BACD British Academy of Childhood Disability

BPNA British Paediatric Neurology Association

Association for Paediatric Palliative Medicine

NPPG Neonatal & Paediatric Pharmacists Group

Position statement 21-03

Off label use of Chloral Hydrate in the Management of Intrusive Movement and Motor Disorders in Children and Young People

Introduction

In October 2021, the MHRA *Drug Safety Update* described a new restriction to use of chloral hydrate and cloral betaine due to the potential for carcinogenic effects, based on animal data. Licensed use is now limited to short-term (maximum 2 weeks) treatment of severe insomnia, only in patients with a suspected or confirmed neurodevelopmental disorder and when the insomnia affects normal daily life.

Chloral hydrate is, however, also used for other, off-label indications. This position statement outlines considerations for off-label use of chloral hydrate to manage distressing symptoms in patients with movement and motor disorder when all other therapies have failed. It also provides recommendations for appropriate discontinuation of chloral hydrate where it is being used to treat insomnia in the absence of movement and motor disorders. Off-label use for other indications, e.g. sedation in paediatric intensive care and procedural sedation is outside the scope of this document.

Take Home Summary

Use of chloral hydrate for insomnia

- In line with the MHRA position, chloral hydrate use for insomnia should be limited to patients with a suspected or confirmed neurodevelopmental disorder, with a maximum duration of 2 weeks.
- Where a patient is currently receiving regular, long-term chloral hydrate for the management of insomnia:
  - They should be reviewed by a relevant specialist and a plan made for discontinuation of the drug. Due to risks associated with sudden cessation of chloral hydrate, this will usually require a gradual, controlled discontinuation. Do not stop abruptly if patients have been taking the drug regularly for over 2 weeks.
  - Alternative pharmacological or non-pharmacological treatments may be required. Consider referring to a local sleep service where appropriate and available.

Use of chloral hydrate in children and young people with movement disorders

- It may be appropriate to use chloral hydrate off-label to manage distressing symptoms in patients with movement and motor disorder when all other therapies have failed OR rapid stabilisation of symptoms is required. This may include:
  - Acute, time-limited regular use to manage symptom exacerbations: this must be under very close, specialist supervision
  - Longer term (duration over 1 month), regular (daily or more frequently) use in children and young people with severe intrusive movement and motor disorders preventing the initiation and maintenance of sleep, after assessment by a consultant with expertise in paediatric neurology.
  - Longer term "when required" use, or repeated short courses for break through symptoms as part of a symptom management plan. Such plans should specify a maximum number of doses per month or continuous days of treatment over which the patient should be reassessed by the relevant specialist team.
- When using chloral hydrate for movement disorders, use the lowest effective dose, at the lowest frequency and for the shortest period possible. The need for ongoing use should be regularly assessed and documented.
- Where use of chloral hydrate is considered appropriate:
  - Informed consent to use chloral hydrate must be obtained and documented.
  - Use must be under the supervision of a named consultant with appropriate experience and competency in paediatric neurology, neurodisability, and/or palliative care. who must regularly review the patient, being alert to signs of inappropriate use and aiming to deescalate wherever possible.
  - A written emergency escalation plan which includes the contact details for the supervising clinical team should be provided to the family and other healthcare professionals. Such plans should specify a maximum number of doses per month or continuous days of treatment above which the patient should be reassessed by the relevant specialist team.
- Hospitals and primary care providers must work together to identify and plan for timely review of all patients currently receiving chloral hydrate. Development of local guidelines to describe the governance arrangements for any ongoing use should be considered.
- Where a chloral hydrate liquid is required, the standardised concentration of 500mg in 5mL should be used.

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Further Information

Chloral hydrate

Chloral hydrate and its prodrug cloral betaine are enterally administered sedative agents which have been widely used in paediatric practice for many years. After absorption, chloral hydrate is rapidly converted to its active metabolite trichloroethanol[1]. The exact mechanism of action of trichloroethanol is unclear, though it may mediate its effects through agonism at GABA receptors[2].

Chloral hydrate has been used for a range of indications including night time sedation; management of dystonia and other movement disorders; sedation in critical care; and sedation for painless procedures[3-6]. Use for night time and procedural sedation has declined in the USA, and the drug is now not readily available in America[5,7]. Reasons cited for the decline include a narrow therapeutic index, no known antidote, prolonged sedation or clinical re-sedation and fatalities associated with chloral hydrate sedation[7]. In 2009, following a national review of safety and efficacy, the MHRA limited the licensed indication for chloral products to "*severe insomnia that is interfering with normal daily life and where other therapies have failed, as an adjunct to nonpharmacological therapies*" [8].

In October 2021, after a further review of published evidence, the MHRA issued a Drug Safety Alert further restricting the licensed indication to the "*short term treatment (maximum 2 weeks) of severe insomnia only when the child or adolescent has a suspected or definite neurodevelopmental disorder and when the insomnia is interfering with normal daily life*" [9]. No new safety concerns had been identified. However, in view of known carcinogenic effects in animal models and a lack of long-term studies in humans, the risk of harm associated with extended use could not be excluded.

Management of movement disorders

Dystonia in children can be particularly challenging, interfering with normal movements, mobility and the delivery of daily care, as well as causing problems with feeding and communication[10]. Dystonia can have a significant adverse effect on quality of life, and is associated with disturbed sleep[11].

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