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ORIGINAL ARTICLE

Aerosol generation during paediatric procedural sedation with continuous-flow nitrous oxide suggests a low risk of airborne viral transmission to health-care workers

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Aim: Inhaled nitrous oxide is a common form of procedural sedation in paediatric care. During the COVID-19 pandemic, concerns about potential aerosol generation and associated viral transmission to health-care workers have led to controversy regarding its use. We aimed to measure the degree of aerosol generation during continuous flow nitrous oxide sedation to inform future guidelines.

Methods: Aerosol numbers in the respirable range were measured using a particle counter during 30 procedures undertaken in children under nitrous oxide sedation in the Emergency Department.

Results: Changes from baseline measurements were greatest in particles in the 0.3 μm range. The mean increase from baseline in 0.3 μm particles per cubic metre was 18 022 (95% confidence interval (CI) 5949–30 096) after the child entered the room, and 2931 (95% CI −4407 to 10 269) during nitrous oxide administration.

Conclusion: Variation of respirable particle numbers from baseline levels was no greater during nitrous oxide administration than for breathing and talking asymptomatic children. These results suggest the additional risk of airborne viral transmission to staff during inhaled nitrous oxide sedation is low.

Key words: aerosols; child; COVID-19; hypnotics and sedatives; viruses.

What is already known on this topic

1 Viruses may be transmitted by aerosols from patient to health-care worker.
2 Recommendations have been made during the COVID-19 pandemic for clinicians to avoid procedures which may generate aerosols.
3 The actual risk of aerosol generation by inhaled nitrous oxide has not previously been documented.

What this paper adds

1 The additional aerosols above baseline generated by a child are mostly below 5 μm in diameter, primarily at the 0.3 μm range.
2 Using continuous flow nitrous oxide delivery with gas scavenging and a cushion mask the aerosol numbers were no greater than for an unmasked asymptomatic child.
3 Recommendations regarding inhaled nitrous oxide need not be restrictive due to concerns about aerosol generation.

Inhaled nitrous oxide (N_2O) is a common agent used for procedural sedation in paediatric practice across a range of subspecialties including Emergency Medicine, Oncology and Radiology.[1] Concerns about aerosol transmission of viral particles to health-care workers (HCW) during the COVID-19 pandemic resulted in the use of N_2O being curtailed by a number of professional bodies and institutions. In the absence of specific evidence, this recommendation was based on concurrent guidelines for high-flow oxygen therapies, in addition to evidence that infected children may be asymptomatic.[2] The guideline from the Australasian College for Emergency Medicine (ACEM) states that there is 'insufficient and conflicting information' about the aerosol-generating potential of inhaled N_2O.[3] The New South Wales Health guideline states that 'Nitrous oxide sedation should be avoided because of high rates of aerosolisation'.[4] No studies published to date have quantified the risk of aerosol generation from the use of N_2O in clinical practice, and this uncertainty has led to conservative decisions designed to protect HCW.

The inclusion of inhaled N_2O as a potentially aerosol-generating procedure (AGP) mostly likely stems from the theoretical risk from a relatively high gas flow over a moist mucosal surface. However, aerosol generation using Hudson facemask oxygen (at 15 L/min) and high flow nasal oxygen (at both 30 and 60 L/min) has now been demonstrated to be low in a laboratory clean room.[5] Continuous flow N_2O might be expected to

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have similarly low levels of aerosol generation and may be even lower due to a more closely fitting mask, the use of a viral filter in the circuit, and scavenging of expired gas into the circuit. Some continuous flow systems have been described as having a very low risk for developing positive pressure in normal spontaneous (non-forced) ventilation, and therefore at low risk for creating aerosols,[1] although aerosol counts from these systems have not been confirmed experimentally.

HCW infection by aerosols depends on the carriage of an adequate number of viable microbial particles before penetration of host tissues.[6] Sampling of aerosols for viral particles is technically very challenging,[7] but measurement of aerosol particle numbers is a reasonable proxy as without aerosol generation airborne transmission is not possible. The aim of this study was to quantify the level of aerosol generation during clinical practice while delivering N_2O by continuous flow for procedural sedation in children, and therefore determine the likely hazard due to aerosol-based viral transmission that this may represent for HCW.

Fig. 1 Particle counter (circled in red) positioned at the head of the bed to simulate staff member face level.

Methods

Setting

The study was conducted from October 2020 to May 2021 in the mixed Emergency Department (ED) of a metropolitan tertiary hospital with 18 000 paediatric presentations annually, situated in Melbourne, Victoria, Australia. All procedures were performed in the same normally pressured procedure room measuring $3.7 \times 2.7 \times 4.6$ m^3 (46 cubic meters) with 6 air exchanges per hour.

Subjects

The study was conducted during medically indicated procedural sedation with N_2O in a convenience sample of 30 patients aged 2–14 years without respiratory symptoms. Procedures performed included fracture reduction and casting, wound suturing, removal of subcutaneous foreign bodies, and eye irrigation.

Equipment and procedures

N_2O and oxygen were delivered with a continuous flow device (Quantiflex MDM, Matrix Medical Inc., Orchard Park, NY, USA) at 6–20 L/min via a disposable circuit with a viral filter attached to a cushion mask. Staff in the procedure room wore personal protective equipment (PPE) as recommended by the state health department at the time. Otherwise, there was no change to the usual process of patient care. Parents and carers present wore surgical masks at all times. The child was the only person in the room not wearing a respiratory mask.

Airborne particle numbers were measured with a particle counter (3016-IAQ; Lighthouse, Freemont, CA, USA) mounted on a stand with the air intake port at a height of 1.45 m to simulate the facial level of standing staff members, and placed against the head of the patient trolley (Fig. 1). Particle numbers were recorded in six particle sizes (0.3, 0.5, 1.0, 2.5, 5.0 and 10 μm) obtained in 60 s intervals at seven standardised time points during the procedural process:

- empty room prior to patient entry (baseline)
- after patient entry to the procedure room (unmasked patient talking)
- during initial N_2O administration
- during the procedure
- during N_2O washout with oxygen
- after mask removal
- after staff and patient had left the room

Positive controls were also obtained after each procedure using a single puff from a salbutamol metered-dose inhaler (MDI), and with 4 mL saline nebulised in a standard Hudson nebuliser with a gas flow of 6 L/min.

On a technical note, devices used for environmental monitoring often report aerosols primarily by particle mass (e.g. PM_5 refers to the mass of all particles below 5 μm in size). However, this is problematic where there is a mixture of particle densities present. Respiratory water-based particles will have a density of close to 1.0 g/cm^3 whereas respirable dust particles have been found to be 4% water and 69% carbon-based organic matter which will have a much greater density.[8] As the Lighthouse particle counter used in this study reports both the number and mass of particles, numerical reporting of particles was selected as the appropriate choice for this study where the measured particles were likely to be a mixture of dust and water.

Particle numbers were downloaded from the counter and analysed in an Excel spreadsheet (Microsoft Corp., Redmond, WA, USA). As baseline particle numbers in the room were slightly different on each occasion, the variance from the initial measurement on each occasion was calculated. Results are reported as mean particles per cubic metre as measured over a 60 second interval in the 30 cases. The study was approved as a quality improvement activity by the Austin Health Office for Research and was determined not to require submission to the Human Research Ethics Committee, nor require patient or carer consent.

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Table 1 Mean airborne particle counts per cubic metre during phases of procedures ($n = 30$)

Particle size	Pre-entry	Post-entry	Nitrous	Procedure	Washout	Mask off	Exit	MDI	Nebuliser
0.3 μm	129 534	147 556	132 465	166 826	137 068	152 677	127 674	839 488	249 203 945
0.5 μm	27 651	37 280	34 031	66 050	43 225	54 478	29 946	323 152	121 955 668
1.0 μm	24 991	32 760	38 681	88 227	60 800	63 413	26 203	338 055	34 733 386
2.5 μm	23 013	33 772	49 687	141 235	96 267	83 319	24 932	268 438	3 852 476
5.0 μm	10 123	14 314	28 240	95 267	60 964	45 414	9264	25 932	45 202
10 μm	6250	10 300	14 479	53 289	25 414	19 376	5768	7098	353

MDI, metered-dose inhaler.

Results

Baseline (pre-entry) particle counts demonstrated that the smallest particles (0.3 μm) predominated. The number of particles decreased as particle size increased (Table 1, Fig. 2). When an unmasked patient (with masked staff and parent) entered the room, the change in particle counts was primarily in particles below 5 μm in diameter, and most prominently in particles of 0.3 μm (Fig. 3).

The mean differences from pre-entry baseline levels (with 95% confidence intervals (CIs)) for 0.3 μm particle counts are demonstrated in Figure 4.

The mean difference in particle count during post-entry (talking unmasked patient: 18 022; 95% CI 5949–30 096) and N_2O administration phases (2931; 95% CI −4407 to 10 269) were also compared to positive controls of an MDI puff (709 954, 95% CI 568 379–851 529) and saline nebulisation (249 203 945, 95% CI 194 685 598–305 150 231) (Fig. 5).

Discussion

Respiratory particles range from 0.5 to 20 μm in diameter, with the larger droplets (>20 μm) likely to fall directly to the ground, smaller droplets (5–20 μm) falling more slowly, and the smallest particles (<5 μm) more likely to be suspended in the air for a longer period.[7] These droplet nuclei (or aerosols) are more likely to be inhaled and reach the lower respiratory tract.[7] The risk of transmission of viruses from larger particles is likely to much greater due to their greater volume and therefore higher viral load, but are relatively more avoidable in medical settings by use of contact and droplet precautions.

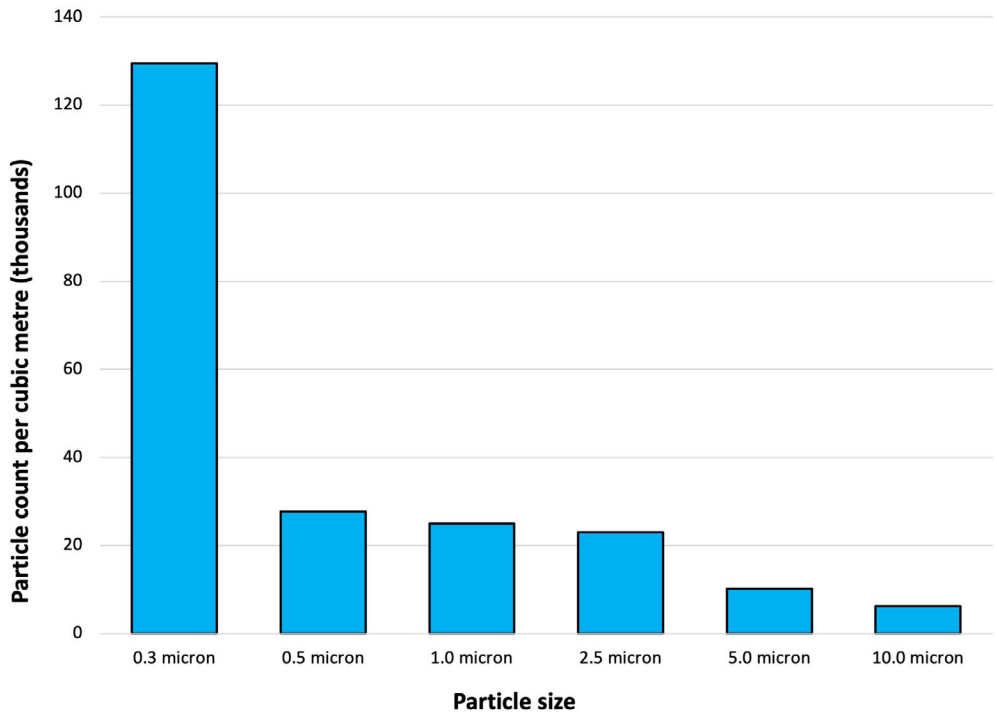

Fig. 2 Particle numbers detected in empty procedure room prior to patient entry.

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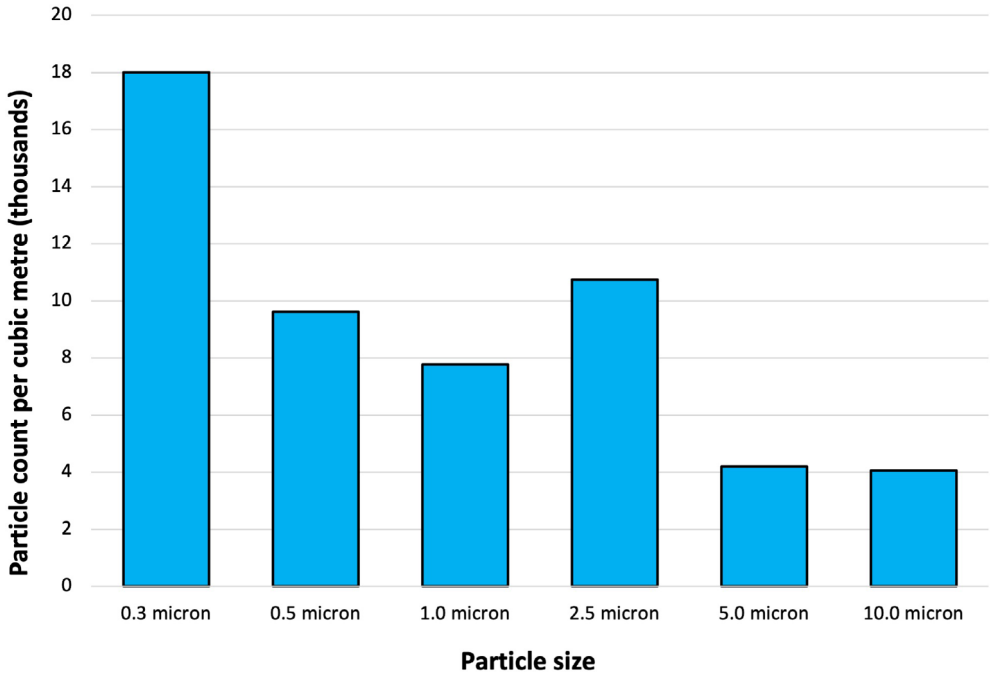

Fig. 3 Variation from baseline (empty room) of particle numbers after patient entry to procedure room.

However, precautions against viruses aerosolised in small particles are more difficult and expensive, requiring filtered masks and face barriers.

Since the beginning of the COVID-19 pandemic, much debate in the clinical sphere has been concerned with defining AGPs which require these greater precautions. AGPs have been defined

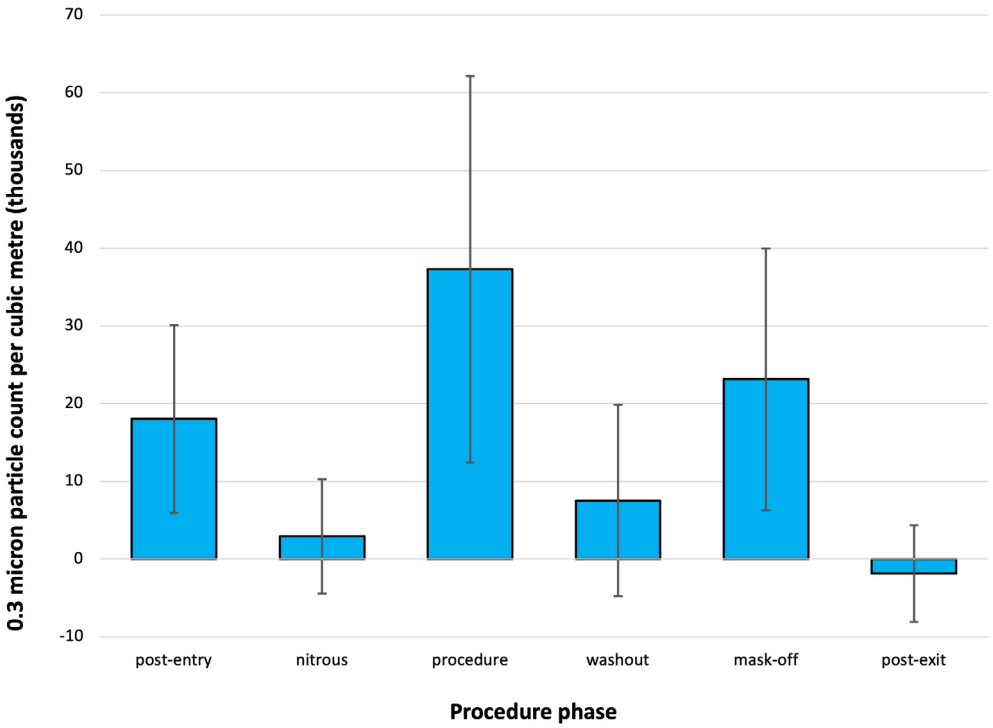

Fig. 4 Variation from baseline of 0.3 μm particles at sequential stages of the sedation procedure (mean values with 95% confidence intervals).

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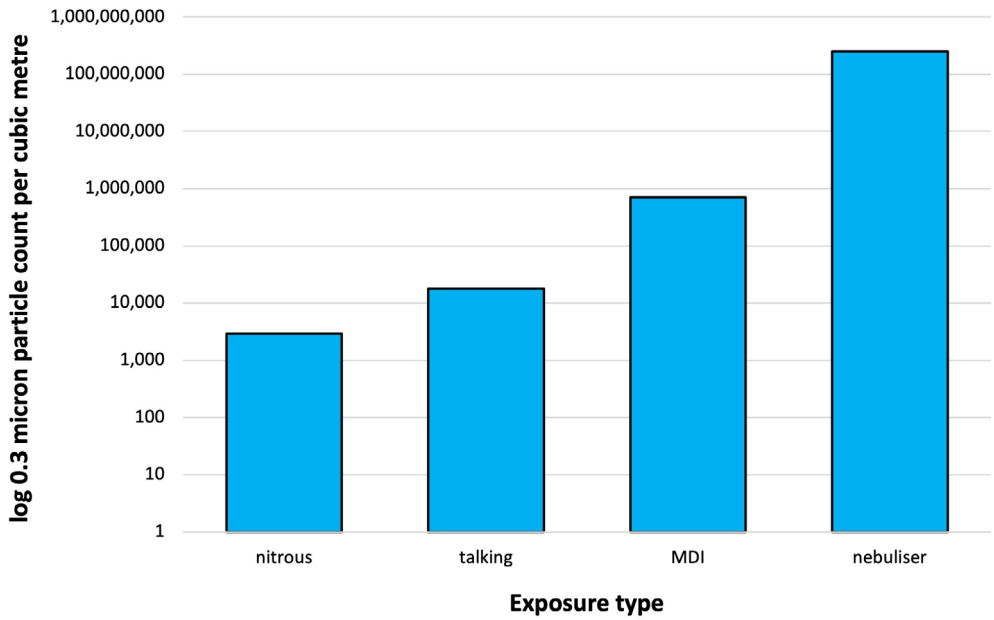

Fig. 5 Comparison of 0.3 μm particle counts for different exposures (logarithmic vertical axis).

as any procedure that 'results in an infectious aerosol beyond that which would normally be released by a patient coughing, breathing, or talking, presenting an increased risk to any HCW in proximity to the patient'.[7] There is little doubt that symptomatic SARS-CoV-2 infection can create aerosols with viable virus,[9] and that AGPs should be avoided in these patients. However, despite routine symptom screening of patients, there are concerns of potential risk from performing AGPs in asymptomatic but nonetheless infectious patients.

Following the previous SARS-CoV-1 epidemic, a systematic review of transmission events to HCW who were most likely protected only by contact and droplet precautions demonstrated a statistically significant association with tracheal intubation, non-invasive ventilation, tracheotomy and manual ventilation before intubation.[6] A statistically significant transmission risk was not found for other procedures such as manual ventilation, endotracheal aspiration, suction of body fluids, bronchoscopy, nebuliser treatment, administration of oxygen, high flow oxygen, manipulation of oxygen or BiPAP masks, defibrillation, chest compressions, insertion of nasogastric tube, chest physiotherapy and collection of sputum.[6] However, since the beginning of the SARS-CoV-2 pandemic, almost all of those procedures have been included in lists of AGPs, including procedures appearing similar to high-flow oxygen such as N_2O sedation. This has an impact not only on the usage of precious high-grade PPE, but also on patients whose care is altered by the consequent changes in practice.

Other medical craft groups have sought to determine the aerosol risk of their normal practice more accurately, as the exclusion of aerosol generation by specific procedures should allow them to be safely continued with contact and droplet precautions during respiratory pandemics. Investigations by groups working in ophthalmology,[10] otorhinolaryngology,[11] and dentistry[12] have sought to determine the aerosol risk of their normal practice. While some devices and procedures designed to reduce aerosol exposure have shown greater risk on empiric testing,[13] some procedures that were initially avoided due to theoretical risks have been demonstrated to be low risk.[10] Fortunately for paediatric practice, children appear to have a lower risk of being infected with SARS-CoV-2, and when infected seem to be less infectious to others than they are with other viruses,[14] possibly due to differences in tissue expression of receptors.[15] However, theoretical risks in paediatric practice have still been stated in relation to nebulised medication, high-flow oxygen therapies, intubation, and inhaled N_2O administration. The often unpredictable behaviours of children, including crying or shouting, are also considered a factor that might increase the risk of aerosol generation.

In our study, the particle counts that HCW were exposed to during N_2O administration were no greater than, and possibly lower than, an unmasked talking child. Higher particle levels during the procedure phase most likely represent movement of staff, and plaster dust in some cases, as particle levels fell again during the washout phase. These results appear to confirm that our longstanding practice of using a close-fitting facemask and gas scavenging during the use of continuous flow N_2O act to prevent an increase in aerosol levels. HCW should therefore be safe in administering inhaled sedation in asymptomatic patients by this method without the need for aerosol precautions.

Limitations

This study is limited by being conducted at a single site and with one type of continuous-flow N_2O system (although common in many Australian EDs), which may limit generalisability. The ideal experimental conditions of near-zero baseline particle levels in a clean room were not possible in this clinical environment, and so a small portable particle counter was required and variance from

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the baseline levels was calculated. This study also measured aerosol generation alone and cannot make any conclusions on the viral load within those aerosols.

Conclusions

Use of continuous-flow nitrous oxide for paediatric procedural sedation in our cohort generated no more aerosol particles than a child who was breathing and talking. It also produced aerosols at least 4 orders of magnitude less than nebulisation therapy. This suggests that nitrous oxide sedation delivered by continuous flow with a close-fitting cushion facemask and gas-scavenging has a low risk of aerosol viral transmission to health-care workers in the event that the child has a subclinical viral infection. Similar techniques could be employed in future to determine the aerosol-generating potential of other clinical procedures.

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