The alternative of oral sedation for pediatric dental care

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In pediatric dentistry, chloral hydrate is habitually selected for sedation of uncooperative children. Although chloral hydrate has been used for decades, various adverse effects are reported and necessity for new alternative drugs has increased. Dexmedetomidine was approved by FDA for sedation at intensive care units (ICU) in 1999. Compared to conventional sedative drugs, dexmedetomidine has not only analgesic and sedative effects but also it barely suppresses the respiratory system. Due to these characteristics, dexmedetomidine is known as safe sedative drug for children and elderly patients. Furthermore, approved by KFDA in 2010 in Korea, the frequency of sedation using dexmedetomidine is increasing. However, due to its intravenous administration method, it was difficult to apply in pediatric dentistry. Recently, intranasal administration method was introduced which might be a new possible alternative of oral sedation.

In this study, we compare the mechanisms, pros and cons of chloral hydrate and dexmedetomidine, introducing new possibilities.

Key Words: Chloral hydrate; Dexmedetomidine; Oral Sedation; Sedation

INTRODUCTION

Visiting dental clinic is scary for young children. This means that sedation could be helpful for them, and many efforts have been made to this day. Oral sedation using chloral hydrate is universally used in pediatric dentistry. The main reasons were long time experience, easy application method and decreased rejection of children and their parents [1]. However, various adverse effects have been reported [2] and social attitudes have changed. This increased the necessity for development of more comfortable and safer drug.

The purpose of the present study is to identify the adverse effects of chloral hydrate and to introduce the recent advances of dexmedetomidine as an alternative sedative drug.

CHLORAL HYDRATE (Pocral®, Hanlim Pharmaceuticals Inc., Seoul, Korea)

Chloral hydrate, synthesized by German chemist Justus von Liebig, was clinically used from 1890 [3]. Chloral hydrate is the most frequently prescribed drug for children and 50-75 mg/kg as sleep inducing dosage without severe adverse effects on respiratory and cardiovascular system is recommended [6]. In 1991, Greenberg et al. [7] reported, administration of 80-100 mg/kg resulted in adverse effects as nausea (14 patients), paradoxical agitation (7 patients), symptoms of respiratory system (4 patients) in 23 out of 295 children (average age; 2.2
y). On the other hand, 40-70 mg/kg was administered to 111 children (average age; 1.9 y) with mild brain, liver and kidney diseases. Despite the mild systemic diseases, no adverse effects associated with chloral hydrate were observed. In another study, use of 75-100 mg/kg chloral hydrate showed decrease of oxygen saturation in 9% of patients [8]. Considering these results, following the recommended dosage is regarded as an important factor for safety.

However, trichloroethylene, metabolite of chloral hydrate, was reported as a potential factor of carcinogenicity [9]. In addition, on drugs which have been practically used without approvals, the Food and Drug Administration (FDA) forced the pharmaceutical companies to receive approval process in June 2006, and prohibited the merchandising of drugs without approvals [10]. Therefore, pharmaceutical companies in America determined production suspension of chloral hydrate in June 2012.

Nevertheless, chloral hydrate is clinically used in several countries including Republic of Korea. It is being avoided by clinicians because of adverse effects such as difficulty of administration due to bitterness, nausea, gag reflex, delusion, severe anxiety and long duration, unpredictable effects [11].

**DEXMEDETOMIDINE**

1. Dexmedetomidine hydrochloride (Orion Pharma, Turku, Finland)

Dexmedetomidine was approved by FDA for sedation of adult patients at intensive care unit (ICU) at 24th, December, 1999. In Korea, it is used since the approval by Korea Food & Drug Administration on June 2010 [12].

Benzodiazepine and propofol, which have been used frequently, mainly affect gamma-aminobutyric acid (GABA) [13,14]. On the other hand, dexmedetomidine is a selective α2-adrenergic agonist and induces sedative effect by affecting α2-adrenergic receptor of central nervous system and cerebrospinal system [15,16]. The half-life is 2-3 hours and in case of condition sensitive half-life, 4 minutes on 10 minutes of continuous administration and 4 hours on 8 hours of continuous administration [17]. This short half-life is an advantage that makes it available for intravenous administration. Dexmedetomidine is rapidly distributed, mainly metabolized at liver, excreted through urine and stool [17].

Dexmedetomidine maintains airway, spontaneous respiration during sedative action and reactivity to CO2 increase and hypoxia, reduces dose of anesthetic drug and inhibits tachycardia [18]. Due to low effect on respiratory function, dexmedetomidine could be very valuable for sedations of children and elderly with weak pulmonary function [19,20]. In 2001, Maze et al, [21] reported decrease in dosage of dexmedetomidine is necessary for patients with liver disease, while it is not necessary for patients with kidney disease. In 2014, Choi et al, [22] reported no difference in complications between the younger group (average age; 56 years old) and the older group (average age; 78 years old) in a study on 50 patients (age; 20-95 y). Tobias et al, [23] reported safe usage of dexmedetomidine in infants and children in 2002. Bradycardia and hypertension was reported in 5-16% of patients associated with dosage of dexmedetomidine. No additional drug treatment for hypertension was necessary and no adverse effect was found [24,25].

Despite many advantages of dexmedetomidine, intravenous administration is a big obstacle for pediatric dentistry.

In the aspect of bioavailability, administration through nasal cavity and oral mucosa showed 82% level compared to intravenous administration, reaching the highest blood concentration within 1.5 hours [26]. In the same study, however, oral administration showed 16% bioavailability due to first-pass effect. In 2007, Yuen et al, [27] reported satisfactory sedative effect of dexmedetomidine by intranasal administration. Therefore, clinical application of dexmedetomidine by intranasal spray is considered as possible alternative of noninvasive sedation for pediatric dental care.
CONCLUSION

General methods for sedation in dentistry are oral administration of antianxiety drugs, N₂O/O₂ inhalation, intravenous administration, analgesic administration. In a sense, usage of various drugs and sedation in dentistry implies deficiency of large sized, well controlled comparative studies about different sedations. The first controversy about oral sedation is safety of Pocral®. Using Pocral® is gradually inhibited in America due to adverse effect on liver function of children. The second controversy is use of benzodiazepine. Although single dose by oral and sublingual administration of triazolam approved by FDA for treatment of insomnia showed effective and safe sedation on patients with moderate anxiety, incremental dose administration and occasional compound use with other sedatives are becoming general.

Recent change was made in sedation for children by utilizing of dexmedetomidine using other methods than intravenous administration. When using intravenous administration, such drug has rapid onset and short duration and often requires infusion pump for control and maintenance of drug effect. Attempts are generally made for intravenous sedation, however, intranasal dexmedetomidine sedation can be useful in terms of accessibility and efficiency. Nevertheless, intranasal dexmedetomidine sedation is likely to induce comparatively deep sedation. Therefore, dental team should be equipped with proper monitoring devices (blood pressure, pulse, respiration) and emergency medical devices, and should be fully aware of emergency situations and skilled in airway management including mask ventilation. If we follow the guidelines for sedation and are prepared for deeper sedation, intranasal dexmedetomidine spray sedation will lead to satisfactory dental treatment to both dentist and parents of patients by its efficiency and safety about sedation.

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