

# Comparison of Behavioral Response between Intranasal and Submucosal Midazolam Administration

Yunhee Kim, Sanghyuk Jung\*, Kwangwoo Baek

*Department of Pediatric Dentistry, Ewha Womans University Graduate School of Clinical Dentistry,*

*\*Department of Preventive Medicine, College of Medicine, Ewha Womans University, Seoul, Korea*

## Abstract

**Purpose.** The objective of this study was to evaluate the behavioral response and assess the effectiveness of additional intranasal (IN) and submucosal (SM) administration of midazolam during pediatric sedation for dental procedure.

**Material and methods.** Thirty-three cases of healthy (ASA I), uncooperative children aged from 24 to 72 month old at pediatric dental clinic of Ewha Womans University Hospital were selected for this study. Children received oral chloral hydrate 50 mg/kg with hydroxyzine 1.0 mg/kg. After waiting for 45 minutes, midazolam 0.2 mg/kg was administered via IN route and via SM route randomly maintaining 50% of N<sub>2</sub>O. A pulse oximeter and a capnograph were used for measuring vital signs (SpO<sub>2</sub>, PR, RR, EtCO<sub>2</sub>) throughout the sedation. Behavioral response was evaluated as Quiet (Q), Crying (C), Movement (M) or Struggling (S) in every 2 minutes for 40 minutes.

**Results.** There were also no statistically significant differences in vital signs of the two groups. The behavioral response for the first ten minutes during sedation was a statistically significant difference ( $P < 0.05$ ) between the two groups. After the first ten minutes, it was revealed that there was no significant difference.

**Conclusion.** This study demonstrated that the addition of IN midazolam to the combination of oral chloral hydrate with hydroxyzine and nitrous oxide/oxygen inhalation is as safe and effective as that of SM midazolam in pediatric sedation for dental procedure.

**Key words :** Sedation, Submucosal midazolam, Intranasal midazolam, Chloral hydrate

## I . INTRODUCTION

It can be very challenging for pediatric dentists to explore the ideal sedatives and regimens to treat the young uncooperative patients more safely and effectively in dental clinic. Various drug regimens and routes of delivery have been introduced to sedate pe-

diatric patients in last three decades<sup>1-4</sup>.

Combination of sedative agents has been used to sedate uncooperative children in pediatric dentistry<sup>5,6</sup>. In Houpt's survey<sup>7</sup>, chloral hydrate (CH) with hydroxyzine (H), and nitrous oxide/oxygen was one of the most frequently used combination for sedation in pediatric dentistry. Despite its popu-

교신저자 : 백 광 우

서울시 양천구 목동 911-1번지 / 이화여자대학교 목동병원 소아치과학교실 / Tel: 02-2650-2660 / E-mail: pedobaek@ewha.ac.kr  
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larity, CH is not the most ideal drug in pediatric sedation. This agent is a sedative hypnotic with variable absorption and wide range of effectiveness<sup>6,8</sup>. Besides, it may cause gastric irritation and respiratory depression<sup>8</sup>. There have been many studies about the effectiveness of CH in pediatric dentistry. Nathan<sup>6</sup> reported success rates ranged from 18 to 90% according to the variable dosage of CH. Some dentists use the CH exceeding the manufacturer's recommended dose (MRD) of 50 mg/kg to raise the success rate<sup>7</sup>. But exceeding MRD (50 mg/kg) leads to serious side effect, such as prolonged patient recovery, central nerve system (CNS) depression and respiratory depression. Recently, the trend has turned to combine CH, not exceeding MRD (50 mg/kg), with different sedative agent such as midazolam, a short acting benzodiazepine<sup>6</sup>.

Midazolam is a water-soluble benzodiazepine having hypnotic, anxiolytic, muscle-relaxant, anticonvulsant, and anterograde amnesic effects<sup>9,10</sup>. The safety and efficacy of midazolam in infants and children has been reported in several literatures<sup>11,12</sup>. Midazolam can be administered through intramuscular, intravenous, rectal, intranasal (IN), submucosal (SM) and oral routes<sup>9-13</sup>.

In 2004, Myers *et al.*<sup>14</sup> reported that SM midazolam combined with oral CH improved the quality of sedation without compromising safety. Other recent studies demonstrated that SM midazolam combined with oral CH, H and N<sub>2</sub>O improved the quality of sedation and the vomiting response<sup>15,16</sup>. In case CH and H orally administrated can not reach adequate sedation, midazolam and N<sub>2</sub>O as an addition can be used occasionally<sup>17</sup>.

There have been many studies to investigate the sedative effect of midazolam in pediatric dentistry<sup>9-14</sup>. Among multiple routes of midazolam, IN and SM routes have the potential advantage of rapid absorption without a hepatic first pass effect<sup>18,19</sup>. Midazolam via IN route can be absorbed into the brain and cerebrospinal fluid directly through the cribriform plate<sup>19</sup>. Because SM route have the rich blood supplies of the oral mucosa, absorption of midazolam is directly into the systemic circulation<sup>18</sup>. For this reason, the bioavailability in children following IN midazolam is 78% with peak plasma concentrations at 10 min<sup>20</sup>. It can be comparable with

74.5% following buccal midazolam<sup>21</sup>. It was suggested that IN route is similar to the SM route according to several studies<sup>22,23</sup>.

Based on the above, the purpose of this study was to:

1. evaluate the safety and efficacy of additionally midazolam administration via SM route and IN route when used for pediatric sedation in dental procedure;
2. estimate the onset time and working time of the two groups (IN midazolam and SM midazolam);
3. compare the vital sign and behavior response between the two groups.

## II . METHODS

### A. Subject selection

All subjects were selected from new patients examined at the Department of Pediatric Dentistry at Ewha Womans University Hospital. Upon selecting candidates for this study, the procedures, possible discomforts and benefits were fully explained to the parents or legal guardians, and their informed consents were obtained before undertaking any procedure. Total 33 (20 male, 13 female) pediatric patients were included in this pilot study.

The followings were inclusion criteria:

1. young children between 24 and 72 months old;
2. healthy subjects without special physical/psychological needs (American Society of Anesthesiologists classification I);
3. more than 2 teeth of extractions or restorations, including amalgam and/or composite restorations, pulpotomy procedures, and stainless steel crowns under local anesthesia;
4. subjects with fearful or refractory behavior as documented by the Frankl Behavior Rating Scale<sup>24</sup>.

A subject reported to have an upper respiratory infection preceding the appointment was excluded from this study.

### B. Study design

A randomized design was used in this study. The principal investigator, who was well aware of the in-

clusion criteria, selected subjects and assigned them randomly into IN group or SM group. After a single investigator performed IN or SM administration on all subjects, two dental operators, who had no information of midazolam route, performed dental treatments under sedation based on American Academy of Pediatric Dentistry (AAPD) guideline<sup>25</sup>.

All subjects received 50 mg/kg dose of oral CH, not exceeding 1,000 mg, with H, and 50% nitrous oxide/oxygen throughout the whole sedation period. All of sedation procedures were recorded on videotapes, and reviewed to analyze behavior response later.

Vital signs monitored by using a pulse oximeter and a capnograph during the whole procedure. They were observed continuously and recorded at 2 minute intervals for 40 minutes. Respiration rate (RR) and end-tidal carbon dioxide (EtCO<sub>2</sub>) were collected for evaluating airway patency and respiratory depression. When the subjects were crying, moving and struggling, RR and EtCO<sub>2</sub> were unreliably recorded because of movement or dislocation of the nasal hood. Therefore, these values were eliminated from the data set.

### C. Procedure

At the sedation appointment, the principal investigator checked each subject's medical history, nothing by mouth (NPO) status and symptoms/signs such as runny nose, or cough. All subjects were evaluated for SpO<sub>2</sub> and PR before administering the sedative agents.

Subjects were randomly assigned to receive SM or IN midazolam administration. Sedation protocol was same for each subject. They received oral CH (Pocral<sup>®</sup>, Hanlim Pharm. Corp, Seoul, Korea) 50 mg/kg and H (Ucerax<sup>®</sup>, Hanlim Pharm. Corp, Seoul, Korea) 1 mg/kg. If the patient refused to take the medicine, the investigator used a needless disposable syringe to deposit the medicine into the buccal vestibule slowly.

The patients were brought to the operative room by their parents or legal guardians on 45 minutes after receiving medication. All monitors were affixed and a videotape recording was started when the subjects were carried into the operatory room. Nitrous oxide/oxygen was delivered from 0% to 50% increasing gradually during first 3 minutes through a full

mask. The patients were secured in a papoose board (Olympic Medical Corp, Seattle, Wash, USA) during sedation. After administrating nitrous oxide/oxygen for 3 minutes, topical anesthesia and local anesthesia were delivered and then midazolam 0.2 mg/kg (Dormicum<sup>®</sup> vial: Bukwang Pharm. Corp, Seoul, Korea) was administrated submucosally on maxillary non-working side of buccal vestibule with a 1-cc tuberculin syringe by the investigator in SM group. In the other group, Midazolam (Dormicum<sup>®</sup> vial: Bukwang Pharm. Corp, Seoul, Korea) 0.2 mg/kg was administered using an atomizer (MAD 300 Mucosal Atomizer, Wolfe Tory Medical, Inc, Salt Lake City, Utah, USA) attached to 1-cc tuberculin syringe. Flumazenil (0.01 mg/kg, IV dose), a reversal agent, was always prepared in case of emergency.

When the patient was fully sedated, the nasal hood was replaced with the full mask. All patients were maintained at 50% nitrous oxide/oxygen at 3 to 5 (L/min) and received 2% lidocaine (1:100,000 epinephrine) in a range of 0.9 to 3.6 cc during treatment not exceeding 3.6 cc. The exact time of midazolam administration and the treatment beginning were recorded. Vital signs and behavior evaluation were also recorded in every 2 minutes throughout the whole procedure.

### D. Data collection and analysis

Gender, age, and weight were checked and induction time, maximum working time, and vital signs were recorded for 40 minutes. Chi-square test and t-test were for statistical test between IN and SM groups.

Each sedation was fixed around 40 minutes which was adequate time to treat at least two quadrants. All data were collected up to 40 minutes from the beginning dental treatment. A single pediatric dentist, who was blinded to drug route, estimated behavior responses by reviewing the video recordings of all sedation procedure. The time of the midazolam administration was recorded and behavior evaluation was initiated from the start of dental treatment at 2 minute intervals. The behavioral response was assessed with using a simple rate described as Q=quiet, no movement; C=crying, no struggling; M=movement, no crying; or S=crying and strug-

gling. In every 10 minutes, the percentage of behavior ratings as Q, C, M, and S was analyzed in the Chi-square test.

All results were analyzed by using SPSS (version 11.0.1, SPSS Inc, USA) statistics program. The statistical difference was judged significant at the  $P < 0.05$ .

### III. RESULTS

Thirty-three subjects participated in this study. The population of sample was 20 males and 13 females, whose aging range was from 25 to 72 months old (mean  $46 \pm 13$ ). The weight of patients was

ranged from 11 to 23 kg (mean  $16 \pm 3$ ). Demographic and weight distribution of IN and SM groups are demonstrated in Table 1. There were no significant differences with respect to gender, age, weight between IN and SM groups ( $P < 0.05$ )(Table 1).

Induction time was recorded as the duration of time from administering the midazolam to displaying calming effect. Mean induction time of IN and SM routes were  $286.3 \pm 74.2$  seconds and  $130.1 \pm 74.0$  seconds respectively. Although these values were not statistically significant, mean induction time of SM group was twice as fast as that of IN group. Mean working time of IN and SM routes were  $56.3 \pm 12.0$  minutes and  $56.8 \pm 13.1$  minutes respectively. These

**Table 1.** Demographic Data

	IN	SM	P-value
Age (months)	$46.5 \pm 14.6$	$44.8 \pm 12.0$	0.295
Weight (kg)	$15.3 \pm 2.1$	$17.3 \pm 3.0$	0.127
Gender (Male/Female)	10/6	10/7	0.829

The values are mean  $\pm$  SD

IN, intranasal spray; SM, submucosal injection

**Table 2.** Distribution of Induction Time and Working Time between IN group and SM group

	IN	SM	P-value
induction time (seconds)	$286.3 \pm 74.2$	$130.1 \pm 74.0$	0.620
working time (minutes)	$56.3 \pm 12.0$	$56.8 \pm 13.1$	0.825

The values are mean  $\pm$  SD

IN, intranasal spray; SM, submucosal injection

**Table 3.** Distribution of Percutaneous Oxygen Saturation (SpO<sub>2</sub>), Pulse Rate (PR), End-tidal carbon dioxide (EtCO<sub>2</sub>), and Respiratory rate (RR) between IN group and SM group

	IN	SM	P-value
SpO <sub>2</sub> (%)	$99.3 \pm 0.3$	$99.0 \pm 0.6$	0.170
PR (beats/min)	$107.0 \pm 10.1$	$108.3 \pm 14.6$	0.451
EtCO <sub>2</sub> (mmHg)	$32.4 \pm 6.7$	$30.4 \pm 5.4$	0.105
RR (breaths/min)	$25.5 \pm 4.7$	$26.9 \pm 4.3$	0.435

The values are mean  $\pm$  SD

IN, intranasal spray; SM, submucosal injection

SpO<sub>2</sub> : percutaneous oxygen saturation

PR : pulse rate

EtCO<sub>2</sub> : end-tidal carbon dioxide

RR : respiratory rate

**Table 4.** Distribution of Behavioral responses throughout Treatment Procedure between IN group and SM group

		Q	M	C	S	P-value
<10 min	IN	62(77.5)	18(22)	0(0)	0(0)	0.010*
	SM	60(70.6)	14(16.5)	5(5.9)	6(7.1)	
10 to 20 min	IN	70(87.5)	9(11.3)	0(0)	1(1.3)	0.195
	SM	76(89.4)	6(7.1)	3(3.5)	0(0)	
20 to 30 min	IN	66(82.5)	11(13.8)	0(0)	3(3.8)	0.197
	SM	75(88.2)	5(5.9)	2(2.4)	3(3.5)	
30 to 40 min	IN	68(85.0)	7(8.8)	1(1.3)	4(5.0)	0.766
	SM	67(78.8)	11(12.9)	1(1.2)	6(7.1)	

Number (%)

IN, intranasal spray; SM, submucosal injection

Q=quiet, no movement; M=movement, no crying; C=crying, no struggling; S=crying and struggling.

\* $P < 0.05$

differences were not statistically significant.

An Independent t-test showed no significant differences in physiologic parameters (SpO<sub>2</sub>, PR, EtCO<sub>2</sub>, RR) recorded at 2 minutes intervals between IN and SM groups (Table 3). There was no serious complication or adverse outcome during sedation sessions. All episodes of oxygen desaturation (below 95 of pulse oximetry levels) were transient and corrected immediately by head repositioning and mouth suction. The pulse rate was increased during local anesthesia, or placement of rubber dam, but quickly decreased into normal range after disappearance of stimuli.

Behavioral responses under sedation were rated in every 2 minutes from the start of the dental procedure for 40 minutes. The subject's behavior was assessed by using a simple category classified as Q, C, M and S to compare the efficacy between IN and SM group. Behavior ratings recorded were respectively converted to percentage at 10 minute intervals for the total of 33 observations (Table 4). A Chi-square test was used to evaluate the significant difference. The behavioral response for the first ten minutes showed a statistically significant difference ( $P < 0.05$ ) between two groups, but it was revealed that there was no significant differences between two groups from 10 to 40 minutes. IN group displayed better behavioral response in comparison to SM group for first 10 minutes (Table 4).

#### IV. DISCUSSION

The combination of sedatives and specific selection of administration routes may maximize effect of drugs, increase safety of patients, and maximize patient acceptability<sup>26</sup>. In pediatric dentistry, the combination of sedatives has been investigated for raising the success rate and achieving the safety of patients under sedation<sup>27</sup>.

Cote *et al.*<sup>28</sup> investigated adverse events in pediatric sedation and concluded that these were associated with drug overdose, drug combination and interactions, three or more sedative agents, and administration of N<sub>2</sub>O in combination with other sedatives. Therefore, it is necessary to find the effective combination of sedatives for the safety of a patient.

Previous studies using CH with H and N<sub>2</sub>O showed 70% of success rates<sup>5,29</sup>. Midazolam has been used in pediatric dentistry because of rapid onset, faster recovery, and amnestic effects<sup>9,10</sup>. Recent studies investigated combining CH with different sedative agents such as midazolam and showed many potential positive interactions<sup>14-16</sup>. These studies demonstrated that adding SM midazolam improved the quality of sedation without compromising safety, not exceeding MRD (50 mg/kg) of CH<sup>14-16</sup>. Furthermore, clinical advantages of SM midazolam are permitting sufficient duration to successfully complete operation, rapid onset and absorption, possible titration, no

need of patient's cooperation, and convenience to use for a dentist<sup>15,16</sup>.

However, disadvantages of the SM injection include the needs of an additional injection, the invasive technique, the discomfort due to needle, and adverse reaction at the injection site<sup>30</sup>. Alfonzo-Echeverri *et al.*<sup>31</sup> discouraged the use of the SM midazolam due to prolonged pain at the injection site. Besides, small amount of vasoconstrictor for SM administration may impose adverse effect on the uptake of midazolam<sup>30</sup>. Recent studies have demonstrated several positive effects of IN midazolam<sup>9-13</sup>. Therefore, IN route of midazolam may be considered as a suitable alternative to SM route to overcome its disadvantages.

In this study, there were no significant differences in mean induction time and maximum working time between IN and SM group. According to Fukuta *et al.*<sup>32</sup>, the initial sedative effect of midazolam via IN route was seen within 5 to 10 minutes. Wilton *et al.*<sup>11</sup> noted a calming effect within 5 min after IN midazolam and this became significant within 10 min. In this study, mean induction time of IN and SM routes were  $286.3 \pm 74.2$  seconds and  $130.1 \pm 74.0$  seconds (Table 2). Overall induction time of both groups is faster than that of previous studies<sup>11,32</sup>. It could be explained for the result of synergic effect of midazolam with other sedative agents.

The data of this study showed that SM midazolam led to twice faster induction time and calming effect, but there was no significant difference. The exact mechanism of IN drug absorption is still not clear, but nasal mucosa is the only direct link to the CNS in the body<sup>9,33</sup>. On the other hand, SM route absorption is directly into the systemic circulation<sup>18</sup>. Although both routes have the same advantage-avoiding hepatic first-pass-effect, their routes for absorption would be different<sup>18,19</sup>. In addition, they will act differently on calming effect related to different agitated status because IN administration may cause nasal burning sensation and general discomfort, which are different from pain of SM injection<sup>4,34</sup>.

Kupietzky and Houpt<sup>9</sup> stated that, in pediatric dentistry, a longer period of sedation was usually required and perhaps the combination of more than one dose would be necessary because of the short duration of midazolam. Lee-Kim *et al.*<sup>35</sup> found that IN midazolam with nitrous oxide/oxygen led to faster

onset time, and somewhat shorter working time. However, this is not sufficient for children to need extensive dental treatment at several times. On the other hand, combination of drugs in this can offer sufficient working time to enable extensive operation in both groups without compromising safety.

There were no significant differences in behavioral responses and vital signs (SpO<sub>2</sub>, PR, RR, EtCO<sub>2</sub>) between two groups. As no significant adverse reactions occurred in any of the sessions, vital signs were maintained within the normal ranges. During injection and increased struggling behavior, PR showed a little increase but sooner fell down within normal ranges. The false reading of RR and EtCO<sub>2</sub> was related to patients' crying and moving while they were holding their breath. All values during these episodes were eliminated from the data set.

All studies of midazolam for children showed that it is relatively safe during the sedation, regardless of its administration route<sup>9-13</sup>. But, when two or more drugs are combined with midazolam, there could be negative synergistic effect such as respiratory depression. Therefore, children must be supervised carefully and a reversal agent, flumazenil, should be available near the operator throughout the whole sedation.

There was a significant difference in behavioral response between IN and SM groups for the first 10 minutes. However, the rest of other sedation periods showed no significant differences in efficacy of behavior. This result would be related to similar bioavailability and peak plasma concentrations of two groups<sup>20,21</sup>. Also, this behavior assessment includes the response from all stimuli such as local injection and rubber dam application. Subjects under IN route, however, showed better behavior for the first 10 minutes of procedures including irritable local injection and rubber dam placement. This can be explained that subjects with IN route showed proper responses from all stimuli, which the operator can proceed the dental treatment. IN group can lead to more adequate sedation for first 10 minutes.

For a possible explanation to the difference in the first 10 minutes described the above, Schwagmeier *et al.*<sup>21</sup> reported that the time to maximum plasma concentration (t<sub>max</sub>) was 30 min following buccal midazolam which is markedly prolonged in comparison to

a tmax of 10 min following IN midazolam. But in that study, buccal midazolam was absorbed not through SM injection but through transmucosal absorption<sup>21)</sup>. Thus tmax of SM injection is probably speculated faster than that of Schwagmeier *et al.*<sup>21)</sup>'s study, 30 minutes, but slower than that of IN route, 10 minutes. Therefore, IN group can reach proper sedation level faster than SM group.

Another possible explanation would be related to obesity; children in IN group (46.5 months old and 15.3 kg) are thinner than those in SM group (44.8 months old and 17.3 kg) respectively. Variable pharmacokinetics deviations of the drugs are associated with obesity<sup>36,37)</sup>. Baker and Yagiela<sup>38)</sup> suggested that lipophilic drugs including most sedatives (e.g., midazolam) act differently in peak blood concentrations of obese patients when dosed on the lean body mass (LBM) unlike hydrophilic drugs. Further studies are required to examine these hypotheses.

Myers *et al.*<sup>14)</sup> have demonstrated that the adding of SM midazolam (0.2 mg/kg) in sedation using the oral CH (50 mg/kg) with 50% nitrous oxide is safe and effective combination, and this would decrease the risk of oversedating children by initially given higher dosage of oral CH. Because oral CH of 50 mg/kg often leads to undersedate the children, by adding SM or IN midazolam in the beginning or middle of dental treatment, the sedation was completed safely and successfully<sup>39)</sup>. Besides its sedative potency, midazolam has the advantage of anterograde amnesia, which may positively effect on future dental treatment or recall visit<sup>13)</sup>.

Two patients in IN group and three in SM group showed vomiting during the sedation. After mouth suction, the procedure was continued without complications or adverse outcome. Unlike other studies, high prevalence (15%) of vomiting in this study was probably due to the reason of the small sample size<sup>5,14)</sup>. Some authors have reported that the IN route required less patient cooperation and it was a convenient, non-invasive, and painless technique<sup>9,10)</sup>. In this study, parents or guardians can accept this technique more easily. But it is impossible to estimate how much amount of sedatives was directly absorbed by the nasal mucosa or swallowed by the patients. And the absorption of midazolam could be influenced by nasal mucosa condition. It is very impor-

tant to optimize IN administration by slow and careful delivery to avoid swallowing.

The possible limitations of this study are that:

1. two operators showed slight difference in working time and procedure;
2. a single evaluator could have subjective ratings of behavior.

Future researches should consider randomized double-blind cross design. This study did not investigate closely about paradoxical reaction, but this reaction was observed in 3 of the 33 cases, two in IN group and one in SM group. More research will be required thereafter about the paradoxical reaction, recovery time, post-operative behavior after adding of midazolam.

## V. CONCLUSION

This study demonstrated that adding of IN midazolam to the combination of oral CH with H and 50% nitrous oxide inhalation is as safe and effective as that of SM midazolam in sedation for uncooperative children.

1. Mean SpO<sub>2</sub>, PR, EtCO<sub>2</sub>, RR were maintained within the normal range for both groups throughout the procedures.
2. Overall behavior under IN and SM was similar pattern. However, IN group displayed better behavioral response in comparison to SM group for first 10 minutes.
3. The advantage of IN midazolam is that it is non-invasive and relatively painless, while it also contains the advantage of SM midazolam - rapid onset and absorption, possible titration, and no need of patient's cooperation.
4. This IN route of administration may offer a suitable alternative to SM route which is invasive.

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국문초록

소아 진정 치료 시 구강 점막 하와 비점막  
Midazolam 투여의 행동 반응 비교

김윤희 · 정상혁\* · 백광우

이화여자대학교 목동병원 소아치과학교실, \*의과대학 예방의학교실

진정법을 이용한 소아환자의 치과치료 시 chloral hydrate와 hydroxyzine을 복용 후 추가로 midazolam을 비점막내로 분무하는 것과 구강 점막 하로 주사했을 때 행동 반응과 진정 효과에 대해 비교하고자 하였다.

미국 마취과학회 신체등급 I급 (ASA I)이며, 협조가 안 되는 24-72 개월 소아 환자 중 진정법을 통해 2개 치아 이상의 보존 치료 및 발치 치료를 받은 33명을 대상으로 하였다. 모든 환자는 chloral hydrate 50 mg/kg 와 hydroxyzine 1 mg/kg 복용하였다. 45분 후 한 군은 비강내로 midazolam 0.2 mg/kg 을 추가 투여하였고 다른 군은 구강 점막 하 midazolam 0.2 mg/kg 을 주사하였다. 치료하는 동안 두 군 모두 50 % nitrous oxide 를 유지하였다. 맥박 산소 측정기와 호기말 이산화탄소 분압 측정기를 이용하여 산소 포화도, 맥박수, 호흡수, 호기말 이산화탄소 분압을 기록하였다. 행동 반응은 Quiet(Q), Crying(C), Movement(M) 그리고 Struggling(S)를 이용하여 총 40분 동안 매 2분마다 기록하고 모든 진정 치료 과정은 비디오로 촬영하였다. 모든 자료는 chi-square test와 two sample independent t-test를 사용하여 분석하였다.

두 군 간의 평균 도입 시간과 최대 치료 시간은 통계학적으로 유의한 차이가 없었다. 또한 활력 생징후도 모두 정상 범위이며 두 군 사이에 통계학적으로 유의한 차이가 없었다. 행동 반응 비교에서는 치료 시작 10분 동안 비강내 투여 군이 점막 하 투여 군보다 개선된 행동 반응을 보였다(P<0.05). 치료 시작 10분 이후에는 두 군사이의 행동 반응에서 유의한 차이가 없었다.

이 연구는 chloral hydrate 와 hydroxyzine 복용 후 nitrous oxide 50%로 유지하는 진정법에 비강내로 midazolam 을 추가 투여하는 것은 점막 하로 추가 투여와 유사한 진정 효과를 가진다. 또한 비강내 midazolam 추가 투여하는 것은 구강 점막 하로 추가 투여의 장점을 가지면서도 비침습적이고 상대적으로 통증이 적다는 이점이 있다. 그러므로 비강내 midazolam 추가 투여는 침습적인 구강 점막 하 추가 투여를 대체할 만한 방법이다.

**주요어** : 진정법, 점막하 미다졸람, 비강내 미다졸람, 크로랄 하이드레이트