outcomes if left untreated for a prolonged period of time. Ideally, a critical sample (i.e., laboratory glucose, insulin, growth hormone, cortisol, serum chemistry, liver enzymes, ammonia, beta hydroxybutyrate, acetoacetate, free fatty acids and lactate) should be obtained when the patient is hypoglycemic, but correction of hypoglycemia should never be delayed for the purposes of specimen collection. In addition to a bolus of IV dextrose, the patient should receive a continuous infusion of fluids containing dextrose to avoid recurrent hypoglycemia.

Hyponatremia

Hyponatremia (serum sodium < 135 mmol/L) is often asymptomatic unless the serum sodium level decreases rapidly or becomes severe (i.e., < 125 mmol/L). Treatment of acute symptomatic hyponatremia requires immediate correction with 3% sodium chloride 4 cc/kg IV administered over 15-30 minutes, with the target end-point being cessation of seizure activity or serum sodium level >

Table 1: Investigations to determine underlying etiology for altered level of consciousness in the pediatric patient.

Etiology	Investigations*
Drugs	acetaminophen, ASA, toxic alcohols, +/- toxicology screen, ECG
Infection	complete blood count, blood culture, +/- CXR** urine routine and microscopy, urine culturecerebrospinal fluid*** for gram stain, culture, glucose, protein, and cell count
Metabolic	blood gases, lactate, glucose, electrolytes, liver enzymes, renal function, ammonia
Structural	neuroimaging (e.g., head CT or MRI)

*EEG should be obtained in patients suspected of having ongoing seizure activity.
**in patients with respiratory symptoms concerning for pneumonia.
***lumbar puncture should NOT be performed in patients with clinical suspicion of increased intracranial pressure.

Table 2: Common toxidromes.

	Signs & Symptoms
Opiates (e.g., oxycodone)	classic triad: respiratory depression, coma, miosis other: bradycardia, hypotension, hypoactive bowel sounds, urinary retention
Sympathomimetics (e.g., cocaine, MDMA)	agitation, seizures, tremor, mydriasis, tachycardia, hypertension+, diaphoresis
Anticholinergics (e.g., diphenhydramine, tricyclic antidepressants)	agitation, delirium, seizures, coma, mydriasis, hyperthermia, flushing, dry mouth and skin, urinary retention
Cholinergics (e.g., organophosphates)	bradycardia, bronchorrhea, lacrimation, salivation, emesis, diarrhea, urinary incontinence
Serotonin syndrome (e.g., SSRIs, other antidepressants, dextromethorphan)	agitation, seizures, sedation, tremors, clonus++, hypertonicity, hyperreflexia, tachycardia, hypertension, hyperthermia, diaphoresis, nausea, vomiting

*+may result in reflex bradycardia; prolonged state may result in hypotension secondary to catecholamine depletion.
++may aid in discriminating between serotonin syndrome and neuroleptic malignant syndrome.

125 mmol/L. Subsequent correction of serum sodium should occur slowly (not exceeding 8-12 mmol/L per day) using isotonic fluids and managing oral free-water intake. Pediatric patients at increased risk of hyponatremia are those consuming improperly mixed infant formula or excess fluids in conjunction with exogenous anti-diuretic agents (e.g. desmopressin for nocturnal enuresis), those receiving hypotonic IV fluids, and those with elevated anti-diuretic hormone levels secondary to medical conditions (e.g, bronchiolitis, meningitis, encephalitis) or in the post-operative period.

Seizures

Patients presenting with seizures should be treated with benzodiazepines, followed by anti-epileptic drugs (e.g., phenytoin, fosphenytoin, phenobarbital) [9]. Persistent seizure activity will require more aggressive management with continuous infusions of GABA-modulating agents, ideally in a pediatric intensive care unit that is able to provide continuous Electroencephalographic (EEG) monitoring. Early and aggressive treatment of status epilepticus is important, as delays in initiating treatment are associated with a cumulative increased risk of progression to refractory status epilepticus [10], a condition associated with significant morbidity and mortality [11]. Seizures secondary to hypoglycemia and / or hyponatremia are not likely to respond to therapy until underlying electrolyte abnormalities are adequately corrected.

Increased intracranial pressure

Clinical suspicion of increased intracranial pressure should be managed by elevating the head of the bed to 30º, administering hypertonic saline, and maintaining CO_2 levels within the normal range. Neuroimaging should be performed in all patients with unclear aetiology for ALC, and should also be considered in patients with intoxication who may have suffered unwitnessed head trauma contributing to alterations in mental status. Patients identified as having space-occupying lesions (e.g., tumor, blood, and abscess) or cerebral edema secondary to head trauma should be managed in consultation with the pediatric neurosurgical team.

Infection

Patients suspected of presenting with ALC secondary to severe sepsis should be treated empirically with broad-spectrum antibiotics (e.g., ceftriaxone and vancomycin) administered within the first hour of identification to optimize survival benefit [12]. Similarly, patients with signs and symptoms of localized central nervous system infection should be treated with systemic antibiotics and acyclovir if viral encephalitis is suspected. Although samples of blood, urine, and cerebrospinal fluid should ideally be obtained prior to administration, antibiotics should never be delayed for the purposes of specimen collection. Lumbar puncture should ONLY be performed if there is no clinical suspicion of increased intracranial pressure and once the patient is stable. Management focused on early and aggressive source control is essential and a thorough physical examination should be conducted to identify potential sources of infection. The pediatric surgical team should be consulted as the clinical scenario dictates.

Specific Situations

Toxic ingestions

Toxic ingestions may be accidental or intentional, and may include multiple substances, particularly in the adolescent patient. Details on history that raise suspicion of a toxic ingestion include acute onset of symptoms, unusual clinical picture, and multi system organ dysfunction, particularly in unsupervised children of young age (< 5 years) and adolescents with access to medication. In the patient with a known history of ingestion it is important for the clinician to determine the substance(s), estimate the amount taken, the elapsed time since ingestion, and any treatments initiated. Physical examination may reveal a toxidrome, or constellation of signs and symptoms that suggest intoxication with a particular substance. Common toxidromes include those of opioids, sympathomimetics, anticholinergics, cholinergics, and the serotonin syndrome (Table 2).

Investigations should include blood gas and serum chemistry to identify alterations in acid-base balance and electrolyte abnormalities.

Presence of a metabolic acidosis warrants calculation of the anion gap, and potentially the osmolar gap. Measurement of serum concentration level for specific substances (e.g., acetaminophen, ASA, toxic alcohols) can be useful, but the utility of the toxicology screen is questionable [13]. Electrocardiogram (ECG) should be obtained as many toxins result in electrical conduction abnormalities of the heart.

Often, treatment must be initiated on clinical suspicion alone and focuses on correction of associated metabolic disturbances and provision of supportive care. In situations where known toxins are present or suspected based on a toxidrome, the regional poison control centre should be notified as early as possible. Although basic principles include decreasing absorption (e.g., removal of the offending agent, decontamination, administration of activated charcoal), altering metabolism (e.g., administering toxin-specific antidotes), and enhancing elimination (e.g., IV fluids, diuretics, urine alkalinization, dialysis), more specific treatment recommendations may be provided.

Diabetic ketoacidosis (DKA)

Pediatric patients with an established diagnosis of type 1 diabetes commonly present in DKA, with as many as 6% requiring hospitalization for this condition each year [14]. Common reasons for this include intentional omission of insulin therapy, mismanagement of insulin dosing during periods of intercurrent illness, and technical issues with the insulin delivery system [15]. Elevated blood glucose levels measured at the bedside should prompt further laboratory investigations, including blood gas, lactate, serum chemistry, and renal function. Patients suspected of intercurrent bacterial infections should also have complete blood count and cultures drawn for microbiology and receive empiric coverage with broad-spectrum antimicrobials.

Treatment of hyperglycemia secondary to DKA requires calculation and replacement of the fluid deficit which should be administered slowly, over 48 hours, using isotonic fluids (i.e. 0.9% sodium chloride or lactated Ringer's). Potassium at a concentrate of 40 mmol/L should be added to the IV fluids once the patient is voiding, unless serum potassium measurements indicate the patient is hyperkalemic, as most pediatric patients presenting in DKA have a deficit in total body potassium and will have further reduction in serum potassium levels due to intracellular shifts when insulin therapy is initiated. Insulin therapy at a rate of 0.05 to 0.1 units/kg/hour should be started 1 - 2 hours after the initiation of IV fluid replacement and continue until the acidosis has corrected, at which time the patient can be transitioned to subcutaneous insulin. It is likely that the blood glucose will normalize at a rate faster than the metabolic acidosis, and dextrose should be added to IV fluids when the plasma glucose level measures 14-17 mmol/L or if it decreases rapidly (> 5 mmol/L/hour) at any time prior. Insulin should be continued as it is required to suppress the lipolysis and ketogenesis responsible for the acidosis. A more thorough review and clinical practice guidelines for the treatment of pediatric DKA are available in the published literature [15].

Metabolic encephalopathy's

Metabolic encephalopathy's that are the result of an accumulation of neurotoxic substrates may progress over hours to days with an acute presentation that includes changes in mental status and non-specific complaints, such as poor feeding and vomiting. In previously well infants and children, signs and symptoms may be the first presentation of an inborn error of metabolism or the signify the onset of significant hepatic or renal failure. Reduced fasting tolerance or family history of recurrent coma, unexplained deaths (especially infants) and consanguinity should raise clinical suspicion. In the patient known to have a metabolic disease, acute decompensation may occur during times of infection, prolonged fasting, or dietary / medication changes.

Physical examination findings suggestive of a metabolic encephalopathy may include Kussmaul respirations, organomegaly, and abnormal body or urine odor. Initial investigations should include blood gas, lactate, glucose, electrolytes, ammonia, liver enzymes, renal function tests, and coagulation studies, as well as serum amino acids, urine organic acids, plasma carnitine, acylcarnitine profile, and pyruvate,.

Elevated concentrations of ammonia (> 150 umol/L) can be extremely toxic with rapidly progressing symptoms. Early consultation with the pediatric critical care team and metabolic specialists is recommended as respiratory depression (with alkalosis) is not uncommon and patients often require intubation and ventilation, and specific therapies directed at correction of the hyperammonemic state. Severe hyperammonemia requires management of intracranial hypertension following the same basic principles used to guide therapy in patients with severe traumatic brain injury. In addition, these patients should initially be kept NPO and provided with a continuous source of IV dextrose 10% at 150% maintenance to avoid the catabolic state, which will also worsen hyperammonemia. L-arginine, an amino acid, should be administered to maintain the urea cycle, and rarely, patients may benefit from lactulose, which can enhance gastrointestinal transit time and reduce bacterial production of ammonia in the gut. Often, continuous infusions of ammonia scavengers (i.e., sodium benzoate, phenyl acetate) are required, and some patients may require dialysis. Hyperammonemic patients presenting with seizures should NOT be treated with valproic acid as this medication inhibits the urea cycle and interacts with carnitine to worsen the hyperammonemic state. Early identification and treatment is essential as many patients with mild to moderate hepatic encephalopathy and hyperammonemia secondary to fulminant hepatic failure will no longer be eligible for transplant if end-stage intracranial hypertension is present.

Conclusion

Although morbidity and mortality rates in infants, children and adolescents presenting with ALC is largely related to the severity of clinical presentation and etiology of disease, outcomes can be improved with early recognition of signs and symptoms, stabilization of airway, breathing, and circulation, and identification and treatment of the underlying pathophysiology of disease.

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