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Original research article

Intravenous Fentanyl and Tramadol in elective craniotomies: Comparison of sedation score

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Abstract

Tramadol is 68% bioavailable after a single oral dose and 100% available when administered parenterally. Peak serum concentration is reached in about 2 hours after oral administration of Tramadol. After parenteral administration, the onset of action is within 20 minutes, and the peak effect is in 30 minutes. Fentanyl depresses the respiratory centers, and cough reflex, and constricts the pupils (miosis). Analgesic blood levels of Fentanyl may cause nausea and vomiting directly by stimulating the chemoreceptor trigger zone. The study was a prospective trial involving 90 patients of the 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. The study was designed to observe sedation up to 30 mins post-operative only by which time all patients were expected to be awake. But on the occasion of a single patient (in the Tramadol group) who remained sedated beyond 30 min, we followed up till the patient was awake and alert (45 min). We also found that in all three groups, there was no significant difference in the time required for obeying simple commands. The mean time required for obeying simple commands was 4.4 min, 4.33 min, and 4.0 min in group L, group F+L, and group T+L respectively.

Keywords: Fentanyl and Tramadol, elective craniotomies, sedation score

Introduction

Lignocaine was synthesized by Lofgren in Sweden in 1943. Anaesthetic properties of Lignocaine were discovered in 1948 by Lofgren and Lundquist. It was introduced into clinical practice by Gordh in 1949. It is an amide type of local anaesthetic. It also has anti-arrhythmic action apart from its local anaesthetic action [1].

The action of the local anaesthetic is on the cell membrane of the axon; they block the sodium conductance. The large transient increase in the permeability to sodium ions necessary for the propagation of the impulse is prevented. The resting membrane potential is thus maintained and depolarization in response to stimulation is inhibited. It raises the threshold for electrical stimulation, reduces the rate of rise of action potential, and closes conduction. The end effect is that it produces electrical stabilization and a failure to propagate an electrical impulse [2].

Tramadol is 68% bioavailable after a single oral dose and 100% available when administered parenterally. Peak serum concentration is reached in about 2 hours after oral administration of Tramadol. After parenteral administration, the onset of action is within 20 minutes, and the peak effect is in 30 minutes [3].

Tramadol is a centrally acting analgesic that relieves pain by opioid-receptor agonism, as well as additional mechanisms. The affinity of Tramadol for the opioid receptor is only 1/6000 that of morphine. However, the primary O-demethylated metabolite of Tramadol is two to four times as potent as the parent drug and may account for part of the analgesic effect. Its affinity for the mu-opioid receptor is low, while that for kappa and delta receptors is very low [4].

Opioids act as agonists at stereo-specific opioid receptors at presynaptic and postsynaptic sites in the central nervous system, mainly in the brain stem, spinal cord, and peripheral tissue. Fentanyl mimics the action of endogenous ligands by binding to the opioid receptor, resulting in the activation of the pain-modulating anti-nociceptive system. It decreases neurotransmission by inhibiting the presynaptic release of neurotransmitters such as acetylcholine, dopamine, norepinephrine, and substance P [5].

Fentanyl depresses the respiratory centers, and cough reflex, and constricts the pupils (miosis). Analgesic blood levels of Fentanyl may cause nausea and vomiting directly by stimulating the chemoreceptor trigger zone.

Fentanyl is known to increase cerebral blood flow and intracranial pressure. It causes progressive slowing of EEG. Fentanyl administration is accompanied by a decrease in mean arterial pressure and

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cerebral perfusion pressure in head injury patients [6].

Objective of the study:
To compare the sedation scores of intravenous Fentanyl and Tramadol in elective craniotomies.

Methodology
The study was a prospective trial involving 90 patients of the 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, a 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 a 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.
The sample size was calculated based on a 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, coughing occurred in 29% of patients in the Tramadol group; whereas in the Fentanyl group, coughing occurred in 52% of cases, and in the Lignocaine group it was 80%. The sample size was calculated by using two independent sample proportions. Accordingly, the 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 time of extubation. post-operative sedation score, post-operative sore throat, and PONV were noted.
In our study, we evaluated that there was no statistical significant difference ('p'> 0.05) in sedation scores across all three groups upto 30 min post-operatively. The study was designed to observe sedation up to 30 mins post-operative only by which time all patients were expected to be awake. But on the occasion of a single patient (in the Tramadol group) who remained sedated beyond 30 min, we followed-up till the patient was awake and alert (45 min). We also found that in all three groups, there was no significant difference in time required for obeying simple commands. Mean time required for obeying

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simple commands was 4.4 min, 4.33 min and 4.0 min in group L, group F+L, group T+L respectively.

Results

Table 1: Distribution of sedation scores in Group L, group T+L, and group F+L

		Sedation score						Total
		0	1	2	3	4	5	
5th min	Group L	0	0	3	20	7	0	30
	Group T+L	0	2	10	9	7	2	30
	Group F+L	1	1	7	13	7	1	30
10th min	Group L	0	0	0	8	21	1	30
	Group T+L	0	0	1	5	20	4	30
	Group F+L	0	0	1	8	18	3	30
15th min	Group L	0	0	0	2	23	5	30
	Group T+L	0	0	1	1	17	11	30
	Group F+L	0	0	0	2	19	9	30
20th min	Group L	0	0	0	0	17	13	30
	Group T+L	0	0	1	0	10	19	30
	Group F+L	0	0	0	1	14	15	30
25th min	Group L	0	0	0	0	13	17	30
	Group T+L	0	0	1	0	5	24	30
	Group F+L	0	0	0	0	9	21	30
30th min	Group L	0	0	0	0	3	27	30
	Group T+L	0	0	0	1	4	25	30
	Group F+L	0	0	0	0	5	25	30

Legend 1: Cells highlighted in green-most patients awake by the 4th minute and obeying simple commands.

Legend 2: Cells highlighted in the patient who received fentanyl were deeply unconscious at the 5th minute, but became drowsy-but- arousable at the 15th min. This patient became easily arousable by the 20th minute.

Legend 3: Cells highlighted in yellow-patient who received tramadol was deeply sedated at the 5th minute and continued to remain very drowsy till the 30th minute when he became slightly less drowsy. This patient went on to become fully awake and alert at the 45th minute.

Table 2: Comparison of median sedation score

	Median Sedation score			'*p*'-value
	Group L	Group T+L	Group F+L	
5th min	3	3	3	0.491
10th min	4	4	4	0.546
15th min	4	4	4	0.323
20th min	4	5	4	0.368
25th min	5	5	5	0.184
30th min	5	5	5	0.688

Conclusion: By using the Kruscal Wallis test p-value > 0.05; therefore there is no significant difference between median sedation scores at any point in observation times.

Table 3: Pair-wise comparison of sedation score by using the Mann-Whitney U test

Sedation score at	'*p*'-values for comparison		
	Group L vs Group T+L	Group L vs Group F+L	Group T+L vs Group F+L
5th min	0.249	0.368	0.817
10th min	0.295	0.951	0.393
15th min	0.138	0.302	0.644
20th min	0.166	0.716	0.328
25th min	0.072	0.288	0.426
30th min	0.430	0.451	0.954

Discussion

Many studies have been conducted to study the use of lignocaine for attenuating cough reflex. However,

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they have shown mixed results; lignocaine by any route is generally not very effective when used alone.
ETT lignocaine has been found to be better in reducing cough during extubation than intravenous lignocaine [6].
10% lignocaine spray on the vocal cord before intubation, has been shown to decrease the incidence of coughing at extubation [10]. The different concentrations of lignocaine spray (4% lignocaine, 10% lignocaine) have been used but it has been found that the cough suppression at extubation does not depend on the concentration of the lignocaine spray [7].
Some recent studies have shown that Lignocaine can be used for inflating the cuff of a polyvinyl chloride endotracheal tube (intracuff use). The intracuff Ligocaine has been shown to reduce coughing during extubation, but only in surgeries that last longer than 1 hour. This is probably because sufficient time is required for Lignocaine to diffuse through the cuff and then to act on laryngotracheal mucosa [8].
Intracuff Lignocaine has been found to be an efficient route to anaesthetize the trachea. The thin polyvinyl chloride membrane of the intracuff allows Lignocaine to diffuse across it. The cuff can act as a potential controlled-release reservoir for local anaesthetic, facilitating diffusion across its membrane and subsequent anaesthesia of underlying tracheal mucosa.
Lignocaine sprayed down the endotracheal tube has been shown to suppress the cough reflex, as well as attenuate the hyperdynamic response to the presence of ETT. The reflex suppression of the cough reflex is attributed to the mucosal anaesthetizing effect.
Local anaesthetics instilled into the trachea are absorbed as rapidly as after intravenous Lignocaine. When Lignocaine is used endotracheally, the plasma concentration achieved is the same or less than that of intravenous Lignocaine.
The plasma concentration of Lignocaine required to suppress the cough reflex during emergence is reported to be 2.3-3 mcg/ml.
The mean serum level of Lignocaine has been found to be 0.43mcg/ml at the time of extubation when 4% Lignocaine 2mg/kg through laryngotracheal instillation of topical anaesthesia was used before extubation. The plasma concentration has been found to be far less than the plasma concentration that is required to suppress the cough. Even at such low plasma concentration of Lignocaine, the cough suppression has been observed at extubation. It suggests that local effect of Lignocaine on laryngotrachea by spraying mucosa is not depend on the serum concentration.
Lin *et al*. and wu *et al*. have obtained 77 to 100% cough suppression using topical Lignocaine administered via LITA tube 15 to 60 min before extubation.
LITA tube is a modified endotracheal tube specially made for laryngotracheal instillation of local anaesthetic agent. It has an additional pilot tube through which local anaesthetic agent can be instilled into larynx via 10 small holes above and below the cuff [9].
Onset of cough reflex suppression and time to achieve peak plasma concentration after intravenous Lignocaine and endotracheal Lignocaine is quite variable. However local anaesthesia is achieved within 2-3 minutes of endotracheal Lignocaine application.
Delinger *et al*. reported that endotracheal instillation of Lignocaine given 5 min before intubation blunted the refex effectively.
Based on these studies, we administered endotracheal Lignocaine 3 min before reversal started [10].

Conclusion

In our study, we evaluated that there was no statistical significant difference (‘p’> 0.05) in sedation scores across all three groups upto 30 min post-operatively. The study was designed to observe sedation up to 30 mins post-operative only by which time all patients were expected to be awake.

References

1. Gonzalez RM, *et al*. Prevention of endotracheal tube induced coughing during emergence from general anaesthesia; anaesth Analg. 1994;79:792-5.
2. Soltani HA, *et al*. the effect of different lidocaine application methods on postoperative cough and sore throat; J Clin Anesth. 2002;14:15-8.
3. Kautto UM, *et al*. Attenuation of circulatory response to laryngoscopy and tracheal intubation: A comparison of two methods of topical anaesthesia; acta Anaesthesiol Scand. 1982;26:599-602.
4. Sconzo JM, *et al*. *In vitro* diffusion of lidocaine across endotracheal tube cuffs; Reg Anesth. 1990;15(1):37-40.
5. Pelton DA, Daly M, Cooper PD, Conn AW. Plasma lidocaine concentrations following topical aerosol application to the trachea and bronchi. Can Anaesth Soc J. 1970;17:250-5.
6. Catterall W, Mackie K. Local anesthetics. In: Hardman JG, Limbird LE, Molinoff PB, *et al*. eds. Goodman & Gilman’s the pharmacological basis of therapeutics. 9th ed. New York: McGraw-Hill, 1996, 331-47.
7. Diachun CA, *et al*. Suppression of cough during emergence from general anesthesia: laryngotracheal lidocaine through a modified endotracheal tube; J Clin Anaesth. 2001;13:447-51.
8. Lin SY, *et al*. New approach to suppress bucking before extubation-lidocaine through modified endotracheal tube. Ma zui Xue za Zhi. 1990;28:23-30.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 09, 2023

9. Takita K, *et al*. Tracheal lidocaine attenuates the cardiovascular response to endotracheal intubation; Can J anaesth. 2001;48:732-6.
10. Denlinger JK, *et al*. Effects of intratracheal lidocaine on circulatory responses to tracheal intubation; Anaesthesiology. 1974;41:409-12.