The Utility of High-Flow Oxygen During Emergency Department Procedural Sedation and Analgesia With Propofol: A Randomized, Controlled Trial

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Study objective: We determine whether high-flow oxygen reduces the incidence of hypoxia by 20% in adults receiving propofol for emergency department (ED) sedation compared with room air.

Methods: We randomized adults to receive 100% oxygen or compressed air at 15 L/minute by nonrebreather mask for 5 minutes before and during propofol procedural sedation. We administered 1.0 mg/kg of propofol, followed by 0.5 mg/kg boluses until the patient was adequately sedated. Physicians and patients were blinded to the gas used. Hypoxia was defined a priori as an oxygen saturation less than 93%; respiratory depression was defined as an end tidal CO_2 greater than 50 mm Hg, a 10% absolute change from baseline, or loss of waveform.

Results: We noted significantly less hypoxia in the 59 patients receiving high-flow oxygen compared with the 58 receiving compressed air (19% versus 41%; $P=.007$; difference 23%; 95% confidence interval 6% to 38%). Respiratory depression was similar between groups (51% versus 48%; difference 2%; 95% confidence interval −15% to 22%). We observed 2 adverse events in the high-flow group (1 hypotension, 1 bradycardia) and 2 in the compressed air group (1 assisted ventilation, 1 hypotension).

Conclusion: High-flow oxygen reduces the frequency of hypoxia during ED propofol sedation in adults. [Ann Emerg Med. 2011;58:360-364.]

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INTRODUCTION

Background

Some emergency physicians administer supplemental oxygen during procedural sedation and analgesia to increase oxygen reserves, thus hoping to minimize the likelihood of hypoxia. The American Society of Anesthesiology and the American Academy of Pediatrics recommend supplemental oxygen for patients undergoing deep sedation and suggest it be considered during moderate sedation.[1,2] However, a previous trial of low-flow nasal oxygen during emergency department (ED) propofol sedation did not identify a clinically significant reduction of hypoxia.[3] High-flow oxygen, however, is more likely to be beneficial because apnea with propofol develops and resolves quickly,[4] and a healthy adult or adolescent when fully preoxygenated can tolerate on average 6 minutes of apnea before oxygen desaturation.[5]

Importance

If high-flow supplemental oxygen can reduce the incidence or severity of hypoxia during procedural sedation with propofol, it could be used routinely for this purpose.

We wished to determine whether high-flow (15 L/minute) supplemental oxygen by nonrebreather mask reduces the incidence of hypoxia by 20% during ED propofol procedural sedation in adults. Our secondary objectives were to compare the frequencies of subclinical respiratory depression and other adverse events.

MATERIALS AND METHODS

Study Design and Setting

We conducted this prospective, randomized, double blind, placebo-controlled study between January 2009 and November 2010 at the Albert Einstein Medical Center, a Level I trauma center in Philadelphia, PA, with an annual census of approximately 100,000 visits. Our institutional review board approved the study, and informed consent was obtained. The trial was not preregistered but was conducted and analyzed in accordance with its original protocol.

Selection of Participants

We included adults (>18 years of age) chosen for propofol procedural sedation in accordance with our standard practice.

Editor's Capsule Summary

What is already known on this topic

It remains unclear whether supplemental oxygen is helpful during procedural sedation.

What question this study addressed

Does adding high-flow supplemental oxygen during propofol procedural sedation reduce hypoxia?

What this study adds to our knowledge

Adding high-flow oxygen decreased the frequency of hypoxia by 23% in this 117-adult randomized double-blind trial.

How this is relevant to clinical practice

There is less hypoxia during propofol procedural sedation when high-flow supplemental oxygen is added.

We enrolled patients 24 hours a day, 7 days a week during the study period. We excluded patients with severe chronic obstructive pulmonary disease, chronic oxygen use, hemodynamic instability, respiratory distress, pregnancy, allergy to any of the study drugs, or inability to provide informed consent.

We used a computer-generated, concealed randomization schedule to assign patients to receive either high-flow oxygen or room air, both administered at 15 L per minute by a nonrebreather mask. The treatment team was blinded by delivering the gases with one of 2 identical-appearing D-tanks marked "A" and "B." Patients wore a capnography nasal cannula under their mask and received 5 minutes of gas administration before an initial propofol dose of 1 mg/kg according to ideal body weight. The treating physicians used their discretion to administer an additional 0.5 mg/kg dose to achieve and maintain the desired level of sedation. The ED staff had standard electronic monitoring (capnography, pulse oximetry, pulse rate, and blood pressure) available to them at all times and applied their usual clinical judgment for monitoring and intervention for adverse events.

Blinded, separate research physicians enrolled patients and recorded data. These individuals had participated in previous sedation studies and were trained in procedural sedation, the study protocol, and the monitoring devices. They had no clinical responsibilities and were instructed to observe and document but not interact with the clinical team or influence their actions.

Age, sex, medical history, medications, allergies, type of procedure performed, and sedation and procedure times were recorded by the research associates, using a standardized data collection instrument. We defined elapsed procedure time as the time from initial propofol administration until the patient returned to baseline alertness.

Research associates recorded sedation depth with a 6-point Ramsay scale[6] (1 point indicating agitation and 6 indicating unresponsiveness) at baseline, 90 seconds after completion of initial propofol administration, and at recovery. The capnography monitor used (Capnostream 20; Oridian, Needham, MA) electronically records data every 5 seconds, and throughout the duration of each sedation, research associates used electronic marking and time stamping to identify specific events, eg, drug administration, beginning and end of procedure, readiness for discharge. They also recorded the time and nature of any intervention for respiratory depression or hypoxia, such as verbal or physical stimulation, airway realignment, use of additional oxygen, and the use of airway adjuncts, assisted ventilation, or tracheal intubation. They identified the occurrence of other adverse events, including hypotension, bradycardia, arrhythmia, vomiting, prolonged ED stay, or admission.

Outcome Measures

Our main study outcome was hypoxia, defined a priori as an oxygen saturation less than 93% for 15 seconds or greater. We defined a priori our secondary outcome of subclinical respiratory depression as an end tidal CO_2 ($ETCO_2$) level of 50 mm Hg or greater, an absolute increase or decrease from baseline of 10% or greater, or a loss of waveform for 15 seconds or greater.[3,7]

To assess these outcomes, we downloaded electronic data from each sedation into a Microsoft Excel (Microsoft Inc, Seattle, WA) database, checked and adjudicated any discrepancies with research associate notations, and generated a graph of the patient's sedation, with the *x* axis showing time and the *y* axis depicting $ETCO_2$, SpO_2, respiratory rate, and pulse rate. Electronic time stamps noted propofol administration, procedure initiation and completion, adverse events, and physician interventions.

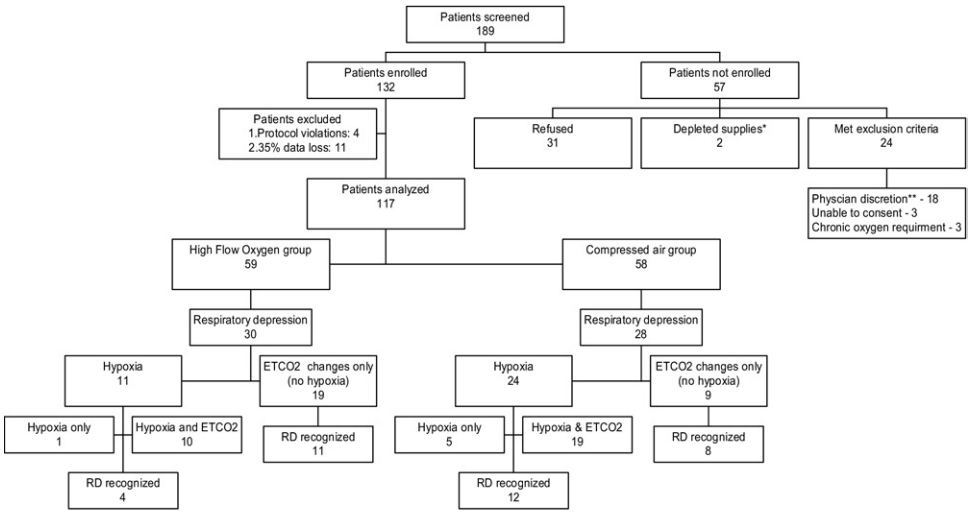
Before study blinding was broken, 3 investigators (K.D., P.D., D.L.) evaluated each graph to code the presence or absence of hypoxia and respiratory depression. We disqualified graphs if they had greater than 35% data loss, unless all 3 evaluators agreed that there was unequivocal evidence of hypoxia or respiratory depression. Lost data were typically due to patient movement (ie, dislodgement of the cannula) or blood pressure cuff insufflations.

Primary Data Analysis

We analyzed our primary outcome with χ^2 (assuming $P<.05$ as significant) and other outcomes descriptively, using SPSS (SPSS, Inc., Chicago, IL). Assuming a 20% absolute reduction in hypoxia as clinically important, we calculated a sample size of 60 subjects in each group (α .05; power 81.5%).

RESULTS

Patient flow is shown in the Figure, and baseline characteristics were similar between groups (Table 1). Hypoxia



*Depleted supplies: Ran out of nasal cannula

**Physician discretion: Physician felt that the patient was not a candidate for procedural sedation or propofol

RD = respiratory depression

Figure. Schematic representation of study results.

Table 1. Patient characteristics.

Demographic	High-Flow Oxygen (n=59)	Compressed Air (n=58)
Median age, y (IQR)	37 (27, 55)	32 (21.5, 45.5)
Sex, female, No. (%) (95% CI)	35 (59) (46–72)	28 (48) (35–61)
Median weight, kg (IQR)	77 (68, 95)	86 (74, 95)
Abscess I & D, % (95% CI)	42 (29–55)	51 (38–64)
Fracture reduction, % (95% CI)	11 (3–19)	17 (7–27)
Joint reduction, % (95% CI)	47 (34–60)	32 (20–44)
Median initial propofol dose, mg/kg (IQR)	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)
Median total propofol dose, mg/kg (IQR)	1.6 (1.1, 2.8)	1.5 (1.0, 2.0)
Median Ramsey scores (90 s after the last dose of preprocedure propofol) (IQR)	4 (2, 5)	4 (2, 5)
Median time from first dose of propofol to return to baseline alertness, min (IQR)	14 (10, 19)	15 (11, 23)

IQR, Interquartile range; *CI*, confidence interval.

was significantly less frequent with high-flow oxygen, whereas capnographic respiratory depression was similar between groups (Table 2).

The breakdown of specific capnographic abnormalities was similar between groups for all patients with respiratory depression (Table E1, available online at http://www.annemergmed.com) and for the subset experiencing hypoxia (Table E2, available online at http://www.annemergmed.com).

For patients with both respiratory depression and hypoxia (n=29), respiratory depression preceded hypoxia in all cases by a median of 45 seconds (interquartile range 29, 68), with these findings similar between groups. The frequency of physician intervention for respiratory depression and hypoxia was similar between groups (Table 3) and is detailed by study subject in Table E3 (available online at http://www.annemergmed.com). When hypoxia was preceded by respiratory depression and an intervention occurred, the majority (13 of 16) of the interventions occurred only after the patient developed hypoxia (Table E3, available online at http://www.annemergmed.com). When hypoxic patients did not receive an intervention, it was because their hypoxia was mild and transient (Table E4, available online at http://www.annemergmed.com).

Two adverse events occurred in the high-flow oxygen group: 1 bradycardia of 40 beats/min lasting 5 minutes and 1 episode of hypotension to 80/50 mm Hg that responded to intravenous fluids in 10 minutes. Two adverse events occurred in the compressed air group: 1 assisted ventilation for 2 minutes and 1 hypotension to 85/40 mm Hg that responded to intravenous fluids in 5 minutes. No patients were admitted as a result of these adverse events, and none were intubated.

LIMITATIONS

We defined hypoxia as an oxygen saturation of less than 93%, a threshold that we believe would prompt most clinicians to intervene to improve oxygenation or ventilation. Using the common threshold of 90% instead would have slightly decreased the incidence of hypoxia in our study but not changed

Table 2. Respiratory depression and hypoxia.

	No. (%)		
	High-Flow Oxygen (n=59)	Compressed Air (n=58)	Difference, % (95% CI)
Patients who developed hypoxia	11 (19)	24 (41)	23, *P*=.007 (6 to 38)
Respiratory depression	30 (51)	28 (48)	3 (–16 to 21)
Hypoxia	10 (17)	19 (33)	16 (1 to 31)
No hypoxia	20 (34)	9 (16)	18 (3 to 33)
No respiratory depression	29 (49)	30 (52)	3 (–21 to 16)
Hypoxia	1 (2)	5 (9)	7 (–15 to 10)
No hypoxia	28 (48)	25 (43)	4 (–14 to 22)

Table 3. Interventions and hypoxia/respiratory depression.

Intervention/No Intervention	High-Flow Oxygen (N=59)	Compressed Air (N=58)	Effect Size, % (95% CI)
Hypoxia, intervention	6	13	12 (–1 to 25)
No hypoxia, intervention	6	5	1 (–9 to 13)
Hypoxia, no intervention	5	11	8 (–4 to 20)
No hypoxia, no intervention	42	30	19 (2 to 35)

our outcome (15% high flow versus 36% compressed air; difference 21%; 95% confidence interval 5% to 35%).

Physicians in this study had real-time access to capnography, as well as standard monitoring. Previous research has shown that the use of real-time capnography during procedural sedation allows clinicians to recognize respiratory depression very early and provide an intervention before an incidence of hypoxia can occur.[7-9] Eleven patients met criteria for respiratory depression in this study, received an intervention, and did not become hypoxic. It is conceivable that a proportion of these patients would have gone on to develop hypoxia. It is possible that our incidence of hypoxic events would have been even higher if we had not used capnography. We believe that the improved safety real-time capnography provides should be part of routine practice, and thus it would not be ethical to blind our clinicians.

DISCUSSION

In this first controlled trial, to our knowledge, of high-flow supplemental oxygen (15 L/minute) during ED propofol sedation, we found that this intervention decreased the incidence of hypoxia to a degree that was both statistically significantly and clinically important. We also reconfirmed our previous observation that capnography provided advance warning of hypoxic events.[3] Thus, assuming that capnography is in place to monitor ventilatory function, our results strongly support the routine use of high-flow oxygen during ED propofol sedation.

Three previous nonblinded, nonrandomized studies have compared sedated patients with and without supplemental oxygen and found conflicting results with respect to respiratory depression and hypoxia.[10-12] We have reported 2 previous controlled trials of low-flow supplemental oxygen showing nonsignificant trends toward decreased hypoxia when sedating with midazolam and fentanyl[3] and propofol.[13]

We found no difference between groups in the incidence of respiratory depression, confirming the findings of previous research that supplemental oxygen does not exacerbate respiratory depression.[7,12]

When our subjects experienced both respiratory depression and hypoxia, the respiratory depression always preceded the hypoxic event. However, in many cases the physicians chose not to intervene until the patient became hypoxic or did not intervene at all (Table E3, available online at http://www.annemergmed.com). We did not assess the physician rationale for delaying or withholding interventions or whether these events were unrecognized altogether. The latter presumption would seem unlikely, given that our observed occurrences of hypoxia without an intervention were transient (Table E4, available online at http://www.annemergmed.com).

Two of our studied capnographic patterns—loss of waveform (apnea) and $ETCO_2$ greater than 50 mm Hg (type 1 or hypopneic respiratory depression)—most frequently heralded subsequent hypoxia (Tables E1 and E2, available online at http://www.annemergmed.com). Also, many patients in this study experienced respiratory depression that did not lead to hypoxia. Our study was not designed to assess the differential predictive value of the various capnographic patterns in predicting subsequent hypoxia, and this is a promising area for further research.

Capnography predicted in advance most hypoxic events in this study, in accordance with our previous sedation research.[3,7] Such early warning may permit the treating physician to intervene, potentially preventing what would have otherwise led to a hypoxic event. However, we observed 5 patients in the compressed air group who developed hypoxia without preceding respiratory depression, and thus capnography cannot be completely relied on in this setting. Patients who receive supplemental oxygen will have greater shift of their oxygen desaturation curves and thus may develop profound respiratory depression yet never experience a hypoxic event. Patients breathing atmospheric oxygen, on the other hand, do not have this shift of the oxygen desaturation curves and thus may desaturate without developing capnographic evidence of respiratory depression.

In summary, we found that high-flow supplemental oxygen significantly reduced the incidence of hypoxia during ED propofol sedation. We believe that such supplementation should be routinely administered, assuming the presence of capnography to monitoring ventilations.

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Author contributions: KD and CRC conceived the study and designed the trial. KD, CRC, and PD supervised the conduct of the trial and data collection. KD, CRC, PD, and YS managed the data, including quality control. PD and DL provided statistical advice on study design and analyzed the data. KD drafted the article. CRC provided editorial support and contributed substantially to its revisions. KD takes responsibility for the paper as a whole.

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Table E1. Distribution of capnographic abnormalities in patients with respiratory depression.

$ETCO_2$ Changes	High-Flow Oxygen (n=30)	Compressed Air (N=28)	Effect Size, % (95% CI)
>10% above baseline, >50 mm Hg	7	8	5 (–28 to 17)
>10% below baseline, loss of waveform	9	8	5 (–28 to 17)
>10% below baseline	11	9	5 (–20 to 29)
>10% above baseline	3	3	6 (–12 to 24)
No changes	29	30	3 (–21 to 16)

Table E2. Relationship of capnographic abnormalities to hypoxic events.

$ETCO_2$ Changes	Resulting Hypoxia: High Flow (N=11)	Resulting Hypoxia: Compressed Air (N=24)	Effect Size, % (95% CI)
>10% above baseline, >50 mm Hg	3	8	5 (–27 to 32)
>10% below baseline, loss of waveform	4	8	3 (–26 to 35)
>10% below baseline	3	2	19 (–5 to 40)
>10% above baseline	0	1	4 (–21 to 20)
No changes	1	5	11 (–19 to 33)

Table E3. Patient interventions and the relationship between hypoxia and respiratory depression.

	RD Criteria	Hypoxia, %	Time From Onset of RD to Onset of Hypoxia	Intervention	When Intervention Occurred Relative to Hypoxia
High-flow group					
1	10% below baseline	88	45 s, after	Airway repositioning	Same time
2	10% below baseline	None	NA	Verbal/painful stim	NA
3	Loss of waveform	None	NA	Verbal stim/airway repos	NA
4	Loss of waveform	85	45 s, after	Airway repositioning	Same time
5	Loss of waveform	None	NA	Airway repo/painful stim	NA
6	Loss of waveform	None	NA	Airway repositioning	NA
7	Loss of waveform	83	65 s, after	Airway repositioning	25 s before
8	Loss of waveform	None	NA	Airway repositioning/verbal/ painful stim	NA
9	Loss of waveform	None	NA	Airway repositioning	NA
10	Above 50 mm Hg	85	40 s, after	Airway repositioning	10 s before
11	Above 50 mm Hg	60	30 s, after	Wall oxygen	Same time
12	none	90	NA	Wall oxygen	NA
Compressed air group					
1	10% below baseline	None	NA	Wall oxygen	NA
2	10% below baseline	75	50 s, after	Wall oxygen	Same time
3	10% below baseline	79	75 s, after	Airway repositioning	Same time
4	10% below baseline	88	20 s, after	Wall oxygen	Same time
5	10% below baseline	None	NA	Verbal/painful stim	NA
6	10% below baseline	60	120 s, after	Airway repositioning/BVM	Same time
7	10% below baseline	80	75 s, after	Airway repositioning	Same time
8	Greater than 50 mm Hg/loss of waveform	None	NA	Verbal stim/airway repositioning	NA
9	Greater than 50 mm Hg/loss of waveform	89	25 s, after	Verbal/painful stim/wall oxygen	Same time
10	Loss of waveform	83	10 s, after	Airway repositioning	Same time
11	Loss of waveform	91	50 s, after	Airway repositioning	Same time
12	Loss of waveform	None	NA	Verbal/painful stim	NA
13	Loss of waveform	None	NA	Verbal/painful stim	NA
14	Above 50 mm Hg	87	35 s, after	Painful stim	Same time
15	Above 50 mm Hg	88	75 s, after	Airway repositioning	Same time
16	Above 50 mm Hg	87	80 s, after	Wall oxygen	25 s before
17	None	88	NA	Wall oxygen	NA
18	None	88	NA	Wall oxygen	NA
19	None	93	NA	Verbal stim	NA

RD, Respiratory depression; *NA*, not applicable; *stim*, stimulation; *BWM,* bag-valve-mask.

Table E4. Patients who developed hypoxia and did not receive an intervention.

RD Criteria		Hypoxia, %	Elapsed Time Between Onset of RD and Onset of Hypoxia	Interval Patient Was Hypoxic
High-flow group				
1	Above 50 mm Hg	87	35 s, after	20 s
2	Loss of waveform	89	100 s, after	30 s
3	Loss of waveform	89	10 s, after	20 s
4	10% below baseline	92	35 s, after	15 s
5	10% below baseline	93	50 s, after	20 s
Compressed air group				
1	Above 50 mm Hg	93	35 s, after	15 s
2	Above 50 mm Hg	85	50 s, Same time	30 s
3	Loss of waveform	89	15 s, after	20 s
4	Loss of waveform	85	35 s	20 s
5	10% change above baseline	79	50 s, after	25 s
6	10% below baseline	87	50 s, after	20 s
7	10% change below baseline	89	20 s, after	20 s
8	10% change above baseline	90	120 s, after	25 s
9	None	79	NA	35 s
10	None	80	NA	20 s
11	None	89	NA	25 s