Severe central nervous and respiratory system depression after sedation with chloral hydrate: a case report

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Chloral hydrate is generally considered a safe sedative-hypnotic drug, and is commonly used for sedation of infants and young children before diagnostic procedures. Even chloral hydrate administered within the recommended maximal dose limits can cause serious morbidity and mortality. Here the authors describe a four-month-old girl with a life-threatening central nervous system and respiratory depression after administration of a therapeutic dose of chloral hydrate. The patient gradually recovered with supportive treatment including ventilation therapy.

Key words: chloral hydrate, respiratory depression, central nervous system depression.

Chloral hydrate (CH) is generally considered a safe sedative-hypnotic drug, and is commonly used for sedation of infants and young children before diagnostic procedures[1-5].

It has no analgesic effect and therefore is not generally used alone for painful operations. CH is completely absorbed and rapidly metabolized to trichloroethanol and trichloroacetic acid, both of which are pharmacologically active. The half-life of trichloroethanol ranges from 9 to 40 hours. The half-life of trichloroacetic acid is even longer than six days[6,7]. Sedation occurs within 30 to 60 minutes at doses of 25 to 100 mg per kg orally or per rectum (max. 1 g). CH is often administered at the highest recommended dosages. Although few reports on its major and minor adverse effects have been published, it is apparently well tolerated. Adverse effects include hypoxia, nausea, vomiting, gastric irritation, hyperactivity, agitation, respiratory depression, acute laryngeal edema, acute laryngospasm, and cardiac arrhythmias[3,7-10].

We describe an infant with a life-threatening central nervous system (CNS) and respiratory depression after the administration of a therapeutic dose of CH.

Case Report

A four-month-old girl with severe respiratory distress was transported to our emergency department from a private hospital with oxygen therapy. CH had been administrated with a dose of 50 mg/kg per kg rectally in a private center because of agitation one day after vaccination. A minute after the CH administration, defecation was observed and the same dose was given orally in the following five minutes. About 10 minutes after the oral administration of CH, respiratory distress was noted. On the physical examination in our center, she had inspiratory stridor, tachypnea with a respiratory rate of 40/min, hyperpnea, tachycardia, and respiratory insufficiency with cyanosis. The pupils were miotic and symmetrically responsive to light. Glasgow Coma Scale (GCS) score was 6 (E2 M3 V1). Blood gas analysis before the intubation revealed severe respiratory acidosis (pH: 7.05, pCO2: 80 mmHg, HCO3: 22 mEq/L, pO2: 48 mmHg). She was intubated immediately because of respiratory distress. During intubation, severe larynx edema was detected. After intubation, spontaneous breathing collapsed. GCS score was 3 (E1 M1 V1). On laboratory investigation, renal and liver function tests were normal but she had leukocytosis and elevated C-reactive protein. High levels of blood glucose level in the acute period slowly reversed to normal during the follow-up, and glycosuria disappeared without treatment. The chest X-ray study before the intubation suggested pulmonary aspiration, and intravenous antibiotic treatment was ordered. The follow-up chest X-ray just

after the intubation was normal. The patient was admitted to the pediatric intensive care unit and ventilation therapy and supportive treatment were given. After six hours of hospitalization, spontaneous breathing was marked and miosis disappeared. She was conscious and was extubated at the eighth hour. After the extubation, she had inspiratory stridor for about one day and in addition to oxygen therapy, inhaler steroid and inhaler adrenaline treatment was given. She was discharged from the hospital on the seventh day.

Discussion

Chloral hydrate is widely used in children to induce sedation during painless imaging procedures. Generally, CH has little effect on respiration, but it can result in oxygen desaturation, including mild or rarely severe hypoxia, especially with repetitive or excessive doses[10]. Significant respiratory depression is rarely associated with CH sedation in children[1,2]. Sanborn et al.[11] reported that the adverse respiratory event rate with CH was 1.2% (8/648) during sedation of pediatric patients for imaging examinations. One of the eight patients required brief positive pressure ventilation with face mask. Keengwe et al.[12] reported two patients with significant respiratory depression after receiving only CH (respiratory rate <12 breaths per minute and arterial oxygen saturation <92). In the study in which CH was administered to 295 children for 326 computed tomography scans, a 1.2% incidence of respiratory symptoms was reported, including wheezing in one child that resolved without intervention, aspiration of secretions in another that required suctioning, and two incidents of airway obstruction by the tongue requiring endotracheal intubation[1]. In a subsequent study evaluating the use of CH for 300 magnetic resonance imaging (MRI) scans, the same investigators reported a 4% (11/300) incidence of hypoxia[2]. Respiratory depression occurred in eight children below 24 months. They suggested that because of smaller airways, infants are more susceptible to respiratory injury than older children when sedated. Heistein et al.[5] retrospectively analyzed 1095 patients sedated with CH (80 mg/kg, maximum 1 g) for echocardiography and determined five (<5% of the total population) adverse events that required major interventions including intubation. The infants younger than six months were under a higher risk for developing serious adverse events. Although CH in therapeutic doses appears not to cause significant CNS and respiratory depression, it may still cause respiratory compromise by relaxing the muscles that support the tongue and upper airway, including the geniohyoid and genioglossus muscles. In fact, this characteristic of CH is mainly responsible for most of the serious adverse events, including upper airway obstruction, hypoxia, and even death. Hershenson et al.[13] described a near fatal respiratory arrest in a child after administration of CH, raising some concerns about possible risks in using this drug for sedation in infants or children with obstructive sleep apnea. Coté et al.[14] culled adverse sedation events from 118 case reports and found 95 incidents resulting in 60 deaths or permanent neurologic injuries. CH was the only drug administered to seven of the affected children. Four received an overdose. The same authors reported a child with cardiac arrest following respiratory depression and bradycardia after receiving 60 mg/kg CH for a cardiology procedure. Postmortem examination of the patient revealed a ventricular septal defect, pulmonary hypertension, and elevated digoxin levels[14]. Malviya et al.[15] reported a 5.3% incidence of significant oxygen desaturation (90% of baseline) in 854 children who received CH alone (mean dose: 65 mg/kg) for nonpainful procedures. Caksen et al.[7] described respiratory arrest due to CH in an infant with clinically diagnosed cyanotic congenital heart disease. Despite the supportive treatment including ventilation therapy, the patient did not survive. In our case, the dose was repeated because of defecation and respiratory failure started a few minutes after the subsequent oral administration. The total given dose was within the recommended dose levels of CH (totally 100 mg/kg). Severe larynx edema was detected during intubation. Although the American Academy of Pediatrics states that CH is an effective sedative with a low incidence of acute toxicity when administered orally at the recommended dosage for short-term sedation and refers to the great deal of experience with CH, the risk of acute laryngeal edema and aspiration in the pediatric group during the procedure should not be forgotten[10].

In conclusion, chloral hydrate is an effective sedative with a low incidence of acute toxicity when administered orally at the recommended

dosage for short-term sedation. There is much experience with CH and most practitioners are familiar with its use. However, even CH administered within the recommended dose limits can cause serious morbidity and mortality. Monitoring of patients who receive CH should be no less rigorous than that used for patients sedated with other sedative medications. We would like to emphasize that CH may cause respiratory arrest in infancy, and we suggest that continuous monitoring of vital parameters and oxygen saturation is recommended in all infants sedated with CH to prevent respiratory arrest. Sedation with CH can last shorter than expected because of the noise of the computed tomography and MRI. It is also not an alternative for minor operations because of the lack of analgesic efficacy. Long-lasting sedation and the deep sleep pattern in the late period require close monitoring after administration. Cardiac toxicity also remains a life-threatening complication. In this regard, it may be appropriate to choose other medications besides CH in the first step in sedation.

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