CHAPTER 2

REVIEW OF THE LITERATURE

The review is divided into five parts as follows:

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2.1 Nitrous oxide usage in dentistry

Pain and anxiety from dental operation are the reasons that patients avoid a regular dental treatment causing poor oral hygiene and other problems of oral health [13]. Especially in children, they sometimes are unable to control their fear and anxiety and usually present those feelings by crying, screaming, kicking or showing any uncooperative behaviors [14].

Uncooperative behavior is managed by both non-pharmacologic and pharmacologic methods. Non-pharmacological behavior management includes verbal and nonverbal communications such as tell-show-do, positive reinforcement, distraction, voice control, active or passive restraint, and hand over mouth exercise (HOME). Dentist should select technique appropriate for each patient. However, those techniques may not succeed in very young or disability patients so pharmacological behavior managements such as N_2O/O_2 inhalation sedation, oral sedation and general anesthesia may be preferred in these cases [15-17]. N_2O/O_2 inhalation sedation has been a technique used to manage dental anxiety for more than 150 years since mid 1800s [3, 18]. Up to this date, N_2O/O_2 is still currently used to control patient's behavior in many countries. There has been an increased use of sedation from a national survey of the members of the American Academy of Pediatric Dentistry (AAPD) in 2000 compared with previous studies in 1985, 1991, and 1995 [15]. That study reported that 47% of surveyed practitioners in the United States of America (USA) used N_2O/O_2 alone as a sedation tool in their practices [15]. From a survey of the members of the AAPD in 2004, N_2O/O_2 inhalation sedation was used around 86% to manage behavior of 3-12 years old patients [17]. However, N_2O/O_2 inhalation sedation is not commonly used in some countries such as Jordan because dentists need more practical training and N_2O/O_2 equipments in that country [19]. However, it may be generally assumed that N_2O/O_2 technique is more acceptable by parents compared to other technique in managing behavior of their children [18].

Eaton et al. [16] surveyed parental attitudes toward behavior management techniques in 2003 and reported that N_2O/O_2 and tell-show-do techniques were the most parents' acceptable behavior management technique because they both are safe and did not seem to be aggressive. Similar result were also reported by Lawrence et al.[20]. Therefore, it may be concluded that N_2O/O_2 is a routine component of dental procedure in the USA [18].

2.2 Properties of nitrous oxide

N_2O is an inhalation agent that is colorless, odorless or sweet smell, and nonirritating to the tissue. It is nonflammable but support combustion [6, 9, 18, 21]. N_2O has the boiling point at -88.5 °C thus it is a gas at room temperature and converts to liquid when it is compressed into the tank [21, 22].

N_2O has very low solubility in blood compared with other gases. Blood-gas partition coefficient of N_2O is 0.47 and N_2O does not combine with hemoglobin so N_2O can enter brain and reach equilibration rapidly resulting in rapid onset within 3-5 minutes after administration [6, 21]. Partition coefficient in tissue, muscles and fat is also very low so N_2O is eliminated rapidly and does not remained in the body [21].

Blood-gas partition coefficient of N_2O is 30 times greater than nitrogen (N_2) so N_2O enter the body space and replace N_2 faster than N_2 can exit that space. As a result, it can increase volume and pressure of body spaces such as bowel, pneumothorax, sinus, eye and middle ear [6, 21].

The potency of N_2O is assessed from Minimum Alveolar Concentration (MAC). Becker and Rosenburg [6] described that MAC is the percent or concentration of the gas at 1 atmosphere that renders 50% of patients unresponsive to a surgical stimulus.

From Table 1, MAC of N_2O is 104-105 making it low potency when compared with other inhalation agents. When single used as inhalation sedation, N_2O cannot induce patient to the general anesthetic level [6, 21].

Table 1 N_2O and other inhalation anesthetic agents [6]

Agent	MAC	Blood: Gas	Fat: Blood
Nitrous Oxide	105	0.47	2.3
Isoflurane (Forane)	1.2	1.4	45
Desflurane (Suprane)	6.0	0.42	27
Sevoflurane (Ultane)	2.0	0.65	48

From its properties, N_2O has many advantages when compared with other inhalation agents. Within 20-30 seconds after administration, N_2O will begin its action and reach the peak onset at 3-5 minutes. When it is compared with other routes of sedation such as nasal, oral and intramuscular (IM), the onset of N_2O is more rapid. Similar to the onset of action, the recovery time of N_2O/O_2 inhalation sedation is more rapid than other routes owing to its properties that it is completely eliminated from the body within 3-5 minutes after N_2O is discontinued [23]. Furthermore, N_2O concentration can be titrated; therefore, the patients reach proper sedation level and oversedation is prevented.

N_2O/O_2 is safe and has very few adverse effects on the body systems such as cardiovascular, respiratory, hematopoietic, endocrine, hepatic or gastrointestinal systems [23, 24]. From the properties of N_2O/O_2, patients are not necessary be admitted in the hospital before and after procedure with N_2O/O_2 inhalation sedation[23].

Although N_2O/O_2 has many advantages as mentioned above, there are some disadvantages from its properties. N_2O is a low potent gas, with the MAC value of 104. N_2O concentration that yields proper sedation level is varying in each patient. There are some patients that do not respond to N_2O even though the high concentration of N_2O is used. Although N_2O/O_2 inhalation sedation is used, dentists should maintain the basic behavior management including verbal and nonverbal communications. Patients should respond and be able to follow dentist's command. If patients are uncooperative and cannot breathe through their noses, N_2O/O_2 inhalation sedation technique is not recommended [9, 23].

Although N_2O/O_2 inhalation sedation is safe and has few adverse effects, long term exposure to N_2O of the dental care team can affect several body systems. Researchers found irreversible changes such as reproductive, hematologic, immunological, neurological, liver and kidney disorders in individuals exposed to high concentration and chronic exposure of N_2O [25-27].

N_2O inactivates vitamin B12 and cobalamine which are necessary cofactors for activate methionine synthetase; therefore, active methionine synthetase is decreased. Inactivated form of methionine synthetase decreases the synthesis of DNA and inhibition of cell division. Effects on reproductive system depend on high concentration and long-term exposure of N_2O more than 24 hours [25-27]. Rowland et al. reported that high levels of unscavenged nitrous oxide affected reproductive system, decreasing ability of being pregnant of female dentist assistant [28]. Moreover, Cohen et al. reported that there was an increased risk of spontaneous abortion among female dental assistants that had been chronic exposed to N_2O [29]. Another effect of chronic exposure to N_2O is hematologic effect. There are the bone marrow suppression that is the result of impaired synthesis of DNA, pernicious anemia, and a vitamin B 12 deficiency diseases [25, 30].

The major sources of gas leakage are from unscavenged mask and an inadequate scavenging system including of equipment leakage, inadequate operatory ventilation and gas leakage from unfitting nasal masks or patient's mouth breathing and talking during procedure. Therefore, the National Institutes for Occupational Safety and Health (NIOSH) recommends a scavenging vacuum line rate of 45 liters/minute with scavenging nasal hood and N_2O concentration is controlled at 25 ppm during administration. All parts and connectors of N_2O machine are rechecked to prevent leakage of gas. Moreover, operator should place gauze on space between nasal hood and bridge of nose and advice patient not to talk or mouth breathe during procedure. Certainly, the important things that should be concerned are periodic maintenance and inspection of N_2O equipments [25-27]. Furthermore, the major disadvantages of N_2O are high cost of the inhalation sedation equipments and insufficient practical dental training to use N_2O/O_2 inhalation sedation [23].

There are many indications for use of N_2O/O_2 inhalation sedation. The most beneficial is to relieve pain and anxiety of fearful or anxious patients in any procedures. N_2O can reduce gag reflex and raise pain threshold of patients hence they are relaxing, more tolerant to long duration of treatment and more cooperative with dental procedure [9]. N_2O can also be used in patients with intellectual disabilities or special needs who can communicate. Faulks et al. [31] used a premixed 50% N_2O/O_2 to sedate the intellectual disability group such as autism, Down syndrome or psychomotor disorder and reported that 91.4% of the cases were successful with no adverse effects. Moreover, the premixed 50% N_2O/O_2 such as Entonox® (Linde

Canada Limited, Ontario, Canada) and Kalinox® (Air Liquid Santé International, Paris, France) are usually used in emergency room or emergency medical services (EMS) to control pain from its analgesic property, rapid onset and no severe side effects [32].

N_2O/O_2 inhalation sedation is not suitable for the patients who unable to communicate and express their feelings during sedation with N_2O/O_2 from their very young ages and severe personality disorders or psychiatric disorder group such as schizophrenia and bipolar disorder [6]. The patients who cannot breathe with their noses because of abnormality of anatomy such as nasal polyps, deviated septum of nose or respiratory disease such as upper respiratory infection, allergic rhinitis, and sinusitis are not recommended for N_2O/O_2 inhalation sedation. Moreover, N_2O/O_2 inhalation sedation is not successful in patients who cannot tolerate nasal mask use from claustrophobia [6, 23]. Respiratory system of normal patients responds to elevated blood carbon dioxide (CO_2) level whereas chronic obstructive pulmonary disease (COPD) patients breathe with hypoxemic drive that responds to lowered blood O_2 tension. When patient with COPD is administered with N_2O with high concentration of O_2, this deactivates the hypoxemic drive and may result in apnea of patients [6, 23].

N_2O/O_2 inhalation sedation should be avoided in the first trimester pregnancy patients to prevent spontaneous abortion or developmental malformation of fetus. Then, pregnant patients should have medical consultation before the use of N_2O/O_2 in any duration of pregnancy [23, 24]. Other contraindications of N_2O/O_2 inhalation sedation are the patients with B12 or folate deficiency/disorders, patients undergoing chemotherapy with Bleomycin drugs. Moreover, patients with latex allergy are also contraindication for N_2O/O_2 inhalation sedation because material of nasal mask is latex [9, 24, 33].

From property of N_2O that can increase volume and pressure of body space hence N_2O/O_2 inhalation sedation is not suitable for patients who have obstructed bowel, pneumothorax, middle ear disease and postoperative retinal surgery [6, 33]. Therefore, dentist should carefully evaluate medical history of patients before N_2O/O_2 inhalation sedation use.

2.3 Administrative techniques of nitrous oxide/oxygen inhalation sedation

Two administrative techniques commonly used in dental treatment are slow titration and rapid induction.

2.3.1 Slow titration technique

After patient received 100% O_2 for 3-5minutes, Malamed [1] recommended beginning with 20% N_2O and 10% of N_2O is incrementally increased every 30-60 seconds until the patient feels relaxed or reaches the ideal stage of sedation. The advantage of this technique is that the patients do not have to receive high percentage of N_2O more than necessary. Furthermore, there is variation between individuals that, with the same concentration of N_2O, the patients will not respond in the same manners. Even in the same individual but different visits, patients may not need the same concentration of N_2O for the ideal stage of sedation. Thus, the dentists should not attach to the N_2O concentration use in the previous treatment or with other patients [2].

From the survey of the University of Southern California School of Dentistry, the proper concentration of N_2O which the patients needed to meet the ideal sedation were from 30% to 40% [1]. In addition, many investigators employed the slow titration technique of N_2O/O_2 inhalation sedation with the range of concentration from 10%-50% N_2O in their studies and serious side effects have never been reported [4, 5, 11, 12, 34-40].

2.3.2 Rapid induction technique

This technique begins with high concentration of N_2O/O_2 up to 50% and this N_2O/O_2 concentration is maintained throughout the procedure [2]. The advantage of this technique is that it can rapidly sedate uncooperative patients thus they reach the sedation level and be calm quickly [2, 41]. Moreover, there is a mixture of 50% N_2O and 50% O_2 in one cylinder distributed in the market such as Entonox® (Linde Canada Limited, Ontario, Canada) and Kalinox® (Air Liquid Santé International, Paris, France) that is usually used in the emergency department, EMS, and pediatric department [32]. The advantage of this equipment is that patients cannot be accidentally received 100% N_2O [41].

On the other hand, the major disadvantage of high concentration of N_2O use is the possibility of producing oversedation [2]. The premixed of 50% N_2O/O_2 cannot administer 100% oxygen in post-operation period and may cause diffusion hypoxia. However, Quarnstrom and Mar [41] reported that there were no clinical signs of diffusion hypoxia in their studies when the premixed of 50% N_2O/O_2 was used during dental procedures. Similarly, many studies reported that 50% N_2O/O_2 premixed was safe and had minor adverse events when it was used in many procedures such as minor superficial surgery, lumbar puncture, venous puncture, burn dressing, fractures, and dental care [42-45].

The ideal stage of sedation can be evaluated from the objective signs and subjective symptoms. Operators should observe and ask the patient's feelings during N_2O/O_2 administration. When patient reaches the proper sedation level, operation can now be initiated. Researchers have described the objective signs of the ideal stage of sedation including relaxed and comfortable feeling, hands opening, feet abduction, and limp legs. Besides observing the patient's objective signs, patient must communicates and responds normally to verbal command. The other symptoms that can be observed in patient sedated with N_2O/O_2 are sleepiness, warmth, floating, heaviness, light-headedness, lips, hands and legs tingling [1, 8, 46].

If patients receive high concentration more than necessary, they will express signs and symptoms of oversedation such as uncooperative or uncomfortable feeling, mouth breathing, nausea and vomiting, sleepiness and dream, hallucination, drowsiness, dizziness, laughing, and confused visual images [8]. Whenever possible, oversedation should be avoided to minimize the serious adverse events.

Cumulative effect of N_2O/O_2 may be seen after long duration of its use. The depth of level of sedation may get deeper although the N_2O/O_2 concentration is not altered. Improper concentration of N_2O/O_2 may lead to oversedation resulting in uncomfortable feeling of the patients [47].

2.4 Recovery from nitrous oxide/oxygen inhalation sedation

The recovery period is the important component in sedation procedure. Fully recover from sedation is necessary prior to patient discharge. Patients should return to their normal status in all aspects including physiologic parameters, signs and symptoms, psychomotor performances and emotional status. If patient is evaluated and met the complete recovery criteria prior to discharge, this protocol can decrease adverse side effects, supporting the safe use of N_2O/O_2 [10, 48]. In recovery periods, many factors should be evaluated prior to patient's discharge as follows:

2.4.1 Diffusion hypoxia

Diffusion hypoxia is the phenomenon that is believed to occur because of the rapid decrease of SaO_2 levels in blood after discontinuation of N_2O/O_2. Fink [49] in 1955 was the first describing diffusion hypoxia, which was originally called diffusion anoxia. The procedures were processed under general anesthesia through endotracheal tube with 75% N_2O/O_2 and 2.5% intravenous thiopental. Fink reported diffusion anoxia, 8% drop in SaO_2 at the end of general anesthesia, in 8 healthy gynecologic patients who recovered in room air.

In the atmospheric air, there are 79.2 % N_2, 20.94% O_2, and 0.04% CO_2 (Figure 1). The blood: gas partition coefficient of N_2O is 0.46 while of N_2 is 0.014. As a result, N_2O can enter space faster than N_2 can exit space resulting in increasing of pressure in any body spaces such as lung alveoli, middle ear, or sinus (Figure 2). When N_2O is immediately discontinued, N_2O from blood and brain will move rapidly into alveoli followed by excretion from the body because of its higher pressure (Figure 3). Because of the rate of N_2O elimination is faster than its N_2 replacement, O_2 concentration in alveoli and blood is decreased and theoretically lead to hypoxia (Figure 4) [1, 6, 50, 51]. Symptoms of diffusion hypoxia are headache, lethargy and nausea [22, 50]. Regarding this theoretic hypothesis, 100% O_2 has long been recommended postoperatively for 3-5 minutes after N_2O is discontinued to prevent diffusion hypoxia by many authors [6, 9, 10, 47, 50].

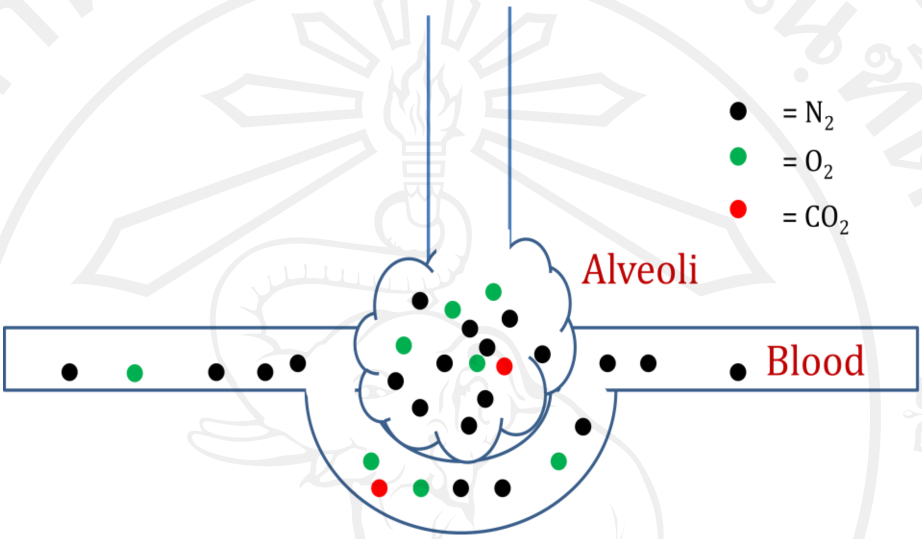

Figure 1 Gases in the atmospheric air

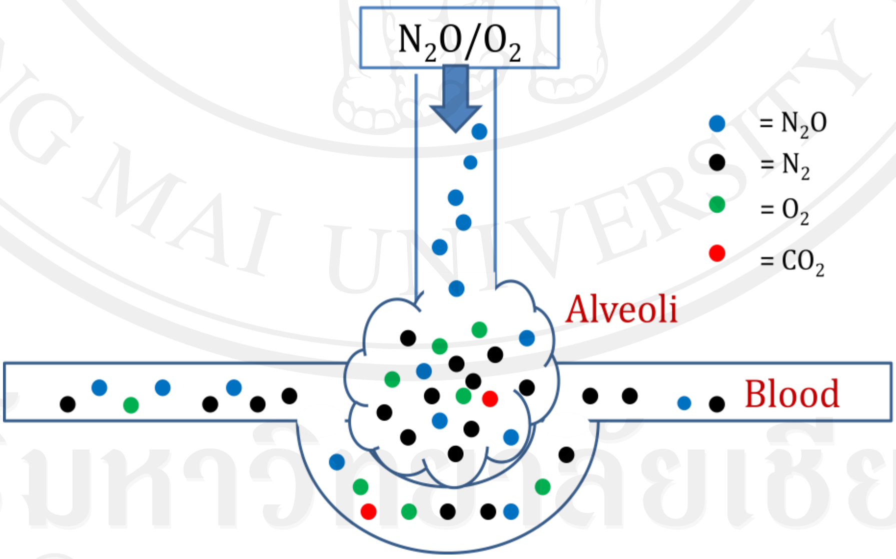

Figure 2 N_2O/O_2 administration

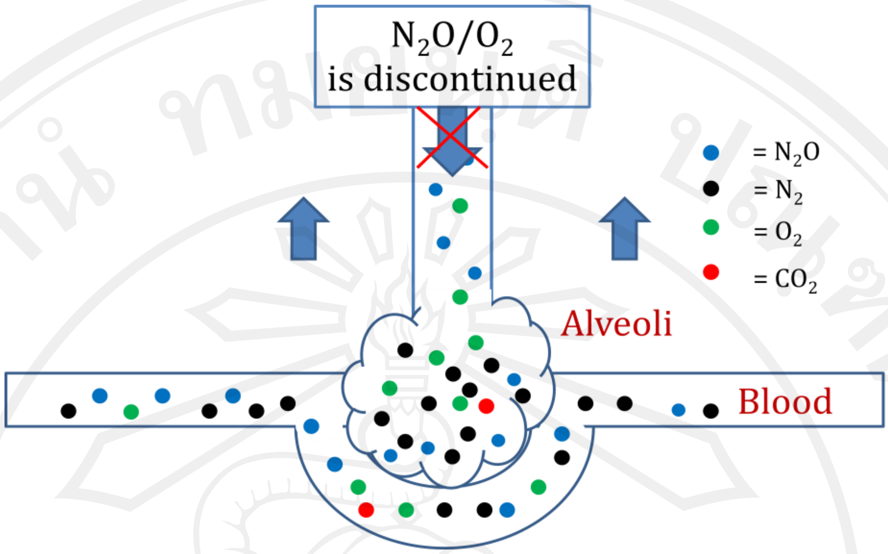

Figure 3 N_2O/O_2 is discontinued

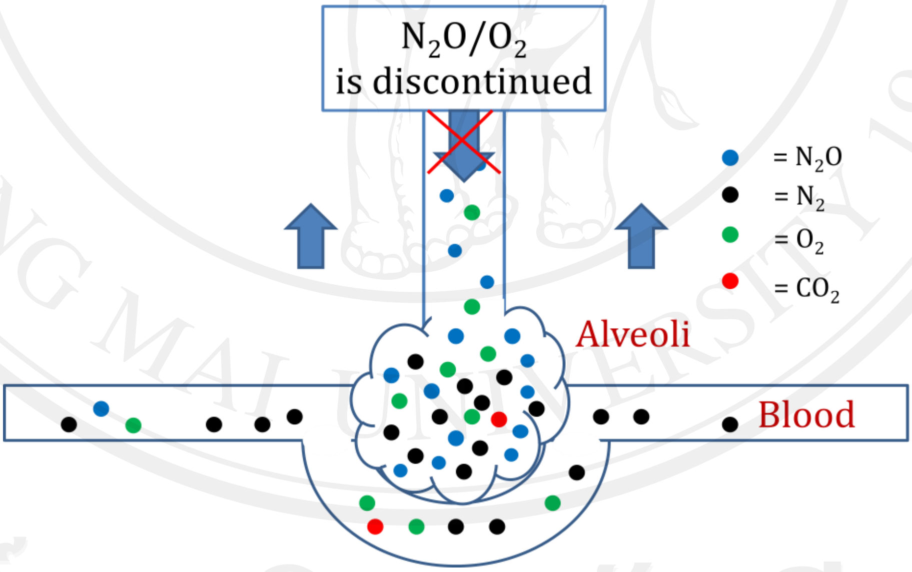

Figure 4 Diffusion hypoxia

Several researchers supported that diffusion hypoxia can occur following discontinuation of N_2O/O_2 without 100% O_2 administration (52-54). Fanning and Colgan (54) in 1969 reported a large drop of SaO_2 after administration of 75% N_2O/O_2 and intravenous thiopental under general anesthesia in both animals and humans.

Similarly, Sheffer et al. [52] in 1972, who used 78.5% N_2O/O_2 and methoxyflurane, also reported a drop of SaO_2 in their study. Moreover, Brodsky et al. [51] in 1988 recommended administering 100% O_2 to prevent hypoxemia in all patients although they found that the major cause of 6% clinically significant hypoxemia ($SaO_2 < 90\%$) in their study was from airway obstruction.

On the other hand, there were many studies that have questioned the necessity of administration of 100% O_2 to prevent diffusion hypoxia. Frumin and Edelist [55] studied in 18 healthy patients who used 79% N_2O/O_2 in variety of operations and received room air instead of 100% O_2 at recovery period. They reported that diffusion hypoxia did not occur when patients had normal ventilation and without respiratory depression. Similarly, Selim et al. [56] in 1970 presented that SaO_2 was only 2 % decrease from the baseline when patient received 79% concentration of N_2O without 100% O_2 post cessation. They discussed that diffusion hypoxia is clinically insignificant when ventilation is adequate.

In dentistry, Quarnstrom et al. [11] studied diffusion hypoxia in 104 adult patients who were administered N_2O/O_2 sedation at an average concentration of 35.6%. Result from their study showed that none of the cases had diffusion hypoxia. Similarly, study of Dunn-Russell et al. [4] that compared diffusion hypoxia between patients who recovered in room air or 100% O_2 after administered slow titration technique of N_2O revealed that SaO_2 recorded by pulse oximeter did not go below 95% in both groups. From that study, they concluded that there was no diffusion hypoxia when the patients were breathing room air instead of 100% O_2 after slow titration technique of N_2O. However, there have been no studies that compare diffusion hypoxia between different administrations (slow titration or rapid induction) and ending techniques (100% O2 or room air).

From the difference in the results of studies mentioned above, Quarnstrom et al. [11] suggested that diffusion hypoxia occurred in Fink, Fanning and Colgan studies may be caused by the higher concentration of N_2O than that of the normal use in dental procedure. N_2O concentration used in dental treatment is usually lower than the one used in general anesthesia. Moreover, respiratory side effect possibly occurred as a result of other anesthetic agent, such as thiopental. Similarly, Becker [6] proposed that, hypoxia only presents if high concentration (>70%) of N_2O/O_2 is used directly by full mask or endotracheal tube. Malamed [22] stated that the occurrence of diffusion hypoxia is rare and clinically insignificant at low N_2O concentration used in dentistry.

Ending with room air may yield some advantages. Jeske et al. [12] suggested that 100% oxygen administration may increase chair time of sedation procedure and dry respiratory tract of the patients. Moreover, there is still a question of the necessity of 100% O_2 in cases when patients vomit during procedure or patients do not want to continue with N_2O/O_2 sedation.

2.4.2 Physiologic parameters

At the recovery period, physiologic parameters should be stable and return to close to the baseline from N_2O property that does not affect cardiovascular and respiratory system [6, 22, 24]. Dentist should monitor physiologic parameters pre-, during, and post- operatively. Malamed [1] recommends the acceptable ranges of parameters as follows: blood pressure within ±20 mmHg/10 mmHg from the baseline, heart rate within ±15 beats/min from the baseline and respiratory rate within ±3 breaths/min . Similarly, Clark and Brunick [10] recommends that postoperative parameters should be blood pressure within 10 mmHg and heart rate within 10 beats/min from preoperative values.

2.4.3 Objective signs and subjective symptoms

Dentist should evaluate symptoms by observing or asking patients of their feelings at recovery period. Subjective symptom that can occur at the recovery period is usually minor such as headache, dizziness, and nausea and vomiting [4]. From the study of Hallonsten et al. in 1983 [57], there were approximately 0.9 % minor adverse effects such as restlessness, vomiting and nausea after treatment. Quarnstrom et al. [11] reported that 11 of 104 volunteer adult patients complained that side effects of average concentration of N_2O at 35.5% included light-headedness, dizziness and decrease in respiration.

The most frequent complications of N_2O are nausea and vomiting. Malamed [47] stated that the incidence of nausea and vomiting was very low. In addition, several studies also reported that the occurrence of nausea and vomiting was less than 0.5% [47]. Similarly, Kupietzky et al. [58] reported that postoperative nausea and vomiting occurred less than 1% after rapid induction of 50% of N_2O/O_2 followed by 100% O_2 for 5 minutes. From the retrospective study of Burnweit et al. [36] in 2004, there were no serious complications after 20-50% of N_2O administration by slow titration technique and nausea and vomiting occurred for a rate of 3%.

Nausea and vomiting may be associated with oversedation, duration of sedation longer than 35 minutes, technique of N_2O/O_2 administration, patient's history of nausea and vomiting, the roller coaster effect, which is the sharp increase and decrease concentration of N_2O/O_2 [6, 47, 58]. On the other hand, Hallonsten et al. [57] reported that there were only mild side effects of N_2O/O_2 such as nausea and vomiting. These effects did not relate to N_2O concentrations, duration of treatment, patient's age and medical conditions. Moreover, Fisher [59] reported that postoperative nausea and vomiting may be affected from other anesthetic agents that combined with N_2O/O_2 such as cyclopropane or propofol. Although Kupietzky et al. [9] demonstrated that there was no difference of the incidence of nausea and vomiting between fasting and non fasting group [58], the AAPD recommended that patients should allow to have only light meal 2 hours before N_2O/O_2 administration[60].

Gall et al. [61] in 2001 reported of adverse effects of sedation with the premixed 50% N_2O/O_2. Major adverse effects, approximately 0.3%, were the adverse event that affected the respiratory system such as oxygen desaturtion, airway obstruction or apnea and cardiovascular system such as bradycardia. The other adverse effects that could be found were oversedation and prolonged sedation more than 5 minutes after N_2O discontinuation. On the other hand, minor adverse effects including euphoria, nausea, vomiting, dizziness and paresthesias were reported to be less than 5%. If patients have any unpleasant feelings, Clark and Brunick [10] recommend giving 100% O_2 and observing until patients get better before discharge.

2.4.4 Psychomotor performance

Many authors investigated effects of N_2O/O_2 on psychomotor ability, memory, and cognition. Psychomotor ability should be evaluated to confirm complete recovery of patients. After the use of N_2O/O_2, patients should be discharged only if they have normal response and function [10]. Thus, there were many psychomotor tests that have been used such as a paper-and-pencil test or a drawing test, an eye-hand coordinate test and an automobile driving stimulation [10, 37, 39, 40, 62].

The Bender Motor Gestalt test is a drawing test that was used on children and adults (Figure 5). It can assess visual-motor function by comparing the functions between pre and post-operational period [63]. Houpt et al. [46] selected four figures from the Bender Motor Gestalt test to evaluate the effects of N_2O/O_2 on psychomotor ability in children. The result was that N_2O at 50% concentration had a small effect on psychomotor ability of children and more errors were found in younger children.

The Trieger test is a modified version of one figure of the Bender Motor Gestalt test proposed by Dr. Norman Trieger in 1967. Lines of figure are replaced by dots and spaced approximately 12-13 mm (Figure 6) [62]. The patients should be tested by asking them to connect all of the dots both pre and post-operatively to compare the accuracy of the test. Each drawing was scored for error such as the number of dots that are missed completely and the distance from dot in millimeters. Moreover, time to complete the test and quality of lines should also be monitored and recorded so this test can evaluate fine visual motor function at the recovery period of the patient [1, 62]. Jeske et al. [12] used the Trieger test to assess psychomotor skills at the recovery period of patients who obtained 35-40 % N_2O/O_2 and completed with 100% O_2 and room air, no difference was found between both groups.

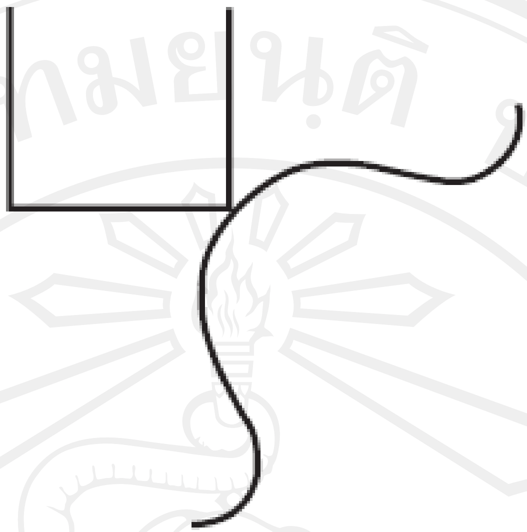

Figure 5 The sample figure of the Bender Motor Gestalt Test [63]

Figure 6 The Trieger test that is modified from the Bender Motor Gestalt Test [62]

Furthermore, Jastak and Orendurff [38] used a driving stimulation test to evaluate safety of automobiles or other complex machinery operation immediately after finishing N_2O/O_2 sedation. After slow titration of N_2O/O_2 was administered and finished with 100% O_2, they evaluated errors in braking, signaling, and speeding. They concluded that the patients could safely operate a motor vehicle after N_2O/O_2 sedation.

Age of patients was not a factor that is associated with psychomotor performance. Norton et al. [40] reported that there was no significant difference of psychological and psychomotor performance between healthy older and younger patients after 30%-46% N_2O/O_2 concentration use. However, psychomotor performances were affected by longer duration of N_2O/O_2 administration. Conry et al. [39] measured psychomotor changes by neuropsychological tests following 90 minutes of exposure to N_2O/O_2 and 100% O_2 after completion. There were psychomotor impairment and this effect was delayed for 10 minutes after terminated N_2O/O_2. So recovery of psychomotor performance may relate to the length of procedure.

When psychomotor impairment was occurred, some studied reported that they rapidly returned to normal following termination of N_2O/O_2. Trieger et al. in 1971 reported that psychomotor impairment measured by a modified Bender Motor Gestalt drawing test after N_2O/O_2 sedation at 25, 50 and 70% concentration can rapidly reverse to normal within three to four minutes after stopping N_2O/O_2 [64]. Similar to the result from the study of Ayer and Lee [37], psychomotor performance which was tested by the Reusch color test and a peg board test were completely reversible immediately after cessation of 35% N_2O/O_2 and full recovery was within 20 minutes after the end of procedure.

2.4.5 Assessing adequate recovery and recovery time

At the recovery period, patients should return to the presedation status. They should have full consciousness and can communicate by answering questions. Patients should feel normal and do not have any unpleasant feelings. Other parameters that should be considered for full recovery are physiologic parameters, objective signs, subjective symptoms and psychomotor performance.

Full recovery time from sedation may vary in each individual because of many factors [(10)]. Takarada et al. [(48)] studied clinical recovery time which is the time from ending of procedure to patient discharge from clinic. Median recovery time after N_2O/O_2 inhalation sedation was 40 minutes which is less than recovery time from intravenous sedation such as propofol and midazolam, from properties of N_2O/O_2 that has rapid onset and very few side effects. Lepere et al. [(65)] suggested that recovery time from conscious sedation was not affected by patient' s age and weight, duration and type of procedure.

There are many tests that can aid in recovery evaluation before discharge. Lepere et al. [(65)] used a modified Aldrete postanesthetic score to determine patient's normal status such as vital signs, responses, and body appearances. Likewise the study of Macnab et al. [(66)] used the Vancouver Sedative Recovery Scale to assess recovery of patient's response, eye appearance and body movement.

2.5 Anxiety and satisfaction assessment

Anxiety is a state of distress about future uncertainties and unpredictable situation. Surgical procedures including dental procedures induce high level of patient's anxiety [(67)] . Okawa et al. [(68)] reported that level of pain related to patient's anxiety at preoperation period; therefore, anxiety reduction is very important to reduce patient's pain during dental treatment. Dental anxiety is related with many factors including of bad experience from earlier treatment, negative attitudes in the family, fear of pain, and perceptions of an unsuccessful previous dental treatment (69).

Patient's anxiety can be assessed from several tests as questionnaires and rating scales. A commonly applied questionnaire is the Corah's Dental Anxiety Scale (DAS) which is the four multiple-choice items dealing with the score ranging from 1-5 so the DAS scores are from 4- 20. Patients were asked to complete DAS to evaluate their anxiety levels to dental procedure (70). Moreover, The State-Trait Anxiety Inventory (STAI) is the self -administered psychological questionnaire which has no time limit for completion. Normally, it takes 15-20 minute to fill this questionnaire (68).

The Visual analog scale (VAS) is an ordinal scale which is a horizontal 100 millimeters line. It has been used in psychological assessment since the early 20th century and successful in many health assessments including pain, quality-of-life and mood (71, 72). VAS is simple to use and have been shown to present high reliability and validity so it is a useful and valid measurement of preoperative anxiety (72-74). Moreover, there is a Global-anxiety visual analog scale (GA-VAS) which is modified from the VAS to make it more easily understand. Williams et al. (71) used the GA-VAS to assess anxiety in generalized anxiety disorder (GAD) patients and presented the reliability, validity, and responsiveness of its use. The VAS is a very simple and easy to understand anxiety assessment tool. Therefore, the GA-VAS is chosen to assess anxiety and the VAS is chosen to assess satisfaction of volunteer in this study.

It can be concluded from the entire review literature that there are controversial opinion of 100 % O_2 administration at the end of procedure to prevent diffusion hypoxia and the difference of administrative and ending techniques may be the factors that affect objective signs, subjective symptoms, psychomotor performance, recovery time and satisfaction in the recovery period. However, no previous studies have ever investigated all these parameters in the recovery period from different administrative and ending techniques of N_2O /O_2.