

Safer employment of nitrous oxide in anesthesia machines—a technical simulation

Thomas Mitterlechner¹, Peter Paal², Daniel C Schroeder³, Volker Wenzel⁴, Holger Herff^{3,*}

1 Department of Anesthesiology, Privatklinik Hochrum, Sanatorium der Kreuzschwestern, Rum, Austria

2 Department of Anesthesiology and Intensive Care Medicine, Hospitaller Brothers Hospital Salzburg, Paracelsus Medical University, Salzburg, Austria

3 Department of Anesthesiology and Intensive Care Medicine, University Hospital of Cologne, Cologne, Germany

4 Department of Anesthesiology, Intensive Care Medicine, Emergency Medicine and Pain Therapy, Friedrichshafen, Germany

*Correspondence to: Holger Herff, M.D., holger.herff@uk-koeln.de.

orcid: 0000-0002-7380-4013 (Holger Herff)

Abstract

Several incidents of anesthesia-attributed mortality in the past were caused by misconnection of gas pipelines resulting in ventilation with pure nitrous oxide. A simple safety feature may be to “mark” nitrous oxide with a lower pressure than oxygen and room air within the hospital’s gas pipeline system. Then, any misconnection of gas pipelines could be detected by pressure differences with a manometer in the anesthesia machine. To check technical suitability, we tested maximum achievable nitrous oxide flows of an anesthesia machine at different pressures in the nitrous oxide supply line. Using decreased pressures for nitrous oxide compared to oxygen did not result in decreased nitrous oxide flows, as long as pressure in the nitrous oxide supply line was > 1500 hPa. A concept of different pressures for nitrous oxide and oxygen could be used to technically differentiate between those two gases, and to avoid potentially fatal misconnections.

Key words: anesthetics; central gas supply; inhalation; misconnection; nitrous oxide; oxygen; pressure; safety

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INTRODUCTION

In order to avoid ventilation with pure nitrous oxide, several technical features have been developed in the last decades such as pin index safety systems, or a mechanical interlock between nitrous oxide and oxygen flow meter controls. Thus, death by ventilation with pure nitrous oxide was considered to be a historical incident of the pre-1990s.¹ However, in an analysis of media sources in the last decade, several fatal nitrous oxide-related cases caused by a misconnection of gas pipelines were discovered in Germany, Austria and Switzerland, the UK, the U.S. and Italy.^{2,3}

Since pressure levels of medical gases are reduced in several steps from high pressure in gas tanks to ambient pressure within the anesthesia machine, there may be a simple and cheap technical strategy to discover dangerous nitrous oxide misconnections when providing anesthesia. The pressure within gas tanks is first reduced to a medium pressure for all gases prior to entering the pipelines of the hospital, and is then being reduced in a last step within the anesthesia machine to ambient air pressure. According to our suggestion, nitrous oxide could be “marked” with a lower pressure than oxygen and room air within the hospital’s gas pipeline system. Subsequently, a simple manometer in the anesthesia machine directly prior to flow meter controls could detect any misconnection of gas pipelines by pressure differences (**Figure 1 A, B**).

However, it is unknown whether a reduced nitrous oxide pressure provides adequate flow to ensure constant tidal volumes. We tested maximum achievable nitrous oxide flows at different pressures within an anesthesia machine. Our formal hypothesis was that there would be no differences in maximum gas flows when using different pressures within the nitrous

oxide pipeline.

MATERIALS AND METHODS

No ethical approval was required for this technical simulation. In contrast to oxygen that can be provided by the anesthesia machine in emergency situations at high flows of > 50 L/min, nitrous oxide is usually used at medium or low flows (< 6 L/min). There may be two situations when high nitrous oxide flows may be necessary: first, for inhalative induction *via* face mask *e.g.* using sevoflurane in children with a nitrous oxide—oxygen ratio of 50:50 or higher; and second, for rapid onset of inhalative anesthesia after intubation generally using a nitrous oxide—oxygen ratio of 70:30. Thus, we measured flows provided by an anesthesia machine (Sulla 808, Draeger, Luebeck, Germany) when changing gas pressures.

In order to control gas pressure in the nitrous oxide supply pipeline, we connected an additional pressure-reducer with an included manometer (WIKA, Klingenberg, Germany). In our research laboratory all gases of the central gas supply are pressurized to 5000 hPa (hecto Pascal; 5000 hPa = 5 bar). The pressure reducer in the nitrous oxide tube connected to the anesthesia machine allowed a stepless nitrous oxide pressure reduction between 5000 hPa and 0 hPa.

We first determined the maximally achievable flow for nitrous oxide that was 10 L/min at a non-reduced pressure of 5000 hPa. Thus, we added 10 L/min oxygen to achieve a mixture of 50% nitrous oxide and 50% oxygen simulating inhalative anesthesia induction *via* face-mask. We then reduced pressure within the nitrous oxide supply line in steps of 500 hPa. When the nitrous oxide flow decreased due to decreased supply line pressure, we decreased the oxygen flow manually at the anesthesia machine to achieve a constant 50:50 nitrous

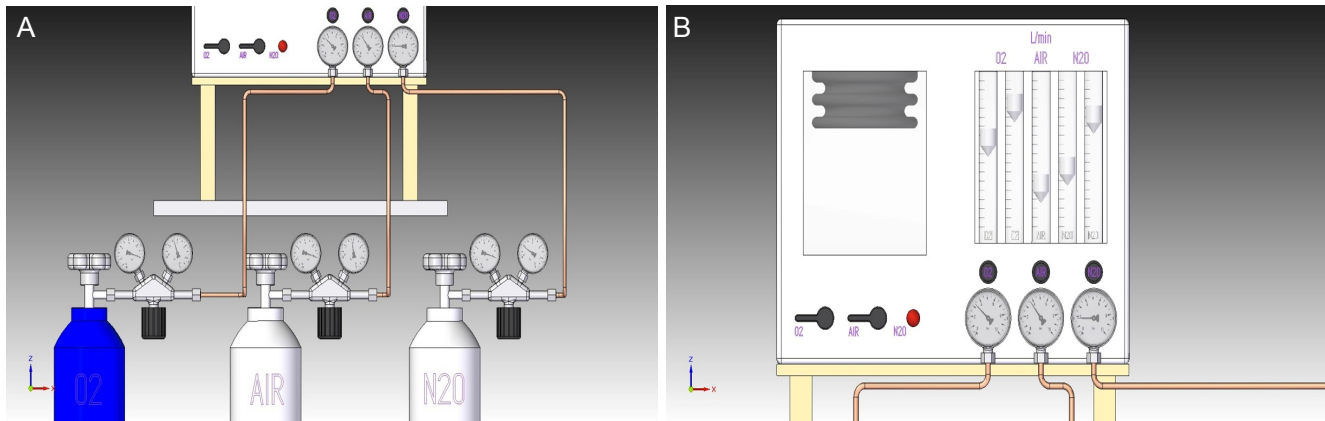


Figure 1: Proposed setting with different pressures.

Note: (A) Gas tanks with the adjustable pressure transducers. All tanks are filled to their maximum pressure (left manometer). Gas pipeline line pressures for oxygen (and air) are explicitly higher than that for nitrous oxide (right manometer). (B) Pressure levels in gas pipelines generated by pressure transducers fixed on the gas tanks can be controlled with a manometer in the anesthesia machine. Any misconnection between nitrous oxide (N_2O) and oxygen (O_2) can be detected there by comparing pressures.

Table 1: Results for gas flows depending on changes of nitrous oxide (N_2O) supply line pressure

Pressure N_2O line (hPa)	O_2 flow at 50% N_2O (L/min)	O_2 flow at 70% N_2O (L/min)	N_2O flow at 50% N_2O (L/min)	N_2O flow at 70% N_2O (L/min)	P between N_2O flows
5000	10±0	4.2±0	10±0	10±0	
4500	10±0	4.2±0	10±0	10±0	
4000	10±0	4.2±0	10±0	10±0	
3500	10±0	4.2±0	10±0	10±0	
3000	10±0	4.2±0	10±0	10±0	
2500	10±0	4.2±0	10±0	10±0	
2000	10±0	4.2±0	10±0	10±0	
1500	10±0	4.2±0	10±0.2	10±0	0.343
1000	7.8±0.2(0.03)	3.8±0.2(0.001)	7.8±0.2(0.001)	9.0±0.4(0.001)	0.001
500	4.2±0.6(0.001)	1.8±0.4(0.001)	4.2±0.6(0.001)	4.0±0.6(0.001)	0.71
0	0±0(0.001)	0±0(0.001)	0±0(0.001)	0±0(0.001)	

Note: N_2O flows automatically decrease in dependence of decreasing pressures in the N_2O supply line (pressure N_2O line). Oxygen (O_2) flows are reduced manually at the anesthesia machine to maintain stable nitrous oxide - oxygen ratios. Data are given as the mean ± SD. Distribution of data was analyzed using Kolmogorov-Smirnov analysis; we used unpaired Student's *t*-test for comparison of nitrous oxide flows at a given pressure between the two gas mixture ratios; we further used paired Student's *t*-test to detect changes in gas flow for each gas in regard of reduced nitrous oxide supply line pressure (comparison within group). Numbers in brackets represent *P* value within group compared to previous result; 1000 hPa is 1 bar.

oxide-oxygen ratio; the pressure in the oxygen supply line was always constant at 5000 hPa. In the next attempt we started at 0 hPa and no flow, and increased in steps of 500 hPa always keeping the 50:50 nitrous oxide-oxygen ratio until we reached 5000 hPa. This setting was performed 10 times. This entire experiment was repeated for the mixture with a nitrous oxide-oxygen ratio of 70:30, representing the phase after intubation. At the maximum nitrous oxide flow of 10 L/min a flow of 4.2 L/min oxygen was necessary to achieve a 70% nitrous oxide fraction in the ventilating gas mixture; the oxygen flow was adapted to a reduced nitrous oxide flow to maintain the ratio of 70:30 accordingly to the previous setting. During the experiment we automatically ventilated a test lung (5600i, Michigan Instruments, MI, USA) (tidal volume 500 mL, respiratory rate 12/min) and surplus fresh gas flow evaded into the exhaust system of the laboratory in order to avoid polluting room air with nitrous oxide.

Statistical analysis

Data are given as the mean ± SD. Distribution of data was analyzed using Kolmogorov-Smirnov analysis; we used unpaired Student's *t*-test for comparison of nitrous oxide flows

at a given pressure between the two gas mixture ratios; we further used paired Student's *t*-test to detect changes in gas flow for each gas in regard of reduced nitrous oxide supply line pressure (comparison within group) (SPSS 15.0, SPSS, Chicago, IL, USA).

RESULTS

Nitrous oxide flows were constant for pressures ≥ 1500 hPa (1.5 bar) in the nitrous oxide supply line using both nitrous oxide and oxygen mixtures and were still sufficiently high for routine use at 1000 hPa. Details are given in **Table 1**.

DISCUSSION

Nitrous oxide use is being controversially discussed in the last 20 years. Despite many “modern” western anesthetists regarding nitrous oxide being obsolete, it is still widely used and may have its indications.⁴⁻⁶ The World Health Organization is still recommending nitrous oxide in the Actual 20th Model List of Essential Medicines (March 2017).⁷ In conclusion, if liked or not by many anesthetists, nitrous oxide will be used in many parts of the world for many further years.⁸

All fatal cases related to ventilation with pure nitrous



oxide were due to misconnection of supply lines prior to the flow meters in the anesthesia machine.^{2,3} When nitrous oxide flows out of the pipelines instead of oxygen, this can only be discovered by oxygen meters that are now mandatory in modern anesthesia machines *e.g.* in the European Union (EN 740).^{2,3} However, these devices obviously failed in our studies in the last decade, and therefore we propose that any additional strategy to increase safety should be used even in the industrialized world. Further, many of our old anesthesia machines have been sold or donated to hospitals in lower income countries and will be on duty for many further years.⁸ Thus, in many places in the world nitrous oxide may be used while oxygen meters may not be standard. This may leave many patients to the potential risk of misconnections.⁸

In contrast to oxygen meters, pressure reducers are automatically present wherever nitrous oxide is used. Since nitrous oxide is stored in liquid form at 51,000 hPa (51 bar) in central gas supply tanks, it has to be depressurized prior to streaming into the supply lines. The use of different pressures for nitrous oxide and oxygen in the pipelines should be technically possible wherever nitrous oxide is used, allowing differentiation between nitrous oxide and oxygen with a simple manometer at the end of supply lines. Further, automated locks for oxygen are integrated in modern anesthesia machines, in case pressure falls below a preset value. We propose that nitrous oxide pressure levels are routinely set below the preset lock pressure for oxygen. Thus, the anesthesia machine would not work if oxygen and nitrous oxide were misconnected even in the oldest and less sophisticated anesthesia machine.

The mixtures with 50% and 70% nitrous oxide in this study were chosen arbitrarily representing high flow employment of nitrous oxide in the induction phase of anesthesia. We further deliberately used an elderly anesthesia machine with mechanic flow meter controls (rotameters); thus, despite potentially less accuracy compared to more modern electronic devices, our values could not be influenced by any unknown calculations within the anesthesia machine depending on pressure changes in gas supply lines.

A possible inaccuracy applies to the mechanical pressure reducer/manometer. However, the purpose of this study was to determine if a pressure of substantially less than the 5000 hPa in the nitrous oxide line results in a sufficient nitrous oxide flow into the anesthesia machine. In regard of a pressure of 1500 hPa being sufficient to achieve the highest possible nitrous oxide flow preset by the anesthesia machine, our mechanical pressure reducer thus seemed to be precise enough to answer the formal hypothesis. There are several further limitations to our study. First, we tested our concept in a laboratory model, which cannot be completely extrapolated to the setting in an operation theatre. Further, we explicitly do not propose any specific pressure that should be used for different gases. We leave that to manufacturers and technicians. There may be technical reasons for minimum or maximum pressures that we are not aware of. Moreover, we limited this experiment to a 70:30 and 50:50 nitrous oxide-oxygen ratio, although other mixtures are possible.

In summary, a concept of different pressures for nitrous oxide and oxygen could be used to technically differentiate between those two gases, and to avoid potentially fatal misconnections.

Author contributions

TM: Investigation, data curation, formal analysis, visualization and original draft preparation. PP: Methodology, conceptualization, formal analysis, review & editing. DCS: Investigation, formal analysis, review & editing. VW: Methodology, supervision, review & editing. HH: Resources, conceptualization, methodology, investigation, formal analysis, visualization and original draft preparation. All authors have read and approved the final version of manuscript for publication.

Conflicts of interest

No author has any competing interests.

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Data sharing statement

Datasets analyzed during the current study are available from the corresponding author on reasonable request.

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Open peer review report

Reviewer: Noritomo Fujisaki, Hyogo College of Medicine, Japan.

Comments to authors: Authors referred fundamental method to avoid patient from inhalation of pure nitrous oxide by checking the different pressure between two gases. To minimize the risk of gas delivery system and to protect the life of a patient in danger from the fatal condition due to the operation, anesthesiologist must avoid oxygen delivery system failure and must check anesthesia machines before the employment of them. But inappropriate connection of gas pipelines was actually difficult to recognize during anesthesia without monitoring of oxygen concentration and was hardly conceivable. Author's efforts for providing a system that can reduce the incidence of human error and technical error to a very low level are to be highly praised.

REFERENCES

1. Caplan RA, Vistica MF, Posner KL, Cheney FW. Adverse anesthetic outcomes arising from gas delivery equipment: a closed claims analysis. *Anesthesiology*. 1997;87:741-748.
2. Herff H, Paal P, von Goedecke A, Lindner KH, Keller C, Wenzel V. Fatal errors in nitrous oxide delivery. *Anaesthesia*. 2007;62:1202-1206.
3. Herff H, Paal P, Lindner KH, von Goedecke A, Keller C, Wenzel V. Fatalities due to nitrous oxide. Complications from mistakes in nitrous oxide supply. *Anaesthesist*. 2008;57:1006-1010.
4. de Vasconcellos K, Sneyd JR. Nitrous oxide: are we still in equipoise? A qualitative review of current controversies. *Br J Anaesth*. 2013;111:877-885.
5. Leslie K, Myles PS, Kasza J, et al. Nitrous oxide and serious long-term morbidity and mortality in the evaluation of nitrous oxide in the gas mixture for anaesthesia (ENIGMA)-II trial. *Anesthesiology*. 2015;123:1267-1280.
6. Myles PS, Leslie K, Chan MT, et al. The safety of addition of nitrous oxide to general anaesthesia in at-risk patients having major non-cardiac surgery (ENIGMA-II): a randomised, single-blind trial. *Lancet*. 2014;384:1446-1454.
7. <http://www.who.int/medicines/publications/essentialmedicines/en/>.
8. Alai AN. Nitrous oxide administration. <https://emedicine.medscape.com/article/1413427-overview#a4>. Accessed 2017-06-14.