Drug choice for pediatric procedural sedation-analgesia and route of adrenaline administration in anaphylaxis treatment

Çocuklardaki tıbbi işlemlerde sedatif-analjezik ilaç seçimi ve anafilaksi tedavisinde adrenalin uygulama yolu

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Dear Editor,

We read the article of Çakmakcı et al. (1) published in the final issue of your journal. The authors presented a pediatric case of anaphylaxis that developed secondary to midazolam administered for the objective of sedation before bone marrow aspiration and lumbar puncture. Based on this case presentation, we would like to mention the drugs that should be preferred for procedural sedation-analgesia in children and the important issues related to the route of administration of adrenaline in the treatment of anaphylaxis.

Administration of anxiolytic, analgesic, sedative, and amnestic drugs, which act by facilitating continuance of the respiratory and cardiovascular functions in interventions that cause pain and anxiety, is called procedural sedation-analgesia. There is no single ideal drug that is used for this objective in children. The type and time of the procedure to be performed, the child's age, the child's anxiety level before the procedure, medical history, and the physician's personal experience and preferences lead to the use of different drugs. The drugs that are most commonly used for procedural sedation-analgesia in children and their properties are briefly summarized below (2–4).

Chloral hydrate has sedative-hypnotic action only and no analgesic action. It is frequently used during imaging and electroencephalogram (EEG) investigations. Adverse effects including airway stenosis and respiratory depression may be observed, especially in children with a history of preterm delivery and/or in young infants.

Benzodiazepines have sedative, amnestic, anxiolytic, and hypnotic actions. In this drug group, midazolam is preferred over diazepam and lorazepam because of its rapid and short-lasting action. They need to be used frequently in combination with opioid group analgesic drugs in painful medical procedures because they do not have analgesic action. When used in combination with opioids, the risk of respiratory depression and apnea is greater.

Barbiturates: This group of drugs includes phenobarbital and thiopental. They have marked sedative, amnestic, and hypnotic actions depending on the dose. These properties are superior compared with benzodiazepines such as midazolam and chloral hydrate. They have no analgesic action. They are frequently preferred for diagnostic imaging. The most common adverse effects include respiratory depression and hypotension.

Etomidate: This drug has sedative and hypnotic characteristics and a rapid and short-lasting action. It has analgesic action. It should be kept in mind that it may lead to transient myoclonus and transient adrenal insufficiency in critically ill children, especially in patients with sepsis and septic shock.

Propofol: This drug has sedative, hypnotic, and amnestic characteristics, and a rapid and short-lasting action. It can be used alone for imaging procedures and in combination with analgesic drugs for painful medical procedures because it has no analgesic action. It may lead to respiratory depression and hypotension. It is contraindicated in individuals who have egg and soya allergy because of the risk for anaphylaxis.

Opioids: Among these drugs with predominant analgesic

characteristics, fentanyl is preferred over morphine because of its rapid and short-lasting action. They are frequently used in combination with midazolam during procedural sedation-analgesia because they have no sedative, amnestic, and anxiolytic action at low doses. Adverse effects include respiratory depression, nausea, vomiting, and chest rigidity, especially with high doses and rapid bolus injections.

Ketamine: Although its analgesic and amnestic actions are prominent, it also has sedative action at high doses. The adverse effect of respiratory depression is considerably rare and facilitates maintenance of airway protective reflexes. In addition, cardiovascular system depression can occur, albeit considerably rarely, and this may lead to hypertension and tachycardia. Owing to of all these characteristics, it has frequently been used alone or in combination with other sedative drugs including midazolam or propofol in procedural sedation-analgesia in children in recent years.

Dexmedetomidine: This drug, which has sedative, anxiolytic, and analgesic actions, has been used alone with a gradually increasing frequency in both painful medical procedures and in painless radiological imaging in recent years. However, one should be very careful in terms of adverse effects including bradycardia, hypotension with slow infusions, and hypertension with rapid administration.

Local anesthetics are locally administered in the region where the procedure is to be performed before wound repair, abscess drainage, foreign body removal, lumbar puncture, and central venous catheter placement. Injection of solutions containing lidocaine or prilocaine or gels containing a mixture of these two, may be used for this objective.

After mentioning all these drugs, we can conclude that sedative and anxiolytic drugs should be used for painless procedures including radiological imaging and EEG, and sedative, analgesic and amnestic (if possible) drugs should be used in combination for painful procedures including lumbar puncture and bone marrow aspiration, which were mentioned to have been performed in the relevant article by the authors in their case (1). The lack of use of analgesic drugs in painful procedures makes the performance of the procedure difficult by decreasing patient comfort and causes use of an increased dose of sedative drug because the patient will feel pain. Increasing the dose of sedative drugs increases the risk of respiratory and circulatory depression. Accordingly, we think that it was not appropriate for the authors to use midazolam alone, as mentioned in their article, because it has no analgesic properties (1). Midazolam should be used in association with analgesic drugs including fentanyl or ketamine before these procedures, which are considerably painful. In addition, we also think that ketamine could be used alone in this patient because its adverse effect of respiratory depression is negligible, besides having analgesic, sedative, and amnestic properties.

In the relevant article, it was stated that lumbar puncture and bone marrow aspiration had been performed seven times previously in this patient by administering midazolam (1). The authors did not discuss the fact that anaphylaxis did not develop after the previous administrations and developed after the eighth administration. We think that anaphylaxis in this patient might be related with different preservative substances contained in commercial preparations of midazolam.

In the treatment of anaphylaxis, it is recommended that 1/1000 adrenaline should be administered by the intramuscular route at a dose of 0.01 mg/kg (maximum dose: 0.5 mg). Intravenous bolus injection is never recommended except for cardiac arrest because of the risk for fatal arrhythmia, hypertension crises, severe tachycardia, and pulmonary edema (5). For all these reasons, we think that it was not appropriate for the authors to administer adrenaline by the intravenous route as mentioned in the relevant article because it carried considerable risk (1).

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Authors' Response

Dear Editor,

We read with interest the interpretations of O.Y. et al. related to our article on our pediatric case of anaphylaxis that developed in relation with midazolam in Pediatric Hematology and Oncology Ward,. However, we observed that the context and objective of our article were not understood. In our article, we aimed to address the risk of anaphylaxis with midazolam, which is commonly used outside the operation room, and therefore, we did not state the routine sedation-analgesia schema being applied in our hospital (1). Although sedation-analgesia used in the childhood age group is outside the context of our article, ketamine could not be administered in our patient because his general status deteriorated following administration of midazolam. Use of midazolam and ketamine in painful procedural sedation-analgesia in children is already recommended and well known (2). We administered intravenous adrenaline because our patient developed bradycardia, his consciousness deteriorated, and a severe picture of anaphylaxis developed. Although intravenous adrenaline can be administered in cases of severe anaphylaxis, we are also in favor of primarily preferring intramuscular adrenaline in anaphylaxis because of its cardiac adverse effects (3, 4). The finding that anaphylaxis did not develop with previous administrations of midazolam in our patient may be explained by the possibility that previous exposures caused sensitivity and anaphylaxis developed with subsequent administration (5).

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