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Midazolam Orally for Sedation during Pediatric Intrathecal Chemotherapy: Unmet Need of Distress-Free Procedures for Cancer Kids in India

Abstract

Preprocedural sedation is the part of standard operating procedures for pediatric intrathecal chemotherapy in developed countries and uses predominantly intravenous route. In India, due to the limited availability of pediatric oncology facilities and the increased patient numbers at those centers, no such intervention is possible. This article discusses this issue and proposes the use of oral midazolam in this context for large-scale utilization.

Keywords: *Intrathecal chemotherapy, midazolam, pediatric*

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Introduction

Intrathecal chemotherapy is an integral part of the treatment in many pediatric cancers. The success story of pediatric acute lymphoblastic leukemia has been possible also because of the central nervous system protective actions of intrathecal chemotherapy. However, the long-term side effects of intrathecal methotrexate with or without cranial radiotherapy are known, and there are attempts to decrease the toxicity without altering the efficacy by de-escalation strategies.

Along with the cognitive, academic, and psychosocial effects of the intrathecal chemotherapy, the other areas of concern are the fear and distress caused by the repeated invasive procedures such as intrathecal methotrexate. As per the treatment protocol, it is given at least 15–20 times to these children. This concern has been discussed earlier in the pediatric community.[1] Earlier in 1990, the American Academy of Pediatrics proposed the guidelines for preprocedural sedation or anesthesia for children undergoing invasive procedures in an emergency room.[2] This article noted that although more research and innovation are needed, every opportunity should be taken to use available methods of pain control. A systematic approach to pain management and anxiolysis, including staff education and protocol development, can have a positive effect on providing comfort to children.

Thereafter, there have been multiple studies to find out the optimum agent to give adequate sedation and to decrease the pain associated with procedures in children. The current drugs that are used for preprocedural sedation in children include ketamine, midazolam, propofol, etomidate, or their combinations. Oral route is always the preferred route in children as the injection anxiety counteracts the purpose. Although there are studies on oral ketamine,[3] the preferred agent for sedation in children remains intravenous (IV) ketamine in combination with propofol.[4] Various institutional protocols have been developed based on the ACEP guidelines which consider IV ketamine as Level A recommendation. Midazolam with or without fentanyl is given as Level B recommendation. Midazolam can be given via IV, oral, intramuscular, intranasal, or per rectal routes.

Midazolam

In 1998, Davies and Waters[5] published a study on oral midazolam for conscious sedation in children undergoing minor procedures. They concluded that at 0.5 mg/kg, oral midazolam appears safe and is effective in sedating most children for minor procedures. Thereafter, multiple studies have been conducted on oral midazolam, and it remains the preferred

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medication for pediatric dentistry and also for other minor invasive procedures.[6] A recent review of safety of oral midazolam in pediatric dentistry noted that significant side effects are rare with oral midazolam.[7] Midazolam is the most common drug used for premedication in the preoperative period to alleviate the separation anxiety before being shifted to the operation theater.

A study from India by Deshmukh *et al*.[8] compared oral and intranasal midazolam in a randomized way and concluded that oral midazolam and intranasal midazolam spray produce similar anxiolysis and sedation, but acceptance of drug and response to drug administration is better with oral route. The sedation and satisfactory separation was 80%–90%. No significant side effects were noted.

Unmet Need in Our Country

The administration of intrathecal methotrexate is done under preprocedural sedation in most of the developed countries. As mentioned, the preferred route is IV and mostly with ketamine or other combinations. In India, there are few pediatric oncology centers, and there is need for a concerted, collaborative, and multidimensional effort to achieve international standards.[9] The large number of pediatric patients seen in the few tertiary centers with lack of adequate infrastructure makes it impossible to consider IV route-based premedication for these children before the intrathecal methotrexate injections.

The separation anxiety and fear is the most common cause of the distress in a child. The pain due to the procedure *per se* is reduced by the application of local anesthetic at the lumbar puncture site. In these institutions, the procedure is done with available human resources by talking to them and holding and fixing them tight during the intrathecal injections. The extent of physical and mental strain to the child and the oncology team is very high.

Role of Oral Midazolam

In this context, oral midazolam at dose of 0.5 mg/kg given 30 min before the intrathecal injection is proposed as a possible effective option for preprocedural sedation in our pediatric patients. Oral midazolam syrups (2 mg/2 ml) are cheap and easily available and can be administered by the oncology nurse as per the body weight. They are consciously sedated and come out of sedation in 40–60 min. The benefit of oral midazolam will be in its application on a larger scale, especially in Indian situations. This, however, initially has to be done in a supervised manner for a small set of children in the presence of the anesthesia colleagues, and once experience is gained can be done by the oncology team.

Conclusion

As we improve the pediatric oncology facilities in our country and aim to be at par with the developed countries, we need to take care of the pain aspect also. Rather than being myopic on the impact of such repeated mental trauma to pediatric cancer patients and their families, we must find out a unique way for our own realities, and this midazolam orally for sedation during pediatric intrathecal chemotherapy protocol may be a useful one.

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Conflicts of interest

There are no conflicts of interest.

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