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Original research article

Comparative study between intravenous Fentanyl and Tramadol for their efficiency in preventing cough during emergence in elective craniotomies

[1]Dr. Sameer Sudhakar Vyavahare, [2]Dr. Nisheed Joseph, [3]Dr. Gayathri Subhash Banasode

[1]Assistant Professor, Department of Anaesthesiology, SMBT Medical College, Dhamangaon, Nashik, Maharashtra, India

[2,3]Assistant Professor, Department of Anesthesiology, Kodagu Institute of Medical Sciences, Madikeri, Karnataka, India

Corresponding Author:
Dr. Gayathri Subhash Banasode

Abstract

The incidence of coughing during emergence is variously reported to be 76-80%. Various techniques used to decrease cough during emergence include deep extubation, administration of Dexmedetomidine, intravenous or topical Lignocaine, intra-endotracheal tube-cuff administration of Lignocaine, use of laryngeal mask airway etc. All patients who were potential candidates for enrolment into the study were informed about its purpose & procedure. A written, informed consent was taken. All patients were investigated as per need and hospital protocols. The use of total intra-operative Fentanyl or Propofol was comparable in all three groups. The mean intra-operative Fentanyl used were as follows: in group L 162.83 mcg, group T+L 174.00, group F+L 167.50mcg. The *'p'* value obtained by using ANOVA test was 0.768 which was not significant. Mean intra-operative propofol used in group L 148.33 mg, group T+L 168 mg, group F+L 132 mg. The '*p*' value obtained by using ANOVA test was 0.449 which was again not significant.

Keywords: Fentanyl, tramadol, cough

Introduction

Most anaesthesiologists pay the greatest attention to haemodynamic changes and other consequent parameters, at induction of anaesthesia and intubation. At the end of the surgery, it is but natural for the concentration to have declined, even by a few degrees. But it is at this stage that we experience varying degrees of problems. The awakening of a patient from anaesthesia and surgery, with all its attendant changes can be quite stressful. The frequency with which haemodynamic surges and coughing leads to complications probably exceeds the problems encountered during intubation, especially in certain surgeries like neurosurgery.

Emergence is classically defined as 'the period between discontinuation of all anaesthetic agents and tracheal extubation'. Recovery from GA and extubation is a period of intense physiological stress for all patients. Tracheal extubation causes a transient increase in Heart rate & Blood Pressure via tracheal and laryngeal stimulation due to catecholamine release. It also causes coughing and occasional bronchospasm. Shivering and pain which are common during emergence from general anaesthesia, are also contributory to metabolic and haemodynamic changes. All of these changes could be detrimental to the patients and their eventual outcome.

The intense haemodynamic changes during extubation and emergence play a very major role in recovery after intracranial procedures in neurosurgery. Tachycardia, systemic hypertension, bronchospasm and coughing may compromise surgical results by contributing to raised intracranial pressure and cerebral oedema. Occasionally, intracranial haemorrhage may develop as a result of intense sympathetic stimulation and worsen post-operative neurological outcome. So, their prevention during emergence from general anaesthesia for intracranial procedures is of utmost importance.

The cough stimulus which begins in the vagal sensory nerves of the airway/ lung is transmitted by synapsing at the nucleus tractus solitarius to the cough centre in the ventrolateral medulla. It therefore stands to reason that in general, anti-tussive effect may be achieved by one or more of the following:

1. Anaesthetizing the nerves in the airway mucosa and preventing the relay of the cough impulse to the nucleus tractus solitarius (action of topical local anaesthetics).
2. Agonist action on the mu receptors in nucleus tractus solitarius and medulla (opiates, Tramadol).
3. NMDA receptor antagonists (Tramadol) [1]

The incidence of coughing during emergence is variously reported to be 76-80% [2]. Various techniques

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used to decrease cough during emergence include deep extubation [3], administration of Dexmedetomidine [4, 5], intravenous or topical Lignocaine [2, 3, 4], intra-endotracheal tube-cuff administration of Lignocaine [3, 4], use of laryngeal mask airway [3, 4] etc.
Deep extubation or replacement of endotracheal tube with an LMA at the end of surgery may not always be possible, nor always feasible. Thus there is a definite place in neuroanesthesia to find a drug which has reliable anti-tussive properties and thereby prevent associated haemodynamic surges and consequences of raised intracranial pressure [6].

Objective of the study:
To compare intravenous Fentanyl and Tramadol for their efficiency in preventing cough during emergence in elective craniotomies.

Methodology
The study was a prospective trial involving 90 patients of American Society of Anaesthesiologists (ASA) grades 1-3, aged 18 to 60 years, who were posted for elective craniotomies.
Approval from the hospital Ethics Committee was taken. A written and informed consent of the patient was obtained prior to the study.

Inclusion criteria were
1. ASA grades 1-3
2. Age 18 years and above
3. Elective craniotomy
4. Glasgow Coma Scale 15

Exclusion criteria were
1. Known allergy to Tramadol, local anesthetic drug.
2. Anticipated large fluid shifts, actual surgery lasting more than 3 hours, or any other intra-operative event that may necessitate mechanical ventilation in the postoperative period.
3. Pregnant patients.
4. Signs of difficult airway.
5. Patients with history of reactive airway disease or COPD.

Sampling procedure
All patients who were potential candidates for enrolment into the study were informed about its purpose & procedure. A written, informed consent was taken. All patients were investigated as per need and hospital protocols.
Sample size was calculated based on percentage of coughing expected i.e. proportion of coughing expected to occur in various treatments. As per the results of various studies on which our study was based, [3] coughing occurred in 29% of patients in Tramadol group; whereas in Fentanyl group, coughing occurred in 52% cases, and in Lignocaine group it was 80%. Sample size was calculated by using two independent sample proportions. Accordingly, sample size of the group Lignocaine versus Tramadol was 65, and the group Lignocaine versus Fentanyl was 23. So overall approximate sample size was 88. But we selected 90 patients which were further divided into three groups by using random sampling. Random code was generated by MS-Excel.
1. Group F+L (Fentanyl+ endotracheal Lignocaine).
2. Group T+L (Tramadol + endotracheal Lignocaine).
3. Group L (only endotracheal Lignocaine).

There was no specific premedication for the purpose of the study. All neurosurgical patients in our hospital are given routine antacid-antiemetic prophylaxis orally 6 hours prior and anti-epileptic medication as applicable.

After taking approval from hospital ethics committee, we screened 120 neurosurgical patients. 90 patients, falling in ASA Grades I-III and having GCS 15/15 were found to satisfy our inclusion and exclusion criteria. After having obtained a written informed consent, patients were allocated to one of three groups, group L (Lignocaine), group T+L (Lignocaine + Tramadol), or group F+L (Lignocaine + Fentanyl).
In the operation theatre, patients were monitored for Pulse, Blood Pressure, ECG, and Oxygen saturation at induction. Train of Four (TOF) monitor to assess muscle relaxation was attached after sedation and supramaximal stimulus for a single twitch was determined.
All patients were premedicated with midazolam and fentanyl, and induced with propofol. Anaesthesia was maintained with O2-air-sevoflurane. Fentanyl, Propofol and muscle relaxant were supplemented intra-operatively as required. The study drugs were administered as planned half an hour before expected

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time of extubation. Presence and severity of coughing was noted. Since there is no guideline to score the severity of coughing at extubation, we devised our own score based on our observations over many past surgeries. We further categorized the score of coughing during extubation into no/minimal coughing (includes no cough, bucking and coughing once) and moderate/severe coughing (coughing on tube >1, 2-5 times, >5 times).

Results

Table 1: Comparison of mean intra-operative fentanyl used in group L, group T+L and group F+L

	Number of patients	Intra op fentanyl mg		'p'-value
		Mean	SD	
Group L	30	162.83	57.44	0.768
Group T+L	30	174.00	65.47	
Group F+L	30	167.50	55.94	

Conclusion: By using ANOVA test p-value > 0.05; therefore there is no significant difference between mean intra-operative fentanyl used in group L, group T+L and group F+L.

Table 2: Comparison of mean propofol (mg) used in group L, group T+L and group F+L

	Number of patients	Propofol mg		'p'-value
		Mean	SD	
Group L	30	148.33	94.40	0.449
Group T+L	30	168.00	160.03	
Group F+L	30	132.00	40.63	

Conclusion: By using ANOVA test p-value > 0.05; therefore there is no significant difference between mean propofol used (mg) in group L, group T+L and group F+L.

Table 3: Comparison of occurrence of coughing in group L, group T+L and group F+L

Cough	Group			'p'-value
	Group L	Group T+L	Group F+L	
Minimal Cough	16	24	25	0.31
Severe cough	14	6	5	
Total	30	30	30	

Conclusion: By using chi-square test p-value > 0.05; therefore there is no significant difference between minimal/severe cough with group.

Table 4: Pair wise comparison by using Chi-square test

Comparison	'p'-value
Group L vs Group T+L	0.028*
Group L vs Group F+L	0.012*
Group T+L vs Group F+L	0.739

* Significant

Discussion

Recent studies have been performed to study efficacy of Remifentanil, Fentanyl and Tramadol for cough suppression and better emergence.

Recent studies have shown that serotonergic (5HT1 receptors) and opioid receptors (mu2, kappa, delta) are involved in antitussive mechanism. Drugs belonging to classses of NMDA receptor antagonists and calcium channel antagonists also have marked cough suppressant effect [1]. Thus some opiates like Remifentanyl and Fentanyl, and NMDA antagonist like Tramadol have been studied to evaluate their central antitussive mechanism.

Moderate coughing is reported when Fentanyl is used intravenously in a dose 1 mcg/kg, and minimal coughing with smooth emergence when dose of Fentanyl 2 mcg/kg. In our study we have used Fentanyl 1 mcg/kg so as to avoid un-necessary post-operative sedation for a quicker assessment of neurological status. We have used Fentanyl 1 mcg/kg along with endotracheal 2% Lignocaine. Both drugs act by different mechanisms. So it helps in reducing cough effectively without having post-operative sedation which can interfere with neurological assessment [7, 8].

When Fentanyl and Tramadol were compared by Lin B F *et al*., Tramadol was found to be better in reducing cough and improving the quality of emergence. They found that Tramadol significantly attenuates cough incidence in non-smokers but no difference was found in the smoker population.

In our institute we have been using endotracheal Lignocaine routinely before extubation to reduce

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coughing and to have better emergence. We thus decided to undertake a study to assess the advantage of addition of IV Tramadol or Fentanyl to ET Lignocaine, over only ET Lignocaine. Ours was a prospective study to evaluate the quality of emergence, incidence of coughing during emergence, post-operative nausea vomiting and post-operative sore throat.

After analyzing the demographic data, the age groups in all three groups were found to be comparable and no statistically significant difference was noted. The '*p'* value obtained by using ANOVA test was 0.083, which was non-significant.

Gender distribution was also comparable in all three groups. The group L included 17 males and 13 females, the group T+L included 15 males and 15 females whereas the group F+L included 16 males and 14 females. The '*p*' value obtained by using Chi-square test was 0.964, which was non-significant.

The comparison of weights amongst the three groups was also statistically not significant ('*p*' value 0.59). Thus all three groups were found to be statistically comparable without any confounding demographic factors.

The use of total intra-operative Fentanyl or Propofol was comparable in all three groups. The mean intra-operative Fentanyl used were as follows: in group L 162.83 mcg, group T+L 174.00, group F+L 167.50mcg. The *'p'* value obtained by using ANOVA test was 0.768 which was not significant. Mean intra-operative propofol used in group L 148.33 mg, group T+L 168 mg, group F+L 132 mg. The '*p*' value obtained by using ANOVA test was 0.449 which was again not significant.

In our study we found that incidence of PONV and POST were not statistically significant between the three groups. By using Fisher's exact test, a '*p'*-value of 0.999 was calculated (> 0.05).

The main aim of our study was to assess the incidence of coughing with endotracheal instillation of 2% Lignocaine and to study the possible anti-tussive effect of either Tramadol or Fentanyl, given as an additional intravenous injection towards the end of surgery.

In our study we have been able to demonstrate that addition of either Tramadol or Fentanyl to an endotracheal instillation of 2% Lignocaine, decreases the coughing severity. When a dose of IV Tramadol 1mg/kg or Fentanyl 1mcg/kg was given half an hour before expected time of extubation, the severity of coughing was decreased significantly. When neither Fentanyl nor Tramadol was added to endotracheal Lignocaine (group L), we found that there was no/minimal coughing in 53.33% patients and moderate/severe coughing in 46.67% patients. In group T+L there was no/minimal coughing in 80% patients and severe coughing in 20%. Whereas in group F+L, 83.33% patients had minimal coughing and 16.67% patients had severe coughing. When a pair-wise comparison across these groups was done, we evaluated that the coughing was significantly decreased in group T+L ('*p'* value 0.028) and group F+L ('*p'* value 0.012) as compared to that in group L. But there was no significant difference in coughing between group T+L and group F+L ('*p'* value 0.739).

A similar study conducted by Lin B F *et al.* [3], compared Tramadol 1mg/kg and Fentanyl 1mcg/kg for emergence in patients undergoing spine surgery. They found that Tramadol was better than Fentanyl to reduce coughing at extubation.

Our results are different from theirs. In our study, we found that both Tramadol and Fentanyl were equally effective in reducing cough when either was combined with endotracheal instillation of Lignocaine.

Conclusion

In our study we have been able to demonstrate that addition of either Tramadol or Fentanyl to an endotracheal instillation of 2% Lignocaine, decreases the coughing severity. When a dose of IV Tramadol 1mg/kg or Fentanyl 1mcg/kg was given half an hour before expected time of extubation, the severity of coughing was decreased significantly. When neither Fentanyl nor Tramadol was added to endotracheal Lignocaine (group L), we found that there was no/minimal coughing in 53.33% patients and moderate/severe coughing in 46.67% patients.

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