



## TOXIC COMA IN CHILDREN – ETIOLOGY AND CLINICAL DIAGNOSIS

Simona Stanca, Mădălina Petran, C. Ulmeanu, Viorela Nițescu

*Emergency Clinical Hospital for Children “Grigore Alexandrescu”, Pediatric Poisoning Centre, Bucharest*

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**Abstract.** Coma is a medical emergency that requires rapid and precise evaluation, especially in a Pediatric Emergency Department. Consciousness refers to the state of awareness of self and environment. Evaluation of consciousness in the pediatric patient must consider age and the appropriate developmental level. Coma is caused by multiple conditions that affect the brainstem or cortex diffusely. In the etiology of coma there are two large categories of coma: traumatic and non traumatic. Each of them includes a lot of cases. Coma is often a manifestation of life-threatening conditions. Therefore, the first evaluation of the child begins with vital functions' stabilization and identification of immediately reversible causes. After stabilization we have to obtain a detailed history and perform a full physical examination. The physical exam can be crucial in finding the toxicants involved. Poisoning is the main cause of coma in children admitted and treated in Emergency Clinical Hospital for Children “Grigore Alexandrescu”.

**Keywords:** neurological status, consciousness, stabilization, etiology, physical examination, history, retrospective study

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### Introduction

Coma is not a disease. It may occur in a lot of critical conditions that involve injuries of the central nervous system and it is the clinical expression for a lot of causes.

Coma represents an acute alteration of consciousness and is one of the main pediatric emergencies, especially in an Emergency Department. In assessing and initiating treatment in coma, time is essential, therefore it is necessary to use specific algorithms.[1]

In coma, the main dysfunctions occur in both cerebral hemispheres and in the reticular-activating system – the central core of the brainstem.

The best practical classification in coma etiology involves:[2]

- Structural causes – head trauma, neoplasm, vascular diseases, infections, hydrocephalus
- Toxic and metabolic causes – hypoxic-ischemic

injury, metabolic disturbances, poisonings, infections, seizures

Poisoning remains a common etiology in coma in children, despite prevention strategies and educational efforts.

Coma is often a life-threatening event. Therefore, a comatose child requires immediate evaluation and stabilization of vital functions, followed by a more accurate history and a thorough physical examination aimed at identifying the etiology of coma and establishing its reversibility. Obtaining this information will allow specific management and prognostic.

Very important in a child brought into the emergency department is making a diagnostic of coma and eliminating other forms of consciousness alterations (confusion, lethargy, stupor, obtundation).

During the initial evaluation of the comatose child, a detailed history is not always available, but a brief history must be obtained in the shortest time possible. The medical history should include a detailed description of all events that came before the onset of coma, giving a particular attention to symptoms that may accompany or precede the neurological manifestations.

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**Simona Stanca**

30-32 Iancu de Hunedoara Bvd, Sector 1, Bucharest

E-mail: simonastanca@yahoo.com

The child's age is another important issue to be reported when evaluating a comatose patient. Consciousness refers to the state of awareness of self and environment. Starting from this definition, as the age is lower, the more difficult it is to classify coma. Therefore there are several ways, none perfect, including standardization and assessment of the depth and severity of coma.

Because of the difficulty and imprecision in using terminology and the need for a truly reproducible assessment of consciousness with good interrater reliability, several behavior rating scales have been developed.

Key objectives in the evaluation and management of coma in children are: to detect the elements of gravity, to appreciate the severity of coma, to observe associated clinical signs, etiologic and differential diagnostic and to establish the appropriate and the best treatment.

**I. Severity signs** are represented by the association of one of these elements in a comatose patient:[3]

- Respiratory syndrome: bradypnea or an irregular respiratory rate with gasps
- Signs of circulatory failure associated with heart rhythm disorders
- Severe neurological disorders: deepcoma, apnea, bilateral slow reactive mydriasis

**II.** Currently, the most widely used neurological assessment method is the **Glasgow Coma Scale** with pediatric adaptations.[4]

order: head, neck, thorax, abdomen, limbs.

**The first step is to stabilize vital functions.**

**Clinical features** of toxic coma are: absence of meningeal irritation and also absence of focal neurological signs (if hypoglycemia is not involved). Usually, neuroimaging reveals no morphological injuries. In the absence of seizures, the patient goes into coma, advancing through various stages of lethargy, confusion and stupor. Deep tendon reflexes, oculo-vestibular and oculo-cephalic reflexes are usually preserved, except for the cases of poisoning with sedative-hypnotic and anticonvulsive medication. Drugs that induce prolonged coma (more than 100 hours) with intermittent periods of awakening usually have an entero-hepatic or entero-enteral circuit and active metabolites inducing cyclic coma.

**Associated physical findings** are essential for the toxic etiology. **Eye exam** is crucial. The eye exam involves evaluating: pupil size, pupil reactivity and nystagmus. Pupil size is always a balance between sympathetic and parasympathetic nervous system activity. In cases of poisoning, pupil sizes are equal, only 20% of patients having up to 0.5 mm in diameter asymmetric pupils. Toxic substances can cause miosis (<2 mm) or mydriasis (> 4 mm). Pupil size is related to the toxic, but does not represent an infallible diagnosis criterion due to multiple interactions with various neurotransmitters.[5]

The photo-motor pupillary reflex is not impaired

| Sign            | GCS                     | Score | PGCS                         | Score |
|-----------------|-------------------------|-------|------------------------------|-------|
| Eye opening     | Spontaneous             | 4     | Spontaneous                  | 4     |
|                 | On command              | 3     | To sound                     | 3     |
|                 | To pain                 | 2     | To pain                      | 2     |
|                 | None                    | 1     | None                         | 1     |
| Motor response  | Obeys commands          | 6     | Normal spontaneous movements | 6     |
|                 | Localizes pain          | 5     | Withdraws to touch           | 5     |
|                 | Withdraws               | 4     | Withdraws to pain            | 4     |
|                 | Abnormal flexion        | 3     | Abnormal flexion             | 3     |
|                 | Extension               | 2     | Abnormal extension           | 2     |
| Verbal response | None                    | 1     | None                         | 1     |
|                 | Oriented                | 5     | Oriented/ coos               | 5     |
|                 | Confused speech         | 4     | Cries but consolable         | 4     |
|                 | Inappropriate words     | 3     | Cries but inconsolable       | 3     |
|                 | Incomprehensible sounds | 2     | Moans to pain                | 2     |
| Max             | None                    | 1     | None                         | 1     |
|                 |                         | 15    |                              | 15    |

**Table I.** Glasgow Coma Scale with pediatric adaptation

**III. Physical examination** and associated findings

It is a complete examination (“from head to toe”), being performed on body segments in the following

in toxic coma, but there are some exceptions. Poisoning with large doses of barbiturates and opiates may cause fixed miosis; fixed mydriasis may occur in anticholinergic poisoning, irreversible to physio-

stigmine. Other causes of mydriasis may include methanol, hypothermia and hypoxia.

Drug-induced nystagmus includes slow horizontal movements and compensatory movement alternative fast side. The most common causes include alcohol, anticonvulsants, hypnotics, sedatives, solvents and quinine. Lithium can produce vertical nystagmus. Phencyclidine, dextromethorphan, phenytoin, hypnotics and sedatives can produce a combination of horizontal and rotator nystagmus. Other sedative hypnotics can produce different movements, such as opsoclonus (involuntary and random eye movement), induced by antidepressants, anticonvulsants, organophosphates, thallium, lithium and haloperidol. Periodic movement type 'ping-pong' has been described in poisoning with monoamine oxidase inhibitors.

Another clinical parameter that can be evaluated in a patient with toxic coma is cranial nerves' dysfunction. Trichlorethylene induces trigeminal sensitive neuropathy, and organophosphates injure more than one cranial nerve, usually bilateral injuries.[6]

**Respiratory movements** are an important factor in assessing clinical response to toxicants. Decreased respiratory rate, regular breaths, <12/min indicate opiates or sedative hypnotics poisoning. These drugs may cause respiratory failure, resulting in an inadequate response to stimulation by increasing the blood concentration of carbon dioxide. Sympathomimetic agents stimulate respiration, inducing tachypnea with increased gas exchange (salicylates, amphetamines, carbon monoxide). Kussmaul breathing (high frequency, regular) is usually associated with metabolic acidosis (methanol, ethylene glycol, salicylates). Another type of breathing pattern in acute poisoning is the Cheyne-Stokes respiration. It is characterized by periods of tachypnea followed by short periods of apnea. This is due to neuronal metabolic disorders. Other complications of drug-induced coma are pulmonary, such as non cardiogenic pulmonary edema (produced by salicylates, opioids, antidepressants, sedative-hypnotics) and aspiration. Pneumonia due to aspiration occurs in approximately 10% of patients admitted after an overdose of drugs and is more common in those with altered mental status.

**Hypertension** is due to sympathomimetics, organophosphates and amphetamines, while hypotension, more frequent, occurs in narcotics, beta-blockers, sedative-hypnotics, calcium channel blockers.

**Skin** examination may help to identify various toxins, like cyanosis unresponsive to oxygen (nitrates, nitrites, phenacetin, benzocaine), red flush (carbon monoxide, cyanide, anticholinergic substances), jaundice (acetaminophen, mushrooms, carbon tetrachloride). Dry skin occurs in

anticholinergic poisoning, while sweating occurs in barbiturates, organophosphates and street drugs (amphetamines, LSD, cocaine).

The **temperature** of the body is increased in anticholinergics poisoning, salicylates, phenothiazines, amphetamines; hypothermia may occur in ethanol, carbon monoxide, sedative hypnotics, clonidine poisoning.

**The severity of poisoning** in toxic coma is related to four factors that must be evaluated from the beginning:[7]

1. Toxic
2. Absorbed dose
3. Time elapsed from exposure
4. Physical and mental status before poisoning

**The physical and therapeutic approaches to a toxic coma child have the following objectives:[8]**

- The history must quickly give a clue about the nature of the toxic, the amount ingested and absorbed, time of ingestion/exposure, time of last meal, primary care at home, age and weight. Very important is to search packages of medicines and other toxic products that exist in the house, also recent medication taken by children or adults.
- Physical examination will focus on vital signs, gravity findings and will appreciate the depth of coma. Any comatose child, whose circumstances are not known, should be suspected as having an exogenous toxic cause. We have to think about toxic etiology in the following conditions: coma, convulsions, acute psychotic manifestations, and acute renal and liver failure.
- Toxicological exam, even if poisoning is well known. Textbooks, computer programs or poison hotlines as the available in our Pediatric Poison Center – TOXAPEL will be used.[9]

A medical practitioner in an Emergency Department must follow **five rules**:

1. All potential poisoning should be considered real;
2. The maximum amount that can be absorbed must be considered absorbed;
3. The time interval between onset of intoxication and primary care must be as short as possible;
4. All oral poisoning, besides the exceptions, must receive gastric lavage
5. Poisonings that can have a bad outcome will be admitted in the hospital for at least 24 hours for monitoring in a special department of toxicology.

Complications that can occur in a toxic coma are as follows:

- hypoventilation with respiratory failure
- circulatory instability
- aspiration pneumonia

- bradycardia, cardiac arrest
- cardiac arrhythmias
- hypo- or hyperthermia
- intracranial hypertension
- brain death.

### Personal study

The following data have been collected from a five-year retrospective toxic coma study in Pediatric Toxicology - Emergency Department in the "Grigore Alexandrescu" Hospital. The conclusion is that toxicants represent the main cause of coma in children. We analyzed 342 coma patients out of a total number of 68.326 admitted in this Department. We analyzed data using the following criteria: consciousness status, type of poisoning, distribution by age, gender or reason for presentation.

Toxic coma was present in 220 cases - 64% of comatose children.

#### Etiology of coma:

- Poisoning: 220 cases - 64%
- Other: 122 cases - 36%
  - MSOF / toxicoseptic shock
  - Resuscitated cardiac arrest
  - Acute respiratory failure
  - Epilepsy – status epilepticus
  - Traumatic brain injury
  - Acute meningo-encephalitis
  - Cerebral hemorrhage

#### Etiology of toxic coma:

- Ethanol: 63 cases - 29%
- Multiple drug poisoning: 46 cases - 21%
- Benzodiazepines: 15 cases - 7%
- Antidepressants: 11 cases - 5%
- Dentocalmin (lidocaine, menthol, phenol) : 11 cases - 5%
- Barbiturates: 9 cases - 4%
- Pesticides: 5 cases - 2%
- Petrol: 3 cases - 1.5%
- Carbon monoxide: 2 cases - 1%
- Heroin: 1 case - 0.5%
- Others: 11 cases - 5%
- Unknown: 44 cases - 20%

#### Intention:

- Intentional poisoning: 155 cases - 70%
- Accidental poisoning: 72 cases - 30%

#### The age range was the following:

- 0-1 year : 42 cases- 13%
- 1-5 years : 66 cases - 19%
- 5-10 years : 62 cases- 18%
- >10 years : 171 cases- 50%

### Discussion

Starting from this study, efforts should be made in the following directions: increasing the efficiency of time spent in the emergency department, devel-

opment of diagnostic algorithms and prevention strategies focusing on the general population and especially on teenagers and increasing security home measures for toxic products.

The use of medicines in combination with ethanol in acute poisoning has become a reality in recent years. These combinations are used as recreational drugs or in suicidal attempts. The combination of ethanol with medicines increases the severity of poisoning and the depth of coma.

The physical exam can reveal an association of signs with particular substances or groups of substances which are known as toxidromes.

Key objectives in the evaluation and management of coma in children are: to detect the elements of gravity, to appreciate the severity of coma, to observe associated clinical signs, etiologic and differential diagnostic and to establish the appropriate and the best treatment.

### Conclusions

Despite its prevalence, toxic coma is still one of the most severe life-threatening situations in pediatric pathology.

Toxic etiology represents the main cause of coma in children admitted and treated in the Emergency Clinical Hospital for Children "Grigore Alexandrescu".

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