

EXTUBATION AFTER ANAESTHESIA: A RANDOMISED COMPARISON OF THREE TECHNIQUES*

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SUMMARY – The mode of ventilation used during awake extubation has not previously been studied. We conducted a randomised controlled trial comparing spontaneous respiration, intermittent positive pressure ventilation, and pressure support ventilation (each n=13) for incidence and severity of peri-extubation complications following routine elective surgery. We found the severity of peri-extubation cough was significantly affected by mode of ventilation used at extubation (p=0.049), with lowest severity grades for those in the pressure support ventilation group. The mean arterial pressure at extubation was lowest in the intermittent positive pressure ventilation group (p=0.007). Other peri-extubation complications and time to extubation following cessation of anaesthesia were not significantly different across the three groups. We suggest that the use of pressure support ventilation for awake extubation may offer an advantage over spontaneous and intermittent positive pressure ventilation extubation strategies.

Key words: *Airway management; Extubation; General anaesthesia*

Introduction

The recent Fourth National Audit Project of the Royal College of Anaesthetists identified a disproportionate incidence of adverse events occurring during emergence or recovery from anaesthesia, accounting for one-third of reported cases¹. Adverse sequelae following tracheal extubation include airway obstruction, laryngospasm, hypoxaemia and cardiovascular instability, in addition to common complications such as cough, hoarseness and odynophagia²⁻⁷. Recently published extubation guidelines by the Difficult Airway Society (DAS) highlight a lack of evidence to guide extubation practice, with many recommendations based upon expert opinion⁸. One aspect not previously studied, and which is also not addressed in the DAS guidelines, is the effect of the mode of ven-

tilation employed during the extubation process. We therefore proposed to conduct a blinded randomised controlled trial comparing three extubation strategies in respect of respiratory complications during and following awake tracheal extubation.

Methods

Approval for the study was obtained from the local research ethics committee, and formal written consent from all participants. We included patients undergoing elective non-oral surgery, aged 18 to 70 years with ASA physical status 1, 2 or 3, and requiring tracheal intubation. Exclusion criteria were predicted or actual difficult intubation (defined by grade 3 or 4 view on modified Cormack and Lehane classification^{9,10}); pathology of the neck, upper respiratory or alimentary tract; the risk of pulmonary aspiration of gastric contents; and body mass index (BMI) greater than 35 kg.m⁻².

For all patients, induction and maintenance of anaesthesia were standardised. Once in the anaes-

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thetic room, an intravenous cannula was sited and pulse oximetry, electrocardiograph and non-invasive blood pressure monitoring applied. All patients were pre-oxygenated *via* facemask until end-tidal oxygen measured greater than 90%. Intravenous fentanyl to a maximum of 200 micrograms was administered and anaesthesia induced with propofol 2-4 mg.kg⁻¹. Neuromuscular blockade was ensured using vecuronium titrated to absence of train-of-four response on peripheral nerve stimulation, following which the trachea was intubated using a cuffed Portex (Smiths-Medical, Ashford, UK) tracheal tube (size 8.5 or 9.0 mm in males and 7.5 or 8.0 mm in females). Anaesthesia was maintained using sevoflurane and air in oxygen. Intraoperatively, intermittent positive pressure ventilation (IPPV) was utilised at a rate and tidal volume to target end-tidal carbon dioxide partial pressure of 35 mm Hg. Neuromuscular monitoring was employed throughout the procedure with additional neuromuscular blocking agent given as required. Ondansetron 4 mg was administered in all patients, but additional analgesia (remifentanyl infusion and/or intravenous morphine, non-steroidal anti-inflammatory agents and infiltration of local anaesthesia) was left to the discretion of the primary anaesthetist. Remifentanyl infusion if used was discontinued a minimum of 15 minutes prior to the end of surgery.

Once the surgical procedure was complete, a researcher supervised extubation. The oropharynx was suctioned, an appropriately-sized oropharyngeal airway inserted and extent of neuromuscular blockade reassessed. Upon appearance of three or more twitches on train-of-four stimulation, neuromuscular blockade was reversed using glycopyrrolate 0.5 mg and neostigmine 2.5 mg. Sevoflurane was discontinued and 100% oxygen administered.

At this time, patients were randomised by computer-generated code to one of three ventilatory modalities for extubation: spontaneous respiration (Spont group), intermittent positive pressure ventilation (IPPV group) or pressure support ventilation (PSV group). Patients with a history of respiratory disease (smoking, asthma or chronic obstructive pulmonary disease) underwent separate randomisation to ensure even distribution across all groups.

Spont group: Patients in the control group were allowed to breathe spontaneously until awake extu-

bation was achieved. The trachea was extubated once spontaneous respiration produced tidal volumes in excess of 6 mL.kg⁻¹ and the patient was able to open the eyes in response to verbal command.

IPPV group: Patients in this group continued to receive IPPV to maintain end-tidal carbon dioxide partial pressure of 35 mm Hg. The trachea was extubated once the end-tidal sevoflurane partial pressure fell below the Minimal Alveolar Concentration (MAC)-awake threshold of 0.2%¹¹, and the patient was responsive to verbal command. Any patient in this group who began breathing spontaneously prior to extubation was changed from mechanical to pressure support mode of ventilation. These patients were analysed on an intention-to-treat basis.

PSV group: Patients in this group were allowed to breathe spontaneously but in addition received pressure support ventilation to maintain end-tidal carbon dioxide partial pressure of 35 mm Hg. Once again, the trachea was extubated once the end-tidal sevoflurane reached 0.2% or less and the patient was responsive to verbal command.

All patients were extubated in supine position on the operating table, and without any form of physical stimulation. Following extubation, oxygen was administered *via* Hudson facemask at a rate of 5 litres *per* minute and the patient transferred to the post-anaesthesia care unit (PACU). Monitoring of oxygen saturation, heart and respiratory rate, and noninvasive blood pressure was continued until subsequent discharge from the PACU.

Baseline characteristics were documented by the researcher present at the time of extubation. Peri-extubation complications were assessed by an independent observer blinded to the ventilation method and randomisation sequence. We utilised PACU staff for this purpose, on the assumption they would not be familiar with the modes of ventilation used during extubation.

The primary outcome measure was the incidence of peri-extubation complications. The following complications were recorded: coughing, biting down on the tracheal tube, breath-holding of greater than three-second duration, laryngospasm, airway obstruction (defined by requirement for airway adjunct or support), apnoea (requiring bag-and-mask ventilatory support), and aspiration of gastric contents. Severity of cough

was subsequently graded according to a four-category scale adapted from Minogue *et al.*¹² (Table 1).

Secondary outcome measures included time to extubation following cessation of anaesthesia; heart rate and mean arterial pressure (MAP) at the time of extubation; and proportional change in heart rate and MAP between discontinuation of anaesthesia and extubation.

Statistical analysis and sample size

Statistical analysis was performed using SPSS version 18.0 (IBM, Portsmouth, UK). This was a parallel three-group study, using Kruskal-Wallis testing for ordinal data, χ^2 -test for nominal data and analysis of variance (ANOVA) for continuous data. Sample size calculation was based upon an assumed incidence of extubation-related complications in the general population of 70%¹³. We anticipated a 40% reduction in complications when using pressure support ventilation. Based on the statistical significance level of 0.05 and power of 80%, we calculated that a sample size of 21 patients was required in each group, giving 63 patients altogether.

Results

Logistical constraints limited enrolment to 42 of the required 63 patients. Data from three further patients were excluded due to unanticipated difficult intubation (all grade 3 Cormack and Lehane laryngoscopic view). Patient allocation and baseline characteristics are shown in Table 2. There were no significant differences in the duration of surgery or opioid consumption among the three groups. The most common category of surgery performed was laparoscopic biliary with 24/39 (62%) patients, followed by urological (5/39, 13%), other laparoscopic (4/39, 10%), general

(3/39, 8%), open biliary (2/39, 5%) and otological surgery (1/39, 3%).

There was no difference in the primary outcome measure of the incidence of peri-extubation complications among the three groups (Table 3). We found the majority of patients in all groups coughed during the extubation process. However, the severity of cough was significantly associated with the mode of ventilation used at extubation ($p=0.049$), with severity grades lowest for those in the pressure support ventilation group. There was a significant difference in severity of cough score between the pressure support ventilation and spontaneous ventilation groups ($p=0.013$, Mann Whitney test, compared to a significance level of 0.017 with Bonferroni correction for three pairwise comparisons). Severe cough was reported in 1/13 (7.7%) patients in the PSV group compared to 5/13 (38%) patients in the Spont and IPPV group each.

Other adverse airway events were relatively uncommon, with all such patients coughing in addition. No difference was found in the incidence of breath-holding, biting on the tracheal tube, and oxygen desaturation to less than 95%. There were no instances of laryngospasm, apnoea, airway obstruction or aspiration of gastric contents.

Secondary outcome measures are reported in Table 4. Cardiovascular stability was well-maintained across all groups, with no significant difference among the three groups in respect of the mean heart rate at the time of extubation or the mean change in heart rate between discontinuation of anaesthesia and extubation. The mean arterial pressure at extubation was significantly lower in the IPPV group compared to both spontaneous and pressure support groups. This effect was transient, however, as MAP for all groups equalised within five minutes of extubation. The mean change in heart rate and MAP during the extubation process was not significantly different either. Finally, the mean time to extubation following cessation of anaesthesia was broadly similar across all three groups, and was not related to the duration of surgery.

Discussion

The choice of ventilatory strategy employed at the time of extubation has historically depended principally on operator preference. Neither the guidelines

Table 1. Grading of cough severity (adapted from Minogue *et al.*¹²)

None	No cough
Mild	Single cough
Moderate	More than one episode of non-sustained cough
Severe	Sustained and repetitive (8 or more discrete episodes) cough

Table 2. Baseline characteristics of patients extubated using spontaneous respiration (Spont), intermittent positive pressure ventilation (IPPV), or pressure support ventilation (PSV). Values are number, mean (SD) or median (IQR [range]), as appropriate

	Spont (n=13)	IPPV (n=13)	PSV (n=13)
Male/Female	5/8	3/10	4/9
Age (years)	43 (14)	48 (15)	52 (17)
BMI (kg.m ⁻²)	28 (5)	26 (4)	29 (4)
ASA grade; 1/2/3	8/5/0	6/7/0	4/7/2
Mallampati score 1/2/3	8/5/0	6/6/1	8/5/0
Laryngeal view 1/2/no record	6/2/5	7/3/3	10/3/0
Bougie required	1	2	1
Duration of surgery (min)	91 (72-119 [55-252])	115 (73-147 [39-226])	100 (75-122 [38-165])
Intraoperative opioid			
Morphine (mg)	8.8 (4.2)	9.5 (5.4)	9.2 (5.3)
Remifentanil infusion	1	2	2

recently published by the DAS⁸ nor those of the American Society of Anesthesiologists¹⁴ make any specific recommendations in this respect, and there is a paucity of extant studies to guide extubation practice.

Our study has demonstrated a significant association between the mode of ventilation used at extuba-

tion and the severity of cough. Differences in the incidence of other complications did not reach statistical significance, possibly due to the insufficient sample size, however, we note the low incidence of severe cough in the PSV group compared to both the Spont and IPPV groups. Conceivably, this difference may have proven significant had the full sample size been achieved.

Table 3. Complications associated with extubation using spontaneous respiration (Spont), intermittent positive pressure ventilation (IPPV) or pressure support ventilation (PSV). Values are number (proportion). Cough grade was not recorded in two patients

	Spont (n=13)	IPPV (n=13)	PSV (n=13)	p value
Peri-extubation complications	13 (100%)	11 (85%)	11 (85%)	NS
Cough incidence	13 (100%)	11 (85%)	11 (85%)	NS
Cough grade				0.049
None	0	2	2	
Mild	1	1	4	
Moderate	6	5	5	
Severe	5	5	1	
Missing data	1	0	1	
Other adverse events*	6 (46%)	3 (23%)	2 (15%)	NS
Breath-holding	4	1	1	
Tube-biting	3	1	2	
Desaturation <95%	1	1	1	

*An individual patient may have suffered more than one adverse event; NS = nonsignificant.

Table 4. Secondary outcome measures: haemodynamic parameters and time to extubation when using spontaneous respiration (Spont), intermittent positive pressure ventilation (IPPV) or pressure support ventilation (PSV). Values are mean (SD)

	Spont (n=13)	IPPV (n=13)	PSV (n=13)	p value
Heart rate at extubation	93 (19)	86 (16)	85 (14)	0.39
Heart rate change (%)	30 (25)	16 (24)	14 (20)	0.19
Heart rate 5 min post-extubation	83 (16)	85 (16)	85 (13)	0.91
MAP at extubation (mm Hg)	103 (19)	86 (16)	106 (11)	0.007
MAP change; %	41 (29)	25 (21)	34 (26)	0.32
MAP 5 min post-extubation	101 (13)	100 (17)	101 (12)	0.96
Time to extubation (min)	17 (7)	14 (7)	15 (5)	0.54

MAP = mean arterial pressure

Although cough is a physiological protective reflex, our findings are significant in that sustained or repetitive cough may cause considerable patient discomfort, and may also result in serious adverse sequelae including raised intracranial, intraocular and intra-abdominal pressures^{4,15}. In addition, severe cough has been demonstrated to acutely increase systolic and diastolic arterial pressures, as well as decreasing coronary flow velocity without altering heart rate¹⁶. Airway irritation that produces cough may itself progress to life-threatening obstruction, laryngospasm or hypoxaemia⁴.

Multiple interacting cough reflex pathways have been identified¹⁷, however, peri-extubation cough is primarily attributable to mechanical airway irritation⁴, with abrupt changes in lung volume or airway pressure also implicated¹⁷. A range of pharmacological adjuncts have been proposed to reduce the incidence or attenuate the severity of perioperative airway irritation, including topical^{12,18}, intravenous¹⁸ or intra-cuff local anaesthetic solution¹⁹, beta-^{20,21}, calcium-channel-^{21,22} or neuromuscular blockade²³, as well as opioid techniques^{24,25}. In addition to these measures, our study suggests that the mode of ventilation used for extubation may be influential, and arguably that pressure support ventilation may be of utility.

The mechanism by which pressure support ventilation might reduce airway irritation is unclear, but intuitively, a ventilatory strategy that encourages spontaneous respiration whilst simultaneously reducing the respiratory workload, and in which peak airway pressures are directly controlled would appear to be optimal²⁶. Pressure support ventilation is well-validated

in Critical Care as a strategy to enable weaning from prolonged mechanical ventilation, primarily through a reduction in the work of breathing²⁷⁻²⁹. Intraoperative pressure support ventilation reduced the time to removal of the laryngeal mask airway following cessation of anaesthesia when compared with mechanical ventilation using pressure control, and also improved intra- and postoperative oxygenation and spirometric parameters, although the clinical difference was limited (2% oxygen saturation)³⁰.

In contrast, elevated peak airway pressures as well as tidal volumes commonly used in conventional IPPV have been associated with development of postoperative pulmonary complications^{31,32}, while unsupported spontaneous respiration may also be detrimental, resulting in atelectasis and hypoxaemia secondary to alveolar collapse as well as load-related inflammatory changes to the respiratory musculature^{26,33,34}. It is therefore plausible that augmentation of patient-triggered breaths using pressure support ventilation may provide a more favourable profile of flow, volume and pressure dynamics at extubation than unsupported spontaneous respiration or mechanical ventilation using IPPV.

In this study, we found that MAP at extubation was significantly lower in the IPPV group than in the Spont and PSV groups, although this effect had equalised within five minutes of extubation. Transient changes in heart rate and arterial pressure have previously been attributed to sympathetic activation at extubation⁴. In the majority of patients, these are probably of little clinical consequence, however, they

may be deleterious in at-risk groups such as those with coronary disease or raised intracranial pressure^{4,35}. However, we suggest the observed difference in MAP most likely reflects relatively greater intrathoracic pressure generated in the IPPV group.

Positive-pressure ventilation is known to impede venous return and hence cardiac output particularly in low-volume states^{36,37}. Conversely, reducing intrathoracic pressure through changes in ventilation rate, volume or pressure, or by increasing spontaneous breaths, usually results in improved haemodynamic parameters^{38,39}. Data from Critical Care suggest the haemodynamic effects of different ventilatory modes are likely to be similar if matched for tidal volume and respiratory rate (as surrogate markers of intrathoracic pressure)²⁹. However, the effect of pressure support ventilation on intrathoracic pressure is variable depending on the level of support provided, changing from a pattern resembling spontaneous respiration at lower levels to one resembling mechanical ventilation at higher levels of pressure support ventilation⁴⁰. Although cardiopulmonary interactions are highly variable depending on individual lung mechanics and pre-existing disease states^{29,41}, conceivably in our study augmentation of patient-triggered breaths at relatively low levels of pressure support ventilation did not elevate intrathoracic pressures to the same extent as occurred with IPPV.

We concede there are several limitations to our study. In particular, logistical constraints prevented us from enrolling patients at the rate anticipated prior to commencement. While we have demonstrated a positive association between the mode of ventilation and the severity of cough, other findings which did not reach statistical significance may have been influenced by the small sample size. However, this is the first study to provide evidence for the influence of the mode of ventilation on peri-extubation complications, and as such we offer our results as a basis for further research.

In addition, our blinding was imperfect. We utilised PACU staff to record the incidence and severity of complications, assuming that they would be unfamiliar with the modes of ventilation employed. This may not have been true in all cases, although we contend it is unlikely to have resulted in any bias.

This is the first study to directly address the mode of ventilation employed during awake extubation. Our

findings suggest that the severity of cough is affected by the mode of ventilation used for extubation, and in this respect pressure support ventilation may offer an advantage over spontaneous and IPPV extubation strategies. Definitive validation through a larger study is recommended.

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Sažetak

EKSTUBACIJA NAKON ANESTEZIJE: RANDOMIZIRANA USPOREDBA TRIJU TEHNIKA

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Dosad nije ispitivan način ventilacije tijekom budne ekstubacije. Proveli smo randomizirano kontrolirano ispitivanje uspoređujući spontanu respiraciju, povremenu ventilaciju pozitivnim tlakom i ventilaciju uz tlačnu potporu (n=13 svaka) u odnosu na incidenciju i težinu periekstubacijskih komplikacija nakon rutinske elektivne kirurške operacije. Nalazi su pokazali da na težinu periekstubacijskog kašlja značajno utiče način ventilacije primijenjen kod ekstubacije ($p=0,049$), pri čemu su najniži stupnjevi težine kašlja zabilježeni u skupini bolesnika kod kojih je primijenjena ventilacija uz tlačnu potporu. Srednji arterijski tlak kod ekstubacije bio je najniži u skupini kod koje je primijenjena povremena ventilacija pozitivnim tlakom ($p=0,007$). Ostale periekstubacijske komplikacije i vrijeme do ekstubacije nakon prestanka anestezije nisu se značajno razlikovale među trima skupinama. Smatramo da bi primjena ventilacije uz tlačnu potporu mogla imati prednost pred strategijama spontane respiracije i povremene ventilacije pozitivnim tlakom.

Ključne riječi: *Zbrinjavanje dišnog puta; Ekstubacija; Opća anestezija*