

# Effect of total intravenous anaesthesia and balanced anaesthesia on the frequency of coughing during emergence from the anaesthesia

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**Background.** The effects of total intravenous anaesthesia (TIVA) and balanced anaesthesia (BAL) on coughing during emergence from the general anaesthesia have not yet been compared.

**Methods.** Fifty patients, aged 18–60 yr, undergoing elective lumbar disk surgery were randomly allocated to undergo TIVA (propofol–remifentanyl) or BAL (fentanyl–nitrous oxide–sevoflurane). Extubation was performed in the knee–elbow position, documented on video, and subsequently evaluated by blinded examiners.

**Results.** There was no difference between TIVA and BAL patients with respect to patient characteristics, proportion of smokers, surgical time, or time of emergence. The median number of coughs was significantly lower in the TIVA group (1, range 0–9) than in the BAL group (4, range 0–20,  $P=0.007$ ). Mean maximal heart rate and mean maximal arterial pressure measured during emergence were also significantly lower in the TIVA group ( $P=0.009$  and  $P=0.006$ , respectively).

**Conclusions.** During emergence from anaesthesia in the knee–elbow position, TIVA is associated with significantly less coughing and reduced haemodynamic response when compared with BAL.

*Br J Anaesth* 2007; **99**: 587–91

**Keywords:** airway, complications; anaesthetic techniques, inhalation; anaesthetic techniques, i.v. infusion; cough

Accepted for publication: June 7, 2007

Tracheal irritation from the tracheal tube, with subsequent coughing, is common during emergence from general anaesthesia<sup>1</sup> and is often thought not to be a complication, but a physiological response to protect the airway from aspiration, although the side-effects of this vital reflex may be highly undesirable in clinical practice.

Coughing not only causes significant patient discomfort, but it may also cause hypertension, tachycardia, and increased intracranial, intraocular, and intra-abdominal pressure, which may lead to coronary ischaemia, arrhythmias, or surgical complications.<sup>2–5</sup>

Various techniques and drugs for the prevention of coughing during emergence have been studied, including extubation in a deep plane of anaesthesia,<sup>6</sup> the use of the

laryngeal mask airway,<sup>7</sup> administration of i.v. agents such as lidocaine,<sup>8</sup> short-acting opioids,<sup>9–10</sup> or dexmedetomidine<sup>11</sup>, and the topical<sup>12</sup> or intra-cuff<sup>13</sup> application of lidocaine. A reliable means of preventing undesired coughing has not been demonstrated to date.

There is a paucity of data regarding the effect of balanced anaesthesia (BAL) using inhalation agents and total intravenous anaesthesia (TIVA) on coughing. Propofol is known as a potent inhibitor of airway reflexes in hypnotic concentrations<sup>14–15</sup> and even subhypnotic doses prevent laryngospasm on extubation in children.<sup>16</sup> Inhalation anaesthetics exert various effects on reflex activity of the airways. In a study comparing airway irritation due to anaesthetic inhalation, sevoflurane was found to be the least

irritative agent when compared with halothane, enflurane, and isoflurane.<sup>17</sup>

However, so far no study has compared the effects of TIVA and BAL with regard to coughing during emergence from anaesthesia. In the present randomized prospective study, we tested the hypothesis that there is at least a 50% reduction in coughing during emergence from anaesthesia after TIVA compared with BAL.

## Methods

After institutional ethics committee approval, written informed consent was obtained from 50 patients, ASA I–II, aged between 18 and 60 yr, and undergoing general anaesthesia for elective lumbar disc surgery in the knee–elbow position. Patients were excluded from the study, if they had signs of a difficult airway, risk factors for perioperative aspiration, chronic coughing, a recent respiratory tract infection, or a history of respiratory disease such as asthma or chronic obstructive lung disease.

All patients were premedicated with midazolam 7.5 mg orally. Routine anaesthesia monitoring consisted of ECG, pulse oximetry, non-invasive arterial pressure at 3 min intervals, capnography, end-tidal concentration of volatile anaesthetics, and train-of-four monitoring (Datex Engstrom AS/3 Anaesthesia monitor; Helsinki, Finland). After random allocation according to a randomization list, patients received either remifentanyl 1 µg kg<sup>-1</sup> (TIVA group) or fentanyl 3 µg kg<sup>-1</sup> (BAL group), and anaesthesia was induced with propofol 2.5 mg kg<sup>-1</sup> followed by rocuronium 0.6 mg kg<sup>-1</sup> after the patient fell asleep. Endotracheal intubation was performed under direct laryngoscopic view by a consultant. We used tracheal tubes with high volume–low pressure cuffs, 7.5 mm inner diameter for women and 8.5 mm inner diameter for men (Mallinckrodt Inc., St Louis, MO, USA). The cuff was inflated with air, and cuff-pressure was monitored and maintained at 20 mbar throughout the procedure.

Anaesthesia was maintained either with remifentanyl 0.25 µg kg<sup>-1</sup>min<sup>-1</sup> and propofol 100 µg kg<sup>-1</sup>min<sup>-1</sup> and an air/oxygen mixture (TIVA group), or with sevoflurane 2 vol% and nitrous oxide 70% in oxygen (BAL group). Controlled ventilation was adjusted to an end-tidal CO<sub>2</sub> of 4.6 (SD 0.5) kPa. The patient was placed in the knee–elbow position with the head resting on a cushion and turned to the side.

Fifteen minutes before the end of surgery, all patients received diclofenac 75 mg for postoperative analgesia. The return of neuromuscular function was confirmed using train-of-four peripheral nerve stimulation. In the case of residual block, neostigmine and glycopyrrolate were administered. After surgery was completed and the drapes removed, anaesthetic agents (sevoflurane or remifentanyl/propofol) were discontinued and a video camera focusing on the patient's abdomen from the side was turned on.

Apart from verbal commands, patients were not stimulated during emergence. After resumption of regular spontaneous ventilation, the trachea was extubated while applying suction through the tube when patients opened their eyes, lifted their head, or attempted self-extubation. After cessation of coughing, the patient was directly transferred from the knee–elbow position to a bed. Any episode of bronchospasm, laryngospasm, or desaturation (SpO<sub>2</sub> < 95%), as well as the duration of surgery, the duration of emergence, maximum increase in heart rate, and arterial pressure during emergence, was recorded.

The video films of the emergence phases were analysed by five independent blinded examiners. A cough was defined as a sudden, strong contraction of the abdomen.

All statistical analyses were performed using the SPSS software package (SPSS Inc., Chicago, IL, USA). Sample size calculation was based on the expectation that using TIVA would reduce the coughing described by Olympio and colleagues<sup>18</sup> to 50%. Permitting a type-I error of  $\alpha=5\%$ , a type-II error of  $\beta=5\%$ , and a power of 95%, 20 patients per group were required. Results are presented as mean (SD) or median (range). Nominal data were compared with  $\chi^2$  analysis and Fisher's exact test where appropriate. Numeric data were analysed using the unpaired Student's *t*-test and the Mann–Whitney *U*-test. *P*-values below 0.05 were deemed statistically significant.

## Results

All patients completed the study without adverse events. Intubation was successful at the first or second attempt in each patient. No difference was found with respect to patient characteristics, proportion of smokers, surgical time, or time of emergence when comparing the 26 patients receiving propofol–remifentanyl anaesthesia (TIVA) with the 24 patients undergoing balanced anaesthesia with fentanyl, nitrous oxide, and sevoflurane (BAL) (Table 1).

During emergence from anaesthesia, the median number of coughs per patient was significantly lower in the TIVA group than in the BAL group. No cough at all was documented in 11 of 26 (42.3%) TIVA patients, and only in four of 24 (16.7%) BAL patients (*P*=0.047). Maximal

**Table 1** Comparative patient characteristics. Data are shown as mean (range) or mean (SD). TIVA, total intravenous anaesthesia; BAL, balanced anaesthesia. There were no significant differences between the groups

	TIVA group (n=26)	BAL group (n=24)
Age (yr)	49.6 (31–60)	54.6 (31–60)
Sex (M/F)	12/14	10/14
Weight (kg)	73.1 (14.6)	80.3 (15.0)
Height (cm)	173.1 (7.9)	172.3 (9.8)
Smokers	9 (34.6%)	5 (20.8%)
Surgical time (min)	65.4 (27.5)	66.7 (29.7)
Emergence time (min)	9.0 (5.1)	7.2 (4.8)

**Table 2** Emergence from anaesthesia. Data are shown as mean (SD) or median (range). TIVA, total intravenous anaesthesia; BAL, balanced anaesthesia

	TIVA group (n=26)	BAL group (n=24)	P-value
Maximal heart rate (beats min <sup>-1</sup> )	66 (12)	75 (11)	0.009
Maximal MAP (mm Hg)	90 (19)	104 (15)	0.006
Lowest SpO <sub>2</sub> (%)	98 (1)	98 (1)	NS
Coughs	1 (0–9)	4 (0–20>)	0.007

MAP and mean maximal heart rate were also significantly lower in the TIVA group (Table 2).

## Discussion

The results of our study demonstrate that, in patients emerging from propofol–remifentanyl anaesthesia in the knee–elbow position, emergence-related coughing occurs significantly less often than in patients having received BAL with fentanyl, nitrous oxide, and sevoflurane. Furthermore, the maximal heart rate and maximal MAP during emergence were significantly lower in the TIVA group.

Coughing during emergence from anaesthesia varies greatly and has been estimated to occur in up to 96% of patients after extubation from the tracheal tube.<sup>19</sup> The stress reaction coupled to coughing may cause hypertension and tachycardia, but can also induce bronchospasm in patients with hyperreactive airways.<sup>2–5</sup> The increased intracranial, intraocular, and intra-abdominal pressure can lead to surgical complications such as bleeding or severe injury.<sup>3–4</sup> Moreover, coughing has the potential to dislodge peripheral and central venous catheters through uncontrolled patient movement.<sup>20</sup>

As the depth of anaesthesia decreases after discontinuing anaesthetic agents, the probability of coughing increases, because the tracheal tube exerts a constant laryngotracheal stimulus. Thus, standardization of the measurement time point is of particular importance when determining cough frequency. In contrast to the induction of anaesthesia, where it is possible, for example using BIS monitoring, to aim for a particular depth of anaesthesia that would reliably prevent intubation stress and coughing,<sup>21</sup> there exists no comparable monitoring procedure for the wake-up phase. In order to guarantee identical study conditions in both groups, we set the extubation and measurement time point in all patients according to generally recognized clinical parameters of the ‘awake state’ (i.e. when patients opened their eyes, lifted their head, or attempted self-extubation).

Previous studies have investigated various techniques and medications for the prevention of coughing during emergence. Although very promising solutions were

found, they were not always applicable in clinical practice. Neither extubation in a deep plane of anaesthesia<sup>6</sup> nor the use of the laryngeal mask airway<sup>7</sup> is generally applicable in patients at increased risk for aspiration or with a difficult airway. I.V. agents such as lidocaine,<sup>8</sup> short-acting opioids,<sup>9–10</sup> or dexmedetomidine<sup>11</sup> involve undesired side-effects and may delay emergence from general anaesthesia.<sup>22</sup> Techniques involving the topical application of lidocaine<sup>12</sup> bear the risk of blocking airway reflexes and may predispose to aspiration.<sup>23</sup> Besides, the endotracheal instillation of fluid may itself induce coughing and agitation. The administration of lidocaine via the tracheal tube requires a modified tube (LITA<sup>TM</sup>)<sup>20</sup> and has not proved to be reliable.<sup>24</sup> Intra-cuff lidocaine<sup>13</sup> can be dangerous if the cuff ruptures.<sup>19</sup> Although all these measures can be used in some patients to prevent coughing during emergence, these studies do not answer the question that we raised in the present study.

Studies on the neuronal pathways regulating the cough reflex have been conducted almost exclusively in animals.<sup>25</sup> The cough reflex is initiated by chemically and mechanically activating sensitive vagal afferent nerves,<sup>26</sup> but other afferent nerve subtypes and nerves innervating other viscera, the chest wall, the diaphragm, and the abdominal musculature also play an important role.<sup>25</sup> It is generally believed that the most important reflexogenic areas are at the level of the larynx and the trachea, whereas the more peripheral bronchial branches are less important as reflexogenic areas.<sup>27</sup> Thus, coughing during emergence is most probably a consequence of local tracheal irritation by the tracheal tube. This also serves as the theoretical basis for topical application of local anaesthetics to prevent coughing.

Propofol is known as a dose-dependent potent inhibitor of airway reflexes in hypnotic concentrations.<sup>14–15</sup> Even subhypnotic doses are effective in preventing laryngospasm on tracheal extubation in children.<sup>16</sup> The suppressive effect of propofol alone on airway reflexes should perhaps not be overestimated. Guglielminotti and colleagues<sup>28</sup> found no suppression of the cough reflex in patients lightly sedated with propofol, and a study conducted by Tagaito and colleagues<sup>29</sup> showed that propofol alone failed to suppress airway reflexes elicited by direct laryngeal stimulation; only the addition of increasing doses of fentanyl reduced the incidence of reflex responses.

The effects of opioids on the haemodynamic response to orotracheal intubation have been extensively studied,<sup>30</sup> but data on the influence of opioids on coughing during emergence are rare. In a study carried out by Mendel and colleagues,<sup>9</sup> alfentanil was effective in reducing coughing before extubation after isoflurane anaesthesia, but extubation time was long in both the placebo and the alfentanil group (19 and 22 min, respectively). Many anaesthetists believe that the administration of opioids at the end of anaesthesia reduces the probability of emergence-induced coughing. However, Shajar and colleagues,<sup>10</sup> after

administering a bolus of remifentanyl ( $1 \mu\text{g kg}^{-1}$ ) before discontinuing inhalation anaesthesia (isoflurane/nitrous oxide), observed no difference in the incidence of coughing during emergence.

Inhalation anaesthetics have been shown to exert various effects on reflex activity of the airways. Therefore, it can be argued that the use of other commonly used inhalation agents such as halothane or isoflurane might have revealed results different from those found in our patients who were anaesthetized with sevoflurane. In a study comparing airway irritation due to inhalation of halothane, enflurane, isoflurane, and sevoflurane, Doi and colleagues<sup>17</sup> reported sevoflurane to be the least irritative agent. This is also confirmed by comparison of the findings of Olympio and colleagues<sup>18</sup> (median 7 coughs) and our findings obtained with sevoflurane (median 4 coughs).

The fact that our data were obtained in patients extubated in the knee–elbow position might be regarded as a possible limitation of our study when applying these results to patients extubated in the supine position. At the end of longer-term anaesthesia in the supine position, secretions often collect in the pharynx or trachea, and suction can possibly cause undesired coughing. When, however, extubation is performed in the knee–elbow position, oropharyngeal or endotracheal suction is rarely required. Olympio and colleagues<sup>18</sup> already showed that prone emergence and extubation after lumbar spine surgery is safe and offers greater haemodynamic stability and less coughing than is the case in patients extubated after returning to the supine position.

In conclusion, our study shows that TIVA offers the advantage of less coughing and less haemodynamic stimulation during emergence from general anaesthesia in the knee–elbow position when compared with an inhalation-based technique with sevoflurane. These results are probably also applicable to other positions, such as the lateral and supine, but further studies are needed to verify this assumption. TIVA may be favoured as the anaesthetic technique of choice when the patient or surgical risk factors require that coughing and hypertension during emergence from anaesthesia be minimized.

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