**Introduction**

Dental fear and anxiety (DFA) is a recognised challenge in the provision of dental treatment and utilisation of dental services. This term refers to the negative feeling associated with dental treatment [1]. The prevalence of DFA, the contributing factors and its impact in children have been widely explored [2-5]. A systematic review looking at DFA among children and adolescents gave an estimated prevalence of 10%, and it was almost always related to dental pain [6].

Effective management of pain and anxiety during dental treatment is important. Non-acknowledgment of this negative emotional state and poor pain management will reinforce DFA. Dental teams treating young children must ensure that patients receive high quality dental treatment with no accompanying harmful physiological or psychological side effects. Managing DFA requires empathy, good behaviour management skills, proficient technical knowledge, effective pain control and in some cases may need pharmacological support such as sedation and general anaesthesia (GA).

Procedural Sedation and Analgesia (PSA) can be used when providing dental treatment. PSA is defined as the use of sedative, analgesic, and dissociative drugs to provide anxiolysis, analgesia, sedation, and motor control during painful or unpleasant diagnostic and therapeutic procedures [7].

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**Keywords:** Nitrous-Oxide, Sedation, Paediatric, Dental

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**ABSTRACT**

Provision of sedation while delivering dental treatment to anxious paediatric patients aims in minimising their discomfort and psychological trauma, managing behaviour as well as controlling patient movements, using a technique with wide margin of safety. Nitrous oxide-oxygen inhalation sedation is one of the sedation methods commonly used to manage dental fear and anxiety. Its beneficial features include; potent anxiolytic effect, its sedative, analgesic as well as amnesic properties, titratability, rapid onset and recovery whilst carrying minimum risk. Modern dental inhalation sedation machines deliver gases in continuous flow mechanism, using nasal hood apparatus therefore allowing treatment to the oral cavity. The machine is equipped with various safety features to avoid adverse events during administration. Operators must be adequately trained and able to manage foreseeable complications. This paper aims to provide an overview on the appropriate practice of nitrous oxide-oxygen inhalation sedation, for paediatric dental patients. Careful case selection, comprehensive preparation by the sedation team, good documentation, the use of appropriate armamentarium, application of titration techniques along with good behaviour management are crucial in producing safe and effective treatment outcomes.
Nitrous oxide-oxygen inhalation sedation (NOIS) is recognised as a safe and effective PSA technique to reduce anxiety, produce analgesia and enhance effective communication between a patient and health care providers [8, 9]. The American Society of Anaesthesiologists affirms that NOIS allows for diminution of pain and anxiety in a conscious patient, while entailing minimal risk [10]. Audits looking at patient safety have also reported very few complications related to NOIS cases [11].

In Malaysia, PSA has been used by the paediatric dental speciality for years. Figure 1 shows part of an audit done from 2014 until 2019, delineating the number and type of sedation given by paediatric dental specialists in the ministry of health. Whilst oral sedation is more commonly used, application of NOIS has slowly increased in recent years. With time, more specialists were trained and centres with NOIS facilities were set up. The speciality is expanding and currently there are 35 paediatric dental departments under the Ministry of Health, Malaysia and some of these centres provide NOIS services.

Figure 1. Oral sedation and NOIS cases performed by paediatric dental specialists, Ministry of Health, Malaysia from 2014 to 2019 [12].

Paediatric dentistry speciality strives to provide good quality oral care to children in a safe environment, while encouraging positive response towards dental treatment. This paper aims to provide an overview on the appropriate practice of nitrous oxide-oxygen inhalation sedation, for paediatric dental patients. The pharmacological properties, specific techniques used and patients’ physiological changes are not covered in depth but clinical management aspects are highlighted to enhance understanding and as guidance to ensure safe and effective usage of this sedation technique in children.

Benefits of NOIS

Nitrous oxide (NO) is an odourless gas with a faint sweet smell tolerable by most patients, that can cause mild depression of the central nervous system and produce a feeling of euphoria [13]. Therefore, NO is an anxiolytic agent but has a superior safety profile as it causes little effect on the respiratory and cardiovascular system [4, 8]. The intact cough reflex results in minimal risk to the patients. There have been no reports of fatalities or serious morbidities when used within the recommended concentrations [8, 14-16].

NOIS also has the advantage of rapid onset and rapid recovery of around two to three minutes. NO can be absorbed quickly from the alveoli, passing through tissues due to pressure gradients and excreted out quickly with pulmonary exhalation. This allows the function of titratability which is an important feature not available with oral sedation [17]. In comparison to intravenous sedation which can also be titrated, NOIS is deemed more
favourable as it negates the need for cannula insertion in a paediatric patient.

NOIS offers sedative effects as well as promotes muscular relaxation and analgesia [18]. In children particularly, this feature helps to expedite delivery of procedures that are lengthy, facilitates procedures that may be uncomfortable but require the patients to be still. A reduction in awareness of pressure-induced pain is an added advantage for dental procedures [19]. Along with the use of good behavioural management techniques, the administration of local anaesthetics can be virtually painless and stress-free for the child, garnering high parental satisfaction at lower costs compared to GA [14, 20].

Patient selection, indications and contraindications

Patients’ medical history should be reviewed prior to the decision to use NOIS. This assessment should include diseases, allergies or adverse drug reactions; current medications; physical abnormalities including pregnancy status; previous hospitalisations; and recent illnesses that may compromise the airway [8]. In a paediatric dental setting, a child needs to have a certain level of cognitive and coping ability to accept wearing a nasal hood and to breathe effectively from the nose. A host of factors often contribute to this including age, emotional attributes, temperament and personality traits, parental, sibling or peer influences, social skills, and past experiences in medical or dental settings [21].

Patient selection is crucial for a successful sedation outcome. The indications and contraindications of NOIS are listed in Table 1. It is worth noting that whilst patients with American Society of Anaesthesiologists (ASA) Physical Grade I and II are deemed fit to undergo NOIS as outpatients at general or specialist practices, patients with ASA III and above need to be treated in a hospital setting. Whenever possible, appropriate medical specialists should be consulted before administering sedative agents to patients with significant underlying medical conditions [8].

Table 1. Indications & Contraindications of NOIS [8, 22, 23].

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
</tr>
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<tbody>
<tr>
<td>● Mild to moderate dental anxiety</td>
<td><strong>Absolute contraindications</strong></td>
</tr>
<tr>
<td>● Unpleasant or lengthy procedures</td>
<td>● Methylenetetrahydrofolate reductase deficiency</td>
</tr>
<tr>
<td>● Medically compromised patients where dental stress could trigger</td>
<td>● Cobalamin (vit B12) deficiency</td>
</tr>
<tr>
<td>exacerbation e.g. cardiovascular disorders, asthma, epilepsy, etc</td>
<td>● Bleomycin (sulphate) treatment</td>
</tr>
<tr>
<td>● Patients with needle phobia</td>
<td></td>
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<tr>
<td>● Heightened gag reflex</td>
<td><strong>Relative contraindications</strong></td>
</tr>
<tr>
<td>● Patients in whom local anaesthesia cannot be obtained (e.g. acute pulpitis, MIH teeth)</td>
<td>● Chronic obstructive pulmonary diseases</td>
</tr>
<tr>
<td>● When other sedation techniques are contraindicated</td>
<td>● Current upper respiratory tract infection</td>
</tr>
<tr>
<td></td>
<td>● Pneumothorax</td>
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<td></td>
<td>● Cystic fibrosis</td>
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<td></td>
<td>● Nasal / facial deformity</td>
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<tr>
<td></td>
<td>● First trimester of pregnancy</td>
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<tr>
<td></td>
<td>● Myasthenia gravis and multiple sclerosis</td>
</tr>
<tr>
<td></td>
<td>● Recent middle ear disturbance or surgery</td>
</tr>
<tr>
<td></td>
<td>● Recent intraocular procedures where gases were used</td>
</tr>
<tr>
<td></td>
<td>● Pre-cooperative age children</td>
</tr>
<tr>
<td></td>
<td>● Severe psychological disorders or drug-related dependencies; compulsive personality</td>
</tr>
<tr>
<td></td>
<td>● Hysterical or defiant patients who refuse the nasal hood due to age, maturity, behaviour or personality disorders [18, 24, 25]</td>
</tr>
</tbody>
</table>
Table 2. Comparison of the nitrous oxide inhalation sedation equipment used by medical and dental personnel

<table>
<thead>
<tr>
<th></th>
<th>Medical device</th>
<th>Dental device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of flow</td>
<td>On demand flow; gas is delivered only when the user breathes in through the mask.</td>
<td>Continuous flow; gas is delivered to the patient irrespective of the patient's breathing pattern.</td>
</tr>
<tr>
<td>Ratio of gases</td>
<td>Preset at a fixed rate of 50% nitrous oxide and 50% oxygen.</td>
<td>Ratio of nitrous oxide and oxygen can be adjusted by the operator.</td>
</tr>
<tr>
<td>Titrination</td>
<td>Titration is not possible.</td>
<td>Operators can titrate/control the level of sedation required.</td>
</tr>
<tr>
<td>Gas delivery</td>
<td>Delivery with a face mask.</td>
<td>Delivery with a nasal hood.</td>
</tr>
<tr>
<td>Scavenging</td>
<td>No scavenging component.</td>
<td>Scavenging nasal hood draws exhaled air away from the patient.</td>
</tr>
<tr>
<td>Example of devices</td>
<td>iii) Nitronox and iv) Kalinox</td>
<td>v) Accutron and vi) Matrix Parker</td>
</tr>
<tr>
<td>Control panel</td>
<td>Pressure indicators displaying content of the cylinders.</td>
<td>Control available to adjust flow rate and ratio of gasses.</td>
</tr>
</tbody>
</table>

* (i),(ii),(iii),(v) photos courtesy of Accutron Inc.  
† (iv) photos courtesy of Kalinox™  
‡ (vi), (vii), (viii) photos courtesy of Porter Instrument
Armamentarium for NOIS

Differences between the medical and dental NOIS devices

A dental inhalation sedation equipment is different from its medical counterpart although both supply nitrous oxide and oxygen via a breathing device. The differences between these devices are outlined in Table 2.

Safety features of a dental NOIS machine

A dedicated dental inhalation sedation machine which complies to good standard of safety features will have these components:

- **Configurated pin and diameter index safety system:**
  These include different configured pin and diameter index safety systems for the respective gas cylinders with colour-coded hoses to prevent inadvertent switching.

- **Oxygen fail-safe mechanism:**
  The flow of nitrous oxide will be automatically terminated should the oxygen supply be depleted.

- **Minimum pre-set oxygen:**
  A minimum pre-set oxygen concentration of at least 30% will ensure patients do not receive less oxygen than the amount available in ambient air.

- **Scavenging nasal hoods:**
  Regarded as the gold standard to minimise nitrous oxide contamination to the environment and avoid complications associated with prolonged exposure.

- **Emergency air inlet:**
  An emergency air intake valve which allows room air to be inhaled when gas flow from the tanks are interrupted.

Preparation for sedation

Conducting NOIS on children needs thorough planning and meticulous preparations. Essentially, all parties have roles and responsibilities to play.

**Patient**

a. Ideally, a pre-sedation visit should be arranged for patient assessment, an in-depth discussion on NOIS and consent-taking.

b. Written information must be provided to patients, explaining the benefits of NOIS, alternative treatment options, pre-procedural instructions, post-procedural precautions and arrangement in the event of complications.

c. Fasting is not required for NOIS, as recommended by guidelines [8, 26, 27].

d. On the day of sedation, reassessment of the current medical status as well as re-confirmation of treatment plan and consent should be done.

e. After completion of treatment, patients will only be discharged if they are deemed fit. The escort accompanying the patient should be capable of caring for the patient.

**Dental Team**

a. All practitioners of NOIS must undertake validated theoretical as well as clinical training and demonstrated an acceptable level of competency [28].

b. All team members including dental nurses and assistants should be capable of providing basic life support at the minimum.

c. Training in paediatric advanced life support is strongly encouraged especially if moderate or deep sedation is practised [27, 29].

d. Clinical protocol should be in place where responsibilities of each member is made clear. An example is patient-monitoring throughout the sedation and recovery period should be done by a member who must be able to recognise any adverse events.

e. Clinical observation of the patient during sedation must include visual monitoring of the depth of sedation, airway patency, skin colour and respiration [8]. Instrumental monitoring such as the use of pulse oximeters and non-invasive blood pressure monitoring is considered good practice [28, 30, 31].

**Equipment and facilities**

a. All equipment should conform to acceptable health and safety standards and be maintained in accordance with the schedule prescribed by manufacturers.

b. Before initial use of the inhalation sedation system for the day, components should be inspected and fail-safe check should be done.

c. Nasal hoods should come in various sizes to ensure good fit and the scavenging system connected to a vacuum pump with a capacity of 45 litres per minute is recommended to
avoid unnecessary exposure to nitrous oxide. Chronic occupational exposure of several hours a week has been associated with adverse health effects [32].

d. Emergency protocols should be in place to allow smooth rescue operations should an emergency situation arise. Clinic settings must permit easy access for emergency services to patients.

**Documentation**

a. Informed consent is mandatory.
b. Clinical records should document sedation details including start time, duration, sedation level, and complications if any.

**Adverse effects**

Serious adverse events associated with NOIS administration in paediatric patients has been reportedly as low. The most commonly reported adverse effect is vomiting and nausea, at 0.5-2.8% [8, 15, 33-35]. Incidence increased with usage of high concentrations of nitrous oxide (>50%), long duration of sedation (> 1 hour), heavy meals prior to sedation as well as fluctuating nitrous oxide levels e.g intermittent nasal and mouth breathing [8, 36, 37].

Diffusion hypoxia is a theoretical risk, but it can be avoided by administering 100% oxygen for 3-5 minutes at the end of the procedure. However, it has been suggested that reoxygenation is clinically unnecessary when nitrous oxide is used as a single agent in healthy patients, at a concentration of less than 70% [38, 39].

Other rare adverse effects include euphoria, hyperexcitability, convulsions, sweating, pallor and vertigo [40]. Rarer still, silent regurgitation and subsequent aspiration can happen. However, this can be avoided by not allowing the patient to clinically go into an unconscious state, thus keeping the pharyngeal-laryngeal reflex intact [8, 23].

The effects of long term exposure to nitrous oxide are not conclusive as studies done were of low methodological quality [41]. Occupational exposure has been linked to bone marrow suppression, reproductive system disturbances, premature deliveries, miscarriages and birth defect of babies [42-44]. Methods to reduce occupational health hazards include the use of effective scavenging systems, ensuring all equipment functions well and good clinical techniques such as using rubber dams, minimising patient talking, crying and mouth breathing [45-47].

**Discussion**

**The role of behaviour management in sedation**

It has been suggested that the lack of experience and operator training may account for the failure of treatment in patients undergoing NOIS [48]. Contrary to some beliefs, NOIS does not eliminate the use of behaviour management when treating anxious patients. In fact, the soothing, calming words and actions of the operator will enhance the relaxing effect of NOIS. Psychological preparation beforehand also has a significant impact on its effect. Pre-sedation visits where the child is introduced to the nasal hood, the use of scented hoods, a description of possible experiences during sedation and the use of audio-visual devices may all play a role in creating a positive experience for the child.

Although NOIS at high concentrations offers mild anaesthesia in the palate, this is inadequate for painful dental procedures. As the administration of local anaesthesia (LA) is the most feared moment in dental care, it is crucial that this procedure be made as comfortable as possible for the child. Useful techniques to consider include the use of topical anaesthesia followed by slow and controlled infiltration of LA agents either manually or with the use of computer assisted devices.

**Managing the risks from NOIS technique**

The American Society of Anaesthesiologists describes sedation as a continuum of states which occur when sedative and analgesic medications are administered [49, 50]. Table 3 delineates the range of sedation states and the clinical characteristics that defines each type of sedation. Sedation and anaesthesia guidelines state that inhaled NOIS when used in combination with sedative agent(s) may produce minimal, moderate or deep sedation or general anaesthesia.
Table 3. Continuum of Depth of Sedation: Definition of General Anaesthesia and Levels of sedation [49].

<table>
<thead>
<tr>
<th></th>
<th>Minimal (anxiolysis)</th>
<th>Moderate/ Analgesia</th>
<th>Deep / Analgesia</th>
<th>General Anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responsiveness</td>
<td>Normal response to verbal stimulation</td>
<td>Purposeful response to verbal or tactile stimulation</td>
<td>Purposeful response following repeated or painful stimulation</td>
<td>Unarousable even with painful stimulus</td>
</tr>
<tr>
<td>Airway</td>
<td>Unaffected</td>
<td>No intervention required</td>
<td>Intervention may be required</td>
<td>Intervention often required</td>
</tr>
<tr>
<td>Spontaneous ventilation</td>
<td>Unaffected</td>
<td>Adequate</td>
<td>Maybe inadequate</td>
<td>Frequently inadequate</td>
</tr>
<tr>
<td>Cardiovascular function</td>
<td>Unaffected</td>
<td>Usually maintained</td>
<td>Usually maintained</td>
<td>May be impaired</td>
</tr>
</tbody>
</table>

Although NOIS is regarded as a safe sedation method, it is not without risks. Thorough preparation is needed to manage any foreseeable emergency situations. The use of nitrous oxide for minimal sedation is defined as the administration of nitrous oxide of ≤50%, without the use of any other sedative, opioid or other depressant drug before or concurrent with the administration of nitrous oxide in an otherwise healthy ASA I or II patient [51]. In this mentioned situation, the sedating team needs to fulfil the preparation and requirements of managing minimal sedation. Should there be changes to the application, i.e. when the percentage of nitrous oxide administered exceeds 50%, the likelihood for moderate or deep sedation increases. The principles of management thus change [10, 52].

Minimal sedation (anxiolysis) entails minimal risk but studies have shown that it is common for children to pass from the intended level of sedation to a deeper, unintended level of sedation [53, 54]. This means that regardless of the intended level of sedation, the sedation of patients may result in respiratory depression, laryngospasm, impaired airway patency, apnoea, loss of protective airway reflexes and cardiovascular instability. It is essential that the team is able to recognize such adverse events and manage them appropriately. In fact, practitioners must have the skills to rescue patients from a deeper level of sedation than that intended for the procedure.

The option of titrating nitrous oxide whilst monitoring the patient’s sedation level is a useful feature of NOIS. While oversedation must be avoided, under-sedation will defeat the purpose of administering sedation and impede the delivery of effective treatment. In general, for a typical patient, a concentration of between 30% to 40% of nitrous oxide can provide an adequate level of sedation for dental treatment [55]. At these concentrations, the patient is awake, relaxed, comfortable, and able to maintain an open mouth to facilitate treatment while having reduced spontaneous movements. A mouth prop should not be forcefully used to hold the mouth open, as this leads to difficulty to assess the level of sedation [56].

The role of general anaesthesia in managing anxious paediatric patients

When providing dental treatment to anxious children, there will be a cohort of patients whom conventional behavioural management techniques do not suffice. Pharmacological support such as sedation or GA is often necessary for this group of children. Given the considerable additional costs, resources and risks incurred for these procedures, many studies have been done to determine which is the most safe, effective and cost-efficient pharmacological method.

Undoubtedly, GA is more suitable in selected cases, particularly in very young patients, those with certain medical issues and special needs, those with severe behavioural problems, children of certain temperaments as well as those requiring complex treatment. Also, those with lack of access to NOIS trained personnel and facilities may best be treated under GA.
Some studies including a systematic review found evidence that NOIS can be a favorable option for children who were otherwise referred for GA [35, 57]. Compared to NOIS, treatment under GA carries higher morbidity and mortality risks, involves more resources and cost compared to sedation. The discomfort and inconvenience of prolonged fasting along with possible admission means more time away from school and work for both the child and caregivers. In addition to this, in some centres, there is a considerable waiting time before a patient may receive this treatment modality.

When considering parental acceptance of the different types of behaviour management techniques, variations exist and this is influenced by ethnic and cultural backgrounds [58]. In a study looking at parental acceptance of advanced behaviour management techniques, NOIS was rated as the most acceptable technique for both emergency and elective treatment compared to other advanced behaviour management techniques such as active or passive restraint and GA [59].

Conclusion

For a long time, dental fear and anxiety has created significant barriers to children's access to good quality dental care, and often these effects have spilled over into adulthood with countless numbers shunning dental care due to childhood trauma. The benefits of providing good sedation for children are numerous, psychologically it decreases patient anxiety and trauma, decreases parental emotional discomfort, improved communication and the provision of dental treatment in a less daunting manner.

Inhalation sedation with nitrous oxide/oxygen is widely accepted as a safe and effective technique in managing anxious dental patients. Nitrous oxide can efficiently be used for procedural sedation in children for a variety of procedures including those that can induce light to moderate pain intensity [60]. Scientific evidence and guidelines support the use of NOIS in children. Careful case selection, thorough planning, comprehensive preparation by trained sedation team, good documentation, the use of appropriate titration techniques and good behaviour management all play a role in increasing the rate of successful dental treatment.

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