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O_2 and N_2O: Between the Rock and the Hard Place

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Abstract

The use of oxygen and nitrous oxide is part of anesthetic practice since ever. These gases follow anesthetic practice in almost all types of clinical settings, procedures and patients. Their indications and limitations of use are well known.

In recent years a great debate either in literature or in scientific meetings has been addressed, concerning the potential poor outcomes related to the use of certain amounts of oxygen and the use of nitrous oxide.

The objective of this review is to gather information related to these two topics, based on the recent most relevant publications (2000-2016).

Results show that both drugs have its advantages and drawbacks, and it is the clinical objective, the procedure, and the type of patient that will contribute the most for the anesthesiologist final decision.

As a conclusion it was found that, 1) oxygen is a lifesaving drug on one side, but its use should be judicious since its high inspired fraction may have direct implications on that lung wellbeing, and 2) nitrous oxide has its known contraindications that should be taken into consideration and preclude its use when not clinically appropriate, however no evidence exists that indicates a formal discontinuation of its use, and in certain clinical scenarios it can be of relevant utility.

Keywords: Oxygen toxicity; Nitrous oxide indications; Contraindications

Introduction

The practice of anaesthesia has been evolving astonishingly fast in the last decades. From the great monitoring progresses to the new ultra short-acting drugs currently available, most have happened in recent years. In addition, the global awareness on what anaesthesia is and could provide to patients makes our specialty particularly exposed and vulnerable to the public opinion. It is not uncommon that our patients and their families, nowadays specially informed, continually evaluate anesthetic practice.

Evidence is being gathered by publications worldwide, in that anaesthesia is no longer innocuous. This idea is growing in several areas, namely about the indication and safety to anesthetize pediatric patients [1], the use of intravenous infusions of opioids that might be related to the development of hyperalgesia [2], the advantages and drawbacks of the amount of oxygen to use [3] or even the current indication for the use of nitrous oxide [4].

Patient satisfaction with overall healthcare provision in a certain clinical scenario relies very often on non-clinical issues, like nontangible factors of the medical profession and the maintenance of almost like-home routine and comfort. These current needs and expectations are some of the great challenges of the modern medical practice.

Anesthesia as a specialty that is focused on patient safety and satisfaction has improved in several areas that meet these needs, namely the control of postoperative acute pain (POAP), the perioperative management of the occurrence of postoperative nausea and vomiting (PONV), the prevention of intraoperative awareness and many others.

The adoption of certain work methodologies and the avoidance of some special practices that directly or indirectly may compromise a good result, have been growing among anaesthesiologists. The choice of the correct inspired fraction of oxygen during anesthesia, or the use of nitrous oxide as part of the anesthetic technic have been subject of huge debates either in the published literature and the scientific meetings worldwide. This editorial commentary will address a summary of the main arguments on these two topics.

Oxygen

The use of oxygen during anesthesia is ubiquitous; everyone uses it with various inspired fractions (FiO_2). Its use starts before anesthesia, as to pre-oxygenate the patient in order to have some reserve for the apnea period of laryngoscopy and intubation [3]. The first choice starts at this moment, what FiO_2 should one use? One hundred percent is a very attractive choice since, a very good reserve will allow some time for laryngoscopy and intubation, and we all know this is a quite thrilled moment [5], nevertheless there is a price for this relief. Atelectasis are prone to develop with the choice of pre-oxygenation with 100% FiO_2 [3], and this is a major issue, that needs a special intervention, namely the use of positive end expiratory pressure

(PEEP) to maintain the lungs open [3], since even recent investigation have shown that if this is not instituted to the patient, the lung will certainly be poorly aerated [6].

During anesthesia, another conflict decision arises. Should a high FiO_2 be used and promote a decreased probability of surgical site infection [7]. Or, in case of a documented high pulmonary vascular resistance, should a high FiO_2 be used to try and mitigate this situation [8]. These problems may be overcome by high-inspired fractions of oxygen, but this again has a price. Animal studies have shown that oxygen itself, as a supplement in spontaneous ventilation, induced higher lung inflammatory infiltrates when compared to room air ventilation [9]. Furthermore, the connection between high-inspired fractions of oxygen and the development of oxidative stress and the occurrence of an inflammatory lung lesion, formerly designated as acute lung injury, has been extensively documented [10,11].

At the end of procedure, before emergence from anesthesia, another critical period is imminent. On this regard, anesthesiologists frequently use high-inspired fractions of oxygen again to assure some reserve for the immediate post-extubation period. This decision is often critical, since this promotes again the occurrence of reabsorption atelectasis [3], which is a major cause of shunt that will accompany the patient to post-anesthetic care unit and the ward. Physiology principles teach us that the natural supporter of open alveoli is the atmospheric nitrogen, since at sea level it is not absorbed to blood stream; the removal of this supporter by high inspired fractions of oxygen will certainly induce alveolar collapse and the formation of atelectasis areas.

Perhaps, the most prudent and advisable practice, when oxygen is to be used, will be to think of it as a lifesaving drug with its undeniable advantages and uses, and at the same time a gas that has to be handle with special care. The thought that hypoxia may be managed by several means (PEEP, recruitment maneuvers) before the decision of a high-inspired fractions of oxygen should be always in our minds. Table 1 summarizes oxygen uses, side effects and complications.

Positive Actions	Reference	Negative actions	Reference
Pre-oxygenation to prevent hypoxia during laryngoscopy	[3]	Formation of atelectasis & shunt	[3]
Post-oxygenation to reduce emergence hypoxia	[3]	Alveolar collapse & shunt	[3]
May decrease surgical wound infection	[7]	Risk of Acute Lung Injury	[10]
Decrease pulmonary vascular resistance	[8]	Higher lung inflammation in spontaneous ventilation	[9]
Use oxygen judiciously, if possible find other means to improve oxygenation before increasing FiO2, remember the advantages of PEEP and recruiting maneuvers [3].			
FiO_2-Oxygen inspired fraction; PEEP – Positive end-expiratory pressure			

Table 1: Oxygen actions.

Nitrous Oxide

Nitrous oxide (N_2O) accompanies anesthesiologists for several centuries now. It is a more soluble gas than nitrogen, in large concentrations is associated to a second gas effect, diffusion hypoxia and expansion of air-filled spaces in the body [12]. Its role has evolved greatly, since a sole anesthetic to a volatile anesthetic vehicle, and it has its place in common practice. A kind of smoothness has been linked to N_2O action when used with volatiles for mask induction; a unique technic used by anesthesiologists for patients with such a need, like children or especially needle scared adults. These characteristics make of N_2O a key tool, which goes in favour of the patient satisfaction.

Nitrous oxide has several pharmacodynamic effects that include: increases respiratory rate, reduces the ventilatory response to hypoxia and hypercapnia, reduces mucociliary function and neutrophil chemotaxis, impels some myocardial depression (despite increasing sympathetic out flow), increases pulmonary vascular resistance, increases cerebral blood flow, cerebral metabolism and intracranial pressure [12]. It has analgesic effect thought to be mediated by activation of opioid receptors in the periaqueductal grey matter of the midbrain, which leads to modulation of nociception pathways and activation of α2 adrenoreceptors in the dorsal horn of the spinal cord [12].

Recent years' evidence has questioned the use of N_2O on several potential or actual negative actions, namely: Inhibition of methionine synthetase (inactivation B12 vitamin) [13], increase closed spaces volume and pressure [14], reduce protein synthesis promoting surgical site infection [15,16], increase vascular risk in perioperative period [17], increase in PONV [16], and a contribution to degradation of ozone layer as a greenhouse effect gas [18].

Believing that the previous experiences with the use of N_2O were not so devastating, the scientific community was impelled to investigate and try and sort out the true impact of N_2O.

Several studies have been published centering the issue in a quite moderate approach; with a prudent stand, addressing that may be, it is still not the time for the N_2O retirement.

Some studies found that the surgical infection rate was somehow similar with and without N2O use [13,19]. Sanders et al found that the occurrence of cardiovascular events did not increase with N2O [20], results aligned with other authors' studies [17,19]. The PONV linked with N_2O were investigated and it was found that there may be a time relation (longer expositions lead to higher incidence of PONV) [21].

A critical global problem is the sustainability of the planet. It is known that N_2O is several times more dangerous for the ozone layer than for example carbon dioxide. Nevertheless, the contribution of N_2O medical use is almost negligible when compared to the major contributors (industry, agriculture and motor cars) that clearly should be regulated [22].

Concern has been raised if the use of N_2O might have any advantages over its non-use. Several studies have shown some usefulness on the prevention of a potential hyperalgesia related to perfusion of some opioids [2], and the decreased occurrence of postoperative chronic pain [23]. Moreover, the use of N_2O has been established has a good practice [24], namely for promoting faster recoveries in the ambulatory surgery scenario [24].

Apart from all these results, care has been taken on the utilization of N_2O and key opinion leaders from scientific societies have sorted out very prudent and reasonable guidelines for its use, which simple state that it has its place and indication. In addition, no evidence exists that recommends, without any doubt, its discontinuation and, most importantly, health professionals are not at risk when N_2O is used in

modern, state of the art operating rooms with adequate scavenging systems [4,24]. Table 2 summarizes the uses of N_2O in clinical practice, its side effects and complications.

Positive actions	Reference	Reported Negative actions	References	Unproven Negative actions	Reference
Decreases hyperalgesia of opioids	[2,23]	Inhibition of methionine synthetase	[13]		
Decreases chronic postsurgical pain	[23]	Increase bowel volume and pressure in closed spaces	[14]		
Good vehicle of volatiles (less dose)	[24]	Reduce protein synthesis promoting surgical site infection	[15,16]	Similar infection rate	[13,19]
		Increased vascular risk in perioperative period	[17]	No increase in cardiovascular effects	[20,19]
		Increase PONV	[16]	Small increase (resolved with one anti-emetic) Depends on duration	[21]
		Greenhouse effect	[17]	Anesthetic use is not a problem compared to agriculture & industry	[22]
Not enough evidence to support Nitrous Oxide exclusion from clinical practice. No effect no health professionals [4,25]					
PONV-Post-operative nausea and vomiting					

Table 2: Nitrous oxide actions.

Conclusion

Regarding the use of oxygen, care should be taken on the decision about what level of inspired fraction should be used. From one side oxygen is needed in order to assure patient safety in key critical moments, but very high oxygen inspired fractions might induce some type of lung lesion.

N_2O has its known contraindications and should not be used in such clinical settings; nevertheless, evidence is lacking that supports its complete discontinuation since in selected patients and /or procedures it might be of great help.

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