Original Article

Role of pre-emptive Huff's manoeuvre and acupressure in reducing the incidence of fentanyl induced cough; a risk factor for postoperative nausea vomiting in female patients: A prospective randomised controlled study

Address for correspondence:
Dr. Parul Jindal, Department of Anesthesiology, Himalayan Institute of Medical Sciences, SRHU, Swami Ram Nagar, Dehradun, Uttaranchal, India.
E-mail: parulpjindal@yahoo.co.in

Received: 16th July, 2019
Revision: 02nd August, 2019
Accepted: 09th August, 2019
Publication: 10th October, 2019

Access this article online
Website: www.ijaweb.org
DOI: 10.4103/ija.IJA_549_19
Quick response code

Parul Gupta, Parul Jindal, Nidhi Kumar
Department of Anaesthesia and Pain Management, Himalayan Institute of Medical Sciences, SRHU, Swami Ram Nagar, Dehradun, Uttaranchal, India

ABSTRACT

Background and Aims: Fentanyl-induced cough is found to occur more often in females and it has been observed to be a risk factor for post-operative nausea and vomiting (PONV). We studied the effect of pre-emptive Huff's manoeuvre and acupressure in reducing incidence of PONV in patients who had fentanyl-induced cough (FIC). **Methods:** This prospective, experimental and randomised study was conducted on 336 patients who were randomly divided into three groups. Group A (n = 112): acupressure was applied, Group B (n = 112): Huff's manoeuvre was performed and Group C (n = 112) was the control group. Thereafter the patients were given a rapid bolus of injection fentanyl at a dose of 2 μ/kg before induction of anaesthesia. Any episode of cough within 60 seconds of fentanyl administration was classified as FIC, and the severity was graded based on the number of coughs (mild 1 – 2, moderate 3 – 4, and severe 5 or more). The occurrence of PONV was recorded. Statistical analysis done using ANOVA test, Kruskal Wallis. **Results:** Incidence of FIC was 8%, 7.1%, and 25.9% in Acupressure, Huff's and control group respectively. The incidence of PONV was found to be higher in patients who had FIC rather than the patients who did not have FIC. **Conclusion:** We conclude that use of Acupressure and Huff's manoeuvre have been demonstrated to be efficacious in reducing FIC and also have an impact in reducing PONV.

Key words: Acupressure, fentanyl, post-operative nausea vomiting

INTRODUCTION

Rapid bolus of intravenous fentanyl is known to provoke an involuntary cough, which is generally transient and benign,[1] and occurs in 18%–65% of patients.[2] Generally, it relieves on its own but at times may be severely explosive and spasmodic and may lead to raised intracranial, intraocular or intra-abdominal pressures in patients, that may be detrimental in patients with ruptured cerebral aneurysms, head trauma, brain herniation or penetrating eye injuries.[3]

The mechanism of fentanyl-induced cough (FIC) is unclear. There is evidence to suggest that central sympathetic system inhibition leading to vagal predominance, stimulation of tracheobronchial tree receptors causing reflex broncho-constriction, pulmonary reflex, or release of histamine may be the causes of this response.[4]

There are numerous pharmacological and non-pharmacological approaches to prevent FIC.

How to cite this article: Gupta P, Jindal P, Kumar N. Role of pre-emptive Huff's manoeuvre and acupressure in reducing the incidence of fentanyl induced cough; a risk factor for postoperative nausea vomiting in female patients: A prospective randomised controlled study. Indian J Anaesth 2019;63:834-40.

Compared to non-pharmacological methods, pharmacological methods may be expensive and may have an added risk of side effects resulting in prolonged hospital stay.[5]

Non-pharmacological methods have shown promising results. Huff's manoeuvre preconditions stretch receptors present in tracheal and bronchial tree, which may prove to be beneficial in preventing FIC. Acupressure has found role in anaesthesia as it can allay anxiety and prevent postoperative nausea and vomiting (PONV). Application of acupressure can effectively reduce cough but the mechanism is not clear.

Previously a study had concluded that both FIC and PONV may have a common trigger.[6] Reviewing the literature we formed a hypothesis that FIC is found to occur more often in young non-smoker females who are also at higher risk for PONV. The study was designed with primary aim to study the effect of Huff's manoeuvre and Acupressure at K27 points in reducing the FIC. The secondary aim was to investigate whether the patient who had FIC during induction of anaesthesia have a higher incidence of PONV.

METHODS

This prospective, experimental, randomised study was conducted following the approval of Institutional Ethics Committee (SRHU/Reg/Int 2017-213 dated 2/5/2017) Written informed consent was obtained from each participant before the surgical procedure. The study protocol adhered to the principles of Declaration of Helsinki. The study included 336 female patients aged 18-60 years with American Society of Anesthesiologists physical status I-III undergoing elective surgical procedures under general anaesthesia and requiring endotracheal intubation. Patients with history of pre-existing lung, renal and cardiac, patients with history of upper respiratory tract infection in previous 4 weeks, pregnant females, smoker, gastrointestinal disorders, patients on treatment with Angiotensin converting enzyme (ACE) inhibitors or antipsychotics in last year, patients with history of any allergy to any study drug and patients with lung or head and neck malignancies who were anticipated to have difficult airway intubation were excluded from the study. The patients were randomly allocated by use of computer generated tables of random number into three study groups. Allocation concealment was established by placing the randomisation sequence in consecutively numbered thick opaque envelopes. In Group A (n = 112) acupressure was applied, in group B (n = 112) patient was asked to perform Huff's manoeuvre and in group C (n = 112) patients were explained about the FIC and reassured.

In Group A, before induction of general anaesthesia, the hollow below the medial end of clavicle was palpated. The index finger of each hand was placed below the collarbone on either side and pressure at the point was held for 1 minute and patient was asked to breathe slowly and deeply.[5] The pressure applied was tolerable to the patient. Within 30 seconds of applying pressure 2 μg/kg fentanyl was given over 30 seconds and the occurrence of FIC was noted over 1 minute of fentanyl administration. In Group B, patients were made to sit straight with chin tilted slightly up and mouth open. Then they were asked to take a deep breath and then hold breath for 2 or 3 seconds and exhale forcefully. They were instructed to repeat this manoeuvre two more times and then follow with one strong cough.[7] The act of huffing lasted for 5 seconds and was standardised to all patients. Fentanyl injection was started within 30 seconds after the completion of huffing manoeuvre. The anaesthetist who either performed acupressure or instructed the patient about performing the Huff's manoeuvre was not involved any further in the study.

At the time of pre-anaesthetic visit the patients were explained to their satisfaction about the non-pharmacological methods that would be used before giving the intravenous dose of fentanyl injection and patient controlled analgesia (PCA) pump they would use after surgery.

All the patients fasted overnight and no premedication was administered to the subjects. Upon arrival in the operating theatre continuous electrocardiogram lead II (ECG), non-invasive arterial pressure (NIBP), Pulse Rate and pulse oximetry (SpO_2) and end tidal carbon dioxide ($EtCO_2$) were instituted using Drager Infinity Vista® monitor (Model MS14750E5394). Peripheral venous access was established with 18 G canula and fluid was started.

No preoxygenation was done in the operation theatre before intravenous bolus of fentanyl. All the patients received fentanyl 2 mcg/kg, prepared as 50 mcg/ml. The primary endpoint was FIC (in terms of both incidence and severity) observed by an independent observer who was unaware of the non-pharmacological method

used. Any episode of cough within 60 seconds of fentanyl administration was classified as FIC, and the severity was graded based on the number of coughs (mild 1 – 2, moderate 3 – 4, and severe 5 or more). Secondary endpoints included any change in heart rate (HR), non-invasive blood pressure (NIBP) observed preoperatively, at induction, 1, 3, 5 and 10 minute (s) after induction of anaesthesia. The incidence of truncal rigidity, apnoea and desaturation were recorded. Apnoea was defined as a pause in breathing for >15 second (s) supported with bag mask ventilation. Truncal rigidity was defined as increased truncal muscle tone that rendered face mask ventilation difficult. It was managed by giving neuromuscular agent. The oxygen desaturation was closely observed and when SpO_2 dropped below 90%, manually assisted mask ventilation was applied immediately.

Anaesthesia was induced with intravenous (IV) propofol at dose of 1.5–2.5 mg/kg, vecuronium at 0.1 mg/kg, followed by intermittent positive pressure ventilation for 3 minute(s). The trachea was then intubated with an appropriately sized endotracheal tube. Anaesthesia was maintained on anaesthetic inhalational agent sevoflurane in an air–oxygen (50:50) mixture with intermittent bolus doses of IV 50 μg fentanyl as needed for intraoperative analgesia. Fifteen minutes prior to the end of surgery IV paracetamol 1 gm was given. Upon completion of the procedure, the volatile anaesthetic was discontinued and residual muscle relaxant effect was antagonised with IV inj neostigmine 2.5 mg and glycopyrrolate 0.2 mg. No prophylactic antiemetic was administered in operation theatre. The tracheal tube was removed upon resumption of spontaneous ventilation, and the patient was then transferred to the post-anaesthesia care unit (PACU). Patients received intravenous injection morphine boluses by PCA pump for subsequent pain complaints.

All postoperative assessments were made by trained nurses who were blind to whether the patient experienced FIC or which method used to reduce incidence of FIC. A staff nurse recorded the incidence of patient complaints of nausea or vomiting. Apfel score was used to predict the possibility of PONV as it has good predictive accuracy. Apfel score has four variables (female sex, history of motion sickness or postoperative nausea and vomiting, non-smokers and opioids in postoperative treatment is planned). PONV can be scored as (0%-10%, 1%-21%, 2%-39%, 3%-61% and 4%-78%). The severity of nausea and vomiting was recorded as a score of 0, 1, or 2 (0 = no nausea or vomiting, 1 = tolerable nausea or vomiting, and 2 = intractable nausea or vomiting requiring iv ondansetron 4 mg). Patients who experienced any degree of nausea or vomiting within the first 24 hours after surgery were classified as having PONV. No prophylactic antiemetics were administered. The on duty anaesthetist assessed the need for antiemetic. All the patients who required a postoperative antiemetic were given IV 4 mg ondanseteron. Evaluation of undesirable effects and complications (respiratory depression, persistent nausea and vomiting, pruritus, constipation and urinary retention.) also followed the same periodicity and were recorded as present or absent. Respiratory depression was defined as respiratory rate lower than 12 breaths per minute. Hypotension was defined as 20% fall in blood pressure of baseline values or systolic blood pressure lower than 90 mmHg in intervals between data collection by nursing staff on medical records. Patients who experienced persistent nausea, vomiting, were given IV inj ondanseteron 0.08 mg/kg and inj metaclopromide 0.35 mg/kg. Patients who developed constipation in postoperative period were started on Syrup Lactulose 2 tsp three times a day.

Estimated sample size was based on incidence of FIC in 32% population based on a previous study.[8] The α was taken to be 95%, the margin of error (*d*) was 5% and the value of *P* was estimated to be 32%. Total sample size was calculated as 334 so we took 112 patients in each group thus making the total sample size 336 for calculation purpose. The method of statistical analysis was decided prospectively and incorporated the intention-to-treat principle.

Interpretation and analysis of obtained results was carried out using Microsoft office Excel. The data were analysed for statistical analysis using Microsoft office Excel 2010 and SPSS IBM version 22, IBM SPSS Statistics base (SPSS South Asia Pvt., Ltd., Bengaluru, India).

Continuous variables were presented as Mean ± SD, and categorical variables were presented as absolute numbers and percentage. Data were checked for normality before statistical analysis using Shaipro Wilk test. Normally distributed continuous variables were compared using ANOVA. If the *F* value was significant and variance was homogeneous, Tukey multiple comparison test was used to assess the differences between the individual groups; otherwise, Tamhane's

T2 test was used. The Kruskal Wallis test was used for those variables that were not normally distributed and further comparisons were done using Mann Whitney U test. Categorical variables were analysed using the Chi-square test. Spearmen's correlation was also used between fentanyl cough dose and FIC severities for all the groups. For all statistical tests, a *P* value less than 0.5 was taken to indicate a significant difference.

RESULTS

A total of 380 consecutive patients were evaluated over a period of 12 months; 44 patients were excluded based on exclusion criteria. The remaining patients were included for further analysis [Figure 1]. The demographic data were comparable in the study groups [Table 1]. The overall incidence of FIC was 13.7% in our study which was statistically significant ($P < 0.001$) among the three group using ANOVA test [Table 2]. Of 29 patients who had FIC in Group C, 15 (13.4%) had mild cough and 12 (10.7%) patients had moderate cough. None of the patients belonging to Group A and Group B had severe cough

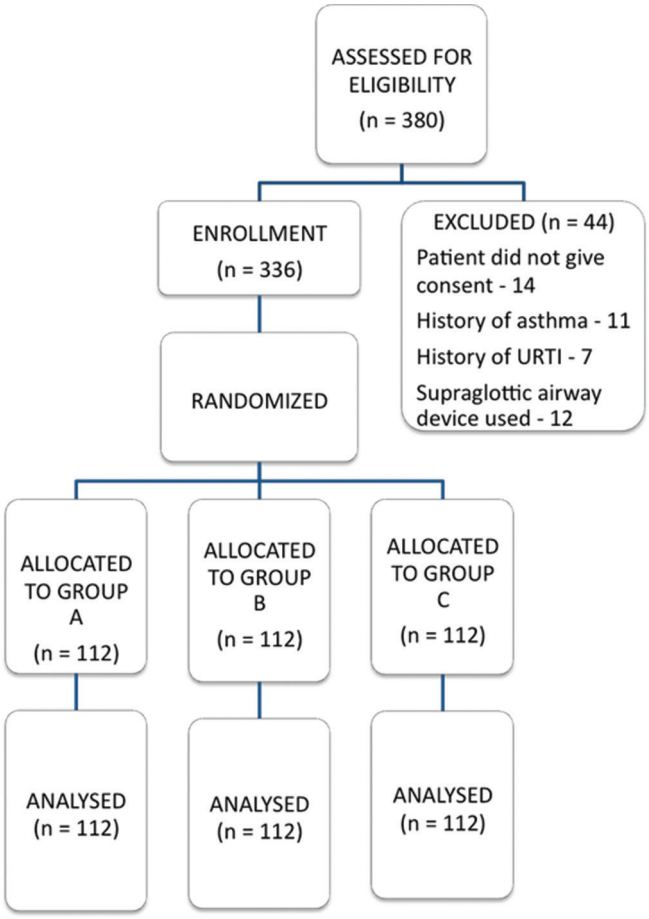

Figure 1: Flow chart showing the selection, exclusion, and randomisation of patients for the study

though Group C had 2 (1.2%) patients with severe cough. There was a highly significant statistical difference in severity of FIC between Groups A, B and C ($P < 0.001$).

No chest wall rigidity, desaturation or apnoea was observed in any patient following IV bolus of fentanyl. Haemodynamic parameters were similar and there was no significant difference between groups in baseline values or after fentanyl injection.

All the patients in our study had Apfel score of 3. The number of times patients used PCA pump for pain relief was recorded and was found to be statistically insignificant ($P > 0.05$) in all the three groups. There was no significant difference between those with or without FIC in terms of patient characteristics or anaesthetic duration. Of 336 patients enrolled in our study, out of which 46 (13.7%) had FIC, we observed that 22 patients had PONV. The incidence of PONV was higher, 15 (32.6%) in patients who had FIC while it was 7 (2.4%) in patients who did not have FIC [Tables 3 and 4]. All the patients who experienced nausea and vomiting were given iv in ondansetron 4 mg and they were relieved thereafter.

The result of multivariate logistic regression analysis showed FIC as the predictive risk factor for the incidence of PONV ($P < 0.001$). Patients showing FIC have 7.8595 greater odds of developing PONV over patients who did not have FIC, that is, patients who have FIC have higher chances of experiencing PONV [Table 5].

In our study, majority of patients [333 (99.1%)] had no complications. In group A, there was only 1 (0.9%) patient who had pruritus for which injection phenaramine maleate was given while in Group C, one (0.9%) patient had constipation which was relieved with plenty of fluids and fibre diet. In placebo group, one (0.9%) patient had an episode of respiratory depression, which was managed conservatively in PACU by giving oxygen via oxygen mask and observation for 24 hours.

DISCUSSION

It has been reported in previous literature that FIC mostly occur within 30 seconds after a rapid iv bolus of fentanyl.[9] We observed all the subjects for 1 minute, which was deemed long enough to detect all FIC. In our study the time of onset of FIC was within

Table 1: Demographic profile, postoperative requirement of morphine of subjects in different groups (Mean±SD)

	Group A	Group B	Group C	*P
Age (years) Mean±SD	41.46±11.99	40.06±11.83	40.56±13.15	0.694
Weight (kg) Mean±SD	55.88±8.62	56.46±8.26	54.67±7.72	0.440
American Society of Anesthesiologist (ASA) physical status I:II	106:6	104:8	101:11	
Duration of anaesthesia (seconds) Mean±SD	146.74±40.86	143.75±43.27	135.13±52.83	0.147
Dose of morphine (mg)	10.40±5.18	10.35±6.11	10.14±5.89	0.997
Number of PCA boluses	14.02±7.92	15.04±12.89	16.30±12.63	0.778

*ANOVA; PCA – Patient controlled analgesia

Table 2: Dose of fentanyl, incidence of FIC and Number of coughs following Fentanyl administration

	Group A	Group B	Group C	*P
Dose of fentanyl (mcg) Mean±SD	116.21±20.81	120.54±19.05	117.22±18.05	0.217
Incidence (n) of cough	9 (8%)	8 (7.1%)	29 (25.9%)	0.001
Time of onset of FIC (seconds) Mean±SD	21.50±4.81	20.75±1.17	16.17±4.69	0.002
No of coughs				
0	103 (92%)	104 (92.9%)	83 (74.1%)	0.001
1-2	5 (4.5%)	3 (2.7%)	15 (13.4%)	
3-4	4 (3.6%)	5 (4.5%)	12 (10.7%)	
≥5	0	0	2 (1.2%)	

*ANOVA; FIC – Fentanyl-induced cough

Table 3: Postoperative nausea vomiting (PONV) observed on shifting the patient from Operation theatre

PONV	(*n*=112) (%)			*P*
	Group A	Group B	Group C	
ON SHIFTING TO PACU (GRADE 0:1:2)	108: 3:1	110:2	108:1:3	0.41
On shifting to PACU 30 min (GRADE 0:1:2)	108:3:1	108:3:1	99:9:4	0.01
On shifting to PACU 1HR (GRADE 0:1:2)	110:2	111:1	105:6:2	0.01
On shifting to PACU 2HR (GRADE 0:1:2)	111:1	111:1	108:4	0.07

*ANOVA. PACU – Post-anaesthesia care unit

Table 4: Patient characteristic data presented as mean (SD) or numbers

	With FIC (*n*=46)	Without FIC (*n*=290)	*P
Age (years)	41.7±11.9	40.6±12.4	0.11
Weight (kg)	54.4±7.5	54.8±8.8	0.11
Duration of surgery (sec)	140±47.0	142.2±46.1	0.20
Dose of fentanyl (μg)	109.5±14.2	119.3±19.7	0.45
PONV	15 (32.6%)	7 (2.4%)	0.03*

*ANOVA for continuous variable. *Chi-square test for categorical variables.
FIC – Fentanyl induced cough, PONV – Postoperative nausea and vomiting

Table 5: Multivariate logistic regression analysis with PONV having Apfel score 3

Factor	Odds ratio (95% CI)	*P*
Age	1.0164 (0.9797-1.0544)	0.3861
Weight	1.0142 (0.9649-1.0661)	0.5784
Duration of surgery	1.0018 (0.9927-1.0110)	0.6930
FIC	7.8595 (4.3455-14.2151)	<0.001
Dose of morphine	0.9934 (0.9195-1.0733)	0.8669

PONV – Postoperative nausea and vomiting

30 second(s) for all patients though we noticed that in Group A and Group B the duration of onset of FIC was increased in comparison to Group C, which was statistically significant ($P < 0.05$). This could be due to a small number of patients 9 (8%) and 8 (7.1%) who elicited FIC in Group A and Group B. Also as only a limited literature is available on the effect of Huff's manoeuvre[7] and acupressure on FICs this finding was not observed in studies done before.[5]

The incidence of FIC observed in our control group (32%) is comparable with that reported by others.[9-11]

In accordance to study conducted by Solanki *et al.*, we observe a significant difference between acupressure and placebo group.[5] Role of Acupressure in anaesthesia practice for prevention of postoperative nausea and vomiting is well documented.[12,13] There are five main acupressure points which are documented in the literature for cough relief in patients with asthma and chronic obstructive pulmonary disease: (CV 22, at the suprasternal notch, K 27, below the medial ends of the clavicles on either side of the manubrium sterni, B 10, one-half inch below the base of the skull and one-half inch out from either side of the spine, Extra Point 17, to the side and just slightly above the vertebra that protrudes at the top of the spine when the head is tilted downward and B 38, between the scapula and

the spine at the level of the heart).[5] Although the mechanism for prevention of cough by acupressure is not fully understood, it significantly reduces the incidence of FIC.

Though opioids are known to suppress cough, paradoxical effect can be seen with a rapid iv bolus of fentanyl causing a sudden severe, self-limiting cough. The actual pathway of FIC in humans is still under study though in previous studies histamine has been proved as the cause for production of FIC.[14] Huff's manoeuvre involves taking a deep breath in, holding it and exhaling. Breathing in and holding it enables air to get behind the mucus and separates it from the lung wall so it can be blown out.[15] A Huffing manoeuvre is sufficient to decrease the cross-sectional diameter of airways sufficient to increase linear velocities and aid secretion movement.[16] The huffing manoeuvre might cause preconditioning of stretch receptors of trachea and bronchial tree and hence prevent FIC.

The mechanism of FIC is unknown but in a research conducted on mice by Kamei *et al*. it was postulated that histamine appears to be involved in production of FIC.[14] In another study of Kimina K, it was concluded that histamine is released during surgical and anaesthetic stress could be correlated with episodes of PONV.[17] Therefore a positive correlation can be established that histamine is a common mediator between FIC and PONV.

In our study, we included only female patients because we used Apfel score of 3 in our study to stratify the risk of PONV. Apfel score is found to have good predictive accuracy to predict possibility of PONV. Apfel score has four variables (female sex, history of motion sickness or postoperative nausea vomiting, non-smoker, opioids in postoperative treatment is planned) and the probability of PONV can be scored (0%-10%, 1%-21%, 2%-39%, 3%-61%, 4%-78%).[6,18]

The limitation of our study was that our study included only female patients and thus we cannot generalise our results for both males and females population undergoing surgery. We included only American Society of Anesthesiologists (ASA) physical status I, II and III and thus we cannot predict how the outcome would change with ASA grading. All the patients in our study had Apfel score of 3 and thus our results cannot be generalised for the patients with lower or higher Apfel score. In our study, we followed our patients for 24 hours in PACU and thus we could not assess the effect of FIC on PONV beyond 24 hours.

CONCLUSION

We found that acupressure and Huff's manoeuvre can effectively decrease the incidence and severity of FIC. The incidence of PONV was found to be higher in patients who had FIC rather than the patients who did not have FIC.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgements

Department of surgery for their encouragement and support for conducting this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Lin JA, Yeh CC, Lee MS, Wu CT, Lin SL, Wong CS. Prolonged injection time and light smoking decrease the incidence of fentanyl- induced cough. Anesth Analg 2005;101:670-4.
2. Lin CS, Sun WZ, Chan WH, Lin CJ, Yeh HM, Mok MS. Intravenous lidocaine and ephedrine, but not propofol, suppress fentanyl- induced cough. Can J Anesth 2004;51:654-9.
3. Shah M, Shah S. The applied physiology of cough. Indian J Pediatr 2001;68:(Suppl 2):S3-10.
4. Lui PW, Hsing CH, Chu YC. Terbutaline inhalation suppresses fentanyl-induced coughing. Can J Anaesth 1996;43:1216-9.
5. Solanki SL, Doctor JR, Kapila SJ, Gehdoo RP, Divatia JV. Acupressure versus dilution of fentanyl to reduce incidence of fentanyl-induced cough in female cancer patients: A prospective randomized controlled study. Korean J Anesthesiol 2016;69:234-8.
6. Li CC, Chen SS, Huang CH, Chien KL, Yang HJ, Fan SZ, *et al*. Fentanyl-induced cough is a risk factor for postoperative nausea and vomiting. Br J Anaesth 2015;115:1-5.
7. Ambesh S, Singh N, Gupta D, Singh PK, Singh U. A huffing manoeuvre, immediately before induction of anaesthesia, prevents fentanyl-induced coughing: A prospective, randomized, and controlled study. Br J Anaesth 2010;104:40-3.
8. Goyal VK, Bhargava SK, Baj B. Effect of preoperative incentive spirometry on fenatanyl induced cough: A prospective randomized controlled study. Korean J Anesthesiol 2017;70:550-4.
9. Yu J, Lu Y, Dong C, Zhu H, Xu R. Premedication with

intravenous dexmedetomidine-midazolam suppresses fentanyl-induced cough. Ir J Med Sci 2012;181:517-20.
10. Pandey CK, Raza M, Ranjan R, Singhal V, Kumar M, Lakra A, *et al*. Intravenous lidocaine 0.5 mg/kg effectively suppresses fentanyl- induced cough. Can J Anaesth 2005;52:172-5.
11. Elmawgoud AA. Effect of tramadol on fentanyl induced cough: A double blind, randomized, controlled study. Egyptian J Anaesth 2013;29:301-4.
12. Lee A, Done ML. The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting: A meta-analysis. Anesth Analg 1999;88:1362-9.
13. Boehler M, Mitterschiffthaler G, Schlager A. Korean hand acupressure reduces postoperative nausea and vomiting after gynecological laparoscopic surgery. Anesth Analg 2002;94:872-5.
14. Kamei J, Nakanishi Y, Asato M, Ikeda H. Fentanyl enhances the excitability of rapidly adapting receptors to cause cough via the enhancement of histamine release in the airways. Cough 2013;9:1-6.
15. Ghuman S, Jaiswal V, Burman D, Ghodey S. To compare the effect of conventional huffing with therapist made huffing device on sputum volume in subjects with acute exacerbation of COPD. IOSR J Dental Med Sci 2017;16:60-3.
16. Pavia D, Agnew JE, Lopez-Vidriero MT, Clarke SW. General review of tracheobronchial clearance. Eur J Respir Dis 1987;153(Suppl 1):123-9.
17. Kimura K, Rusch C, Strasser M, Lengkong H, Wulf M, Koller M, *et al*. Influence of histamine release on postoperative vomiting (POV) following gynaecological laparoscopic surgery. Inflamm Res 2004;53:148-53.
18. Apfel CC, Lara E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: Conclusions from cross-validations between two centers. Anesthesiology 1999;91:693-700.