Nitrous oxide/oxygen mixture (EMONO) for pain control in children

Daniel Annequin (MD)
daniel.annequin@trs.aphp.fr
Pediatric Pain Unit Children Hospital Armand Trousseau Paris

National French guideline for EMONO use (1)

EMONO is the reference product for painful procedures and care in children as it possesses a series of original properties: speed and reversibility of action, analgesic/anxiolytic effect and a good risk/benefit profile (Grade A). It does not cover all painful procedures and care. Depending on the indications, the child's age and the experience of the healthcare providers, 10 to 30% failure is observed. Children under the age of 2 have less pronounced effects.

The main uses of EMONO are as follows:

- any procedure involving skin breakage (in association with local anaesthesia), fitting of a drip, venous puncture, lumbar puncture, myelogram, intra-articular injection, bladder catheter, dental care, small and superficial burn dressing (Grade A).
- fitting of a stomach tube, bronchial and digestive endoscopy, kidney, liver or muscle biopsy (Grade B).

Any form of premedication (psychotropic drugs, opioid...) requires increased vigilance (professional agreement). The respiratory risk due to potentiation by these products remains an exceptional event. EMONO safety is maximum when used alone, without any drug combination (Grade C).

Self-administration should be preferred (Grade C). Application of the mask to the face may induce major distress; forceful application should be avoided. Inhalation should last at least 3 minutes, with no leak between mask and face. Verbal support during inhalation is recommended. The patient should be observed permanently. Patient preparation is essential: the effects of EMONO and the procedure used should be explained.

The adverse effects are generally reversible within a few minutes of terminating treatment: nausea and vomiting has no clinical impact (the gag reflex is present). Occasionally, deeper sedation is observed. Repeated and/or prolonged administration may induce a "well-being" state that can lead to abusive use.

EMONO should be administered in adapted premises, by specifically trained medical or paramedical staff whose knowledge is periodically reassessed.

In the event of prolonged administration at a given location a gas venting system must be fitted. Failing this, regular airing of the room, combined with the use of a mobile cylinder allowing administration at the patient's bedside, or in a different room, represent simple measures that can be used to control problems associated with occupational exposure to N2O. When these precautions are taken, no significant effects on healthcare personnel, associated with the occasional intermittent use of EMONO has been observed.
1 **PEDIATRIC PAIN UNIT TROUSSEAU HOSPITAL**

- Dr Annequin = Anesthesiologist + Psychiatrist
  - Director of pediatric pain unit since 1993 (biggest in France …)
  - Dr Tourniaire, Dr Andreu Gallien, Dr Gallo, pediatrician full time
  - Dr Tonelli, Dr Gatbois, Dr Le Goff

- Acute pain service
  - 2 nurses full time

- Chronic pain consultation (700 new patients/year)
  - 85 % migraine and chronic daily headache
  - 2,5 psychologists full time

2 **DISCREPANCIES BETWEEN COUNTRIES RELATING EMONO USE**

- High support
  - France, UK, Australia, New Zealand, some US states …
  - Common use, official guidelines

- Suspicious support
  - *sometimes we could use it but we need more data…it is a very old fashioned product, modern pain control need modern tool…*

- Opposite
  - *N2O is too dangerous for the planet, humans, it has to be banned*

- Lack of knowledge
  - *N2O can be used out the OT without anesthesiologist ??
  - *N2O have analgesic properties ??*

3 **CHALLENGE OF THIS COURSE**

- Increase knowledge
  - Decrease misconceptions

- Double evidence
  - Review of the literature
  - Clinical benefits for children, parents and health professionals
4 PROCEEDURE PAIN PROBLEM

Without paediatric efficient sedation, strong physical restraint is very often needed to administer painful or anxiogenic treatments to children. Indeed, restraint is used in 54% of wound closures. Moreover, a total of 28% of pediatric emergencies in Melbourne required strong restraint despite the use of a sedation protocols (2), and this figure was a striking 80% in Denmark. The term "brutacaine" was even coined to describe these extreme cases (3-5).

5 EMONO CLINICAL EFFECTS (6)

- Anxiolysis, euphoria (“laughing gas”)
- Light analgesia (increase pain threshold)
  - EMONO is not able to provide general anesthesia
- Conscious sedation
  - the patient can talk, react to environmental stimulations..
- Dissociative state emotional/sensorial
  - Modification of sensory perceptions: visual, auditory
- Protective airway reflex still functional

6 FUNDAMENTAL MECHANISM

- N-methyl-D-aspartate receptor antagonist (7,8)
- Opioid release (9)
- GABA receptor (10)
- Stimulation of noradrenergic neurons in the brainstem, activation of adrenoceptors (11)
GREENHOUSE GAS

MEDICAL USE OF N2O IS < 0,1 % OF TOTAL N2O EMISSIONS
9 VIT B12 DEFICIENCY AND NEUROLOGICAL TOXICITY (chronic exposure or risk patient) (12;12;13;13;14;14-19)
- Chronic, sustained inhalation (G.A, addiction)
- Inhibition of methionine synthetase required for myelin phospholipids
- Vitamin B12 deficiency produces spinal dorsal cord degeneration.
- Clinical symptoms
  - myelopathy, peripheral axonal neuropathy, or both, with combinations of paraesthesia, gait ataxia, sphincter disturbance and pyramidal weakness
  - Reversible after 3 days substitutive treatment.

10 CONTROVERSY WITH N20 DURING GENERAL ANESTHESIA
- Homocysteine level (20)
  - Exposure to < 2 h nitrous oxide is not associated with increase in postoperative plasma total homocysteine concentrations in children (21)
- Postop complications (22)
  - “with nitrous oxide (N2O) 33% decreased odds of 30-day mortality, 17% decreased odds of in-hospital morbidity and mortality, and 41% decreased odds of pulmonary morbidity compared with patients anesthetized without N2O” (23).
- DNA damage(24)
  - Transient effect, clinical validity? (25)
- Postsurgical pain (26)
  - nitrous oxide administration is associated with a reduced risk of chronic postsurgical pain

11 OCCUPATIONAL EXPOSURE
- Slight decrease fertility among 19/7000 dental assistant (>5 h/week) (27)
- No effect (spontaneous abortion) among 4000 Swedish midwives (28)
- “No significant effects on healthcare personnel, associated with the occasional intermittent use of EMONO has been observed” (1)
- “limited data to clearly substantiate concerns about the reproductive toxicity of occupational exposure to N2O at levels below the currently recommended and accepted guidelines” Joseph D Tobias 2013 statement (29)

12 SIMPLE WAYS TO LIMIT EXPOSURE
- Scavenging systems must be available if EMONO still used in the same place
- Moving tank + space ventilation
- Collecting pipe through the window
SAFETY AND RISKS OF NITROUS OXIDE LABOR analgesia (30)

- Nitrous oxide labor analgesia is safe for the mother, fetus, and neonate and can be made safe for caregivers.
- It is simple to administer, does not interfere with the release and function of endogenous oxytocin, and has no adverse effects on the normal physiology and progress of labor

TERATOGENICITY

- N2O” teratogenicity demonstrated in rats cannot be extrapolated to humans” (31;32)
  - Registry study of 5405 cases: frequency of congenital malformations, not higher among women who received nitrous oxide at the time of surgical anesthesia during the first trimester of pregnancy (33)

HISTORICAL BACKGROUND

- Born in UK 1961 for labour pain
- Entonox® (BOC)
- Ambulances, hospital wards, ED, physiotherapy.
- Millions of inhalations achieved in the dental office (adults and children) without any serious adverse effect.

FRANCE

- In the late eighties, EMONO, anecdotal used only in the pre-hospital care and in some delivery rooms.
- In 1990, EMONO (Trousseau Hospital) introduced in hemato oncologic ward: lumbar punctures, bone marrow aspiration…
- Changes in the inhalation system (whistle, colored flavored masks…) to improve pediatric use.

TROUSSEAU CHILDREN HOSPITAL EXPERIENCE

- Academic Hospital; 350 beds
- 25 cylinders (1,5 /3 m3) used daily in 15 different wards
- 2012: 3918 m3 used for 28600 inhalations
- 98% inhalations performed by trained nurses
15.2.1 EMONO Cylinder consumption for 2 weeks in the Hospital Trousseau hematology department

15.3 Inhalation number/year
16  EMONO MULTICENTRIC  FRENCH SURVEY (34)

Side effects during 1019 inhalations

<table>
<thead>
<tr>
<th>Effect</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>62.8 %</td>
</tr>
<tr>
<td>Euphoria</td>
<td>20.1 %</td>
</tr>
<tr>
<td>Change in visual or auditory perception</td>
<td>7.0 %</td>
</tr>
<tr>
<td>Dream</td>
<td>5.7 %</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>3.7 %</td>
</tr>
<tr>
<td>Deep Sedation</td>
<td>2.1 %</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>1.7 %</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1.6 %</td>
</tr>
<tr>
<td>Restlessness</td>
<td>1.5 %</td>
</tr>
<tr>
<td>Nightmare and hallucination</td>
<td>1.2 %</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>1.9 %</td>
</tr>
</tbody>
</table>

17  PAEDIATRIC PROCEDURAL SEDATION BASED ON NITROUS OXIDE AND KETAMINE: SEDATION REGISTRY DATA FROM MELBOURNE ED (35)

- Hospital ED; 67 000 patients/year; 4 years review (2004-2008)
- 2002 patients underwent procedural sedation (PSA); median age 5.7 years
- Nitrous oxide used in 1625 (81%), ketamine in 335 (17%) and midazolam in 39 (2%)
- Laceration repair (38%) orthopedics procedures (33%)
- 89% had no adverse events
- Most adverse events were mild, mainly vomiting (8%)
- Serious adverse events were desaturation in 12 patients, seizures in two patients and chest pain in one patient. The maximum required airway support was bag mask ventilation. No patients aspirated or required intubation
18  ADVERSE EVENTS OF PREMIXED NITROUS OXIDE AND OXYGEN FOR PROCEDURAL SEDATION IN CHILDREN, 7511 INHALATIONS (36)

- 18 months, 46 centers
  - inhalation time: 3 - 50 min ; mean 11 min (SD 6.6)
- Major adverse events in 25 procedures.
  - All events resolved within minutes after discontinuation
  - No patient needed intervention to maintain their airway

19  PROSPECTIVE SAFETY STUDIES WITH EMONO AND N20

Strong and solid data are available
- 1205 EMONO administrations achieved in 661 patients for dental care ; 93% successful (37)
- 600 patients (mean age : 5.45 ) pediatric emergency (38).
- 1018 urinary catheterisation (median age :4.8 ans) cystography; 70 % N20 ; nurse administred (39)
- 1221 administrations 543 patients uncooperative for dental care (40)
• 3 310 administrations mostly pediatric (84 %), (41)
• 35 828 administrations 191 French centers included (42))

20 NATIONAL GUIDELINES FOR EMONO WITH EBM CRITERIA
• “appropriate for pain procedures in children who are able to cooperate” Scottish Intercollegiate Guideline Network.(43)
• “safe for procedural sedation in children, effective for painful procedures in children” Management of procedure-related pain in children and adolescents The Royal Australasian College of Physicians(44)

21 INDICATIONS
Short minor procedures ( less than 30 minutes)
• Lumbar puncture , bone marrow aspiration
• Emergency:
  o laceration repair, clip removal, cast remodelling, pin removal or section, bladder catheterization, nasal packing, fracture with minor deplacement, nail surgery, foreign body, laceration exploration, abscess drainage
• Surgical dressing, burn dressing
• Venous canulation, punctures: lymph nodes, renal biopsy, hemATOMA
• Dental care

22 CONTRA INDICATIONS (very rare)
• Increase intra cranial pressure.
• Head injury
• Bowel obstruction
• Pneumothorax, severe emphysema
• Recent cardiopulmonary bypass, intraocular gas injection

23 DRUG COMBINATION
• local anesthesia (emla cream, lidocaine ....)is needed when skin effraction
• Potential increase of sedation level with opioids or psychotropic (benzodiazepines…) agents is real
• Combination needed when EMONO is inefficient.

24 PREPARATION
Technique is explained with much details to the child with appropriate words.
• Children are encouraged to examine and play with the mask and apply it to their faces.
• "strange" sensations describe and anticipate
• excitement, sensation of warmth, heaviness of the limbs, laughing, paresthesia…
• It must be emphasized that the child will no be asleep and that pain will be relieved, although not necessarily abolished

25  CROSS THE BARRIERS
• Strong safety  efficiency data
• Patient centred medicine (child need)
• Ethical aspect
Excessive misconceptions
• adverse effects, side effects, toxicity, pollution, overestimated
• This method is still underused, and it should be readily available in each emergency and paediatric (adult …) department.

26  TRAINING VIDEO (FRENCH)
http://www.youtube.com/watch?v=pL3Tw_jSAus

27  EMONO USED BY A NURSE FOR DAILY DRESSING AFTER ABSCESS DRAINAGE COMBINATION WITH NALBUPHINE (WEAK OPIOID)
https://www.youtube.com/watch?v=zeiSq0UzQnw
Le MÉOPA pour avoir moins mal

Qu’est-ce que c’est ?
Le MÉOPA est un mélange de deux gaz, l’oxygène et le protoxyde d’azote.

À quoi ça sert ?
Ce médicament spécial permet d’éviter que tu ais mal quand on doit te faire des examens ou des soins qui sont douloureux.

Ce que tu vas faire
1. Tu prends le MÉOPA par une prise d’air dans le masque et tu respiras le mélange pendant que les soins sont effectués.
2. Tu respireras de manière normale et naturelle, sans forcing, lorsque le traitement sera terminé.
3. Si tu as du souci à cause du masque, tu peux prescrire la propranolol.

Ce que tu vas ressentir
Le MÉOPA n’a pas d’effets particuliers. Il peut provoquer une légère pâleur de la peau, une petite douleur au cœur et un petit accès de sueur. Il peut aussi provoquer des brûlures de la gorge si le temps est trop chaud.

On peut utiliser le MÉOPA pour faire :
- des points de suture
- la prise d’une perfusion
- des soins dentaires
- des soins à domicile

En savoir plus sur le MÉOPA :
www.sparadrap.org

© Association SPARADRAP
References


12. Iwata K, OKeefe GB, Karanas A. Neurologic problems associated


(38) Kalach N, Barbier C, el Kohen R, Begon-Lours J, Nyombe-Nzungu P,


