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Is high-concentration Nitrous oxide the safest option for short periods of procedural sedation in Paediatric Emergency Medicine

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Dear Editor,

Since the 1990's there has been an increase in the number of invasive procedures being performed in paediatric emergency departments (PEDs) using procedural sedation and analgesia (PSA)[1,2]. A recent survey of British and Irish PEDs found that 82% of departments preformed PSA[2].

Timely PSA provides rapid pain relief and by allowing procedures to be completed in the PED reduces the need for hospital admission. While there are many benefits of PSA, as yet there is no perfect medication or combination of medications that provides PSA without any risk of adverse event.

Nitrous Oxide (N_2O) is a commonly used agent for PSA in PEDs. In general, N_2O at concentrations up to 50% provides minimal sedation, with a low reported incidence of severe adverse events (SAEs). At concentrations of 50% -70% it is more likely to generate moderate or deep sedation (with, in theory, greater potential for SAEs)

To inform PSA practice, we preformed a literature review to identify the incidence of SAEs, significant interventions in response to SAEs and unplanned hospital admissions, occurring in children aged one to seventeen years, undergoing PSA using N_2O at concentrations between 51% and 70% in the PED setting.

Methodology from preferred reporting items for systematic reviews and meta-analyses statement (PRISMA) was followed. A comprehensive search of three electronic databases: Cochrane Central Register of Controlled Trials, Ovid MEDLINE and PubMed Central was completed.

SAEs were defined as: apnoea, laryngospasm, hypotension, bradycardia, complete airway obstruction, clinically apparent pulmonary aspiration, permanent neurologic injury, or death[3]. Significant interventions were defined as: positive pressure ventilation, endotracheal intubation, administration of vasoactive medication, administration of neuromuscular blockade or performance of chest compressions[3].

An assessment of the risk of bias in included randomised controlled studies was performed using the of the Cochrane Bias Assessment Tool for randomised trials. An assessment of the risk of bias in included observational studies was performed using the Cochrane Risk of Bias in Non-randomized Studies tool.

Three RCTs (878 PSAs) and five observational studies (2,552 PSAs) were identified. The incidence of SAEs was 0.3 per 1,000 PSAs (1 episode of bradycardia which responded to the administration of oxygen). There was no reported case of intervention in response to SAEs. The incidence of unplanned hospital admission was 0.3/1,000 PSAs. The risk of bias assessment found two studies at low risk of bias, five studies at moderated risk of bias and one study at high risk of bias.

The incidence of SAEs identified is significantly lower than that reported with other commonly used PSA agents used in the PED (ketamine, propofol, midazolam, chloral hydrate)[4].

Given the risk of bias assessment, a concern is that underreporting of SAEs in studies could lead to underestimation of the incidence of SAEs. However, the incidence of SAEs, interventions in response to SAEs and unplanned hospital admissions, were all low.

In summary, high-concentration N_2O is identified as having a lower incidence of SAEs than other PSA agents. The favourable safety profile should be considered when choosing a PSA agent in the PED.

Declarations of Conflicts of Interest:

None declared.

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