Pharmacological and Non-pharmacological Prevention of Fentanyl-Induced Cough : A meta-analysis

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Ji Eun Kim

− ABSTRACT −

Pharmacological and Non-pharmacological Prevention of Fentanyl-Induced Cough: A meta-analysis

Fentanyl-induced cough (FIC) is often observed after intravenous bolus administration of fentanyl during anesthesia induction. This meta-analysis assessed the efficacy of pharmacological and non-pharmacological interventions to reduce the incidence of FIC. We searched for randomized controlled trials comparing the pharmacological or non-pharmacological interventions with the controls to prevent FIC; we included 28 studies retrieved from Pub-Med, Embase, and Cochrane Library. Overall incidence of FIC was approximately 31%. Lidocaine [odds ratio (OR) = 0.29, 95% confidence interval (CI) 0.21 – 0.39], *N*-methyl-D-aspartate (NMDA) receptor antagonists [OR = 0.09, 95% CI 0.02 – 0.42], propofol [OR = 0.07, 95% CI 0.01 – 0.36], α_2 agonists [OR = 0.32, 95% CI 0.21 – 0.48], β_2 agonists [OR = 0.10, 95% CI 0.03 – 0.30], fentanyl priming [OR = 0.33, 95% CI 0.19 – 0.56], and slow injection of fentanyl [OR = 0.25, 95% CI 0.11 – 0.58)] were effective in decreasing the incidence of FIC, whereas atropine [OR = 1.10, 95% CI 0.58 – 2.11] and benzodiazepines [OR = 2.04, 95% CI 1.33 – 3.13] were not effective. This meta-analysis found that lidocaine, NMDA receptor antagonists, propofol, α_2 agonists, β_2 agonists, and priming dose of fentanyl were effective in preventing FIC, but atropine and benzodiazepines were not. Slow injection of fentanyl was effective in preventing FIC, but results depend on the speed of administration.

Keyword: Anesthesia, Fentanyl-induced cough, Meta-analysis, Prevention

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Ⅰ. INTRODUCTION

Fentanyl-induced cough (FIC) is often observed after intravenous bolus administration of fentanyl during anesthesia induction. The incidence of FIC is from 18% to 65% (Lin et al, 2004; Lin et al, 2005) although is usually brief and self-limiting. However, coughing is undesirable during anesthesia induction because it is associated with increased intracranial (ICP), intraocular, and intra-abdominal pressures. Furthermore, severe FIC can cause multiple conjunctival and periorbital petechiae, (Tweed and Dakin, 2001) and lead to upper airway obstruction that might require immediate intervention. (Ambesh et al, 2009) Therefore, it is clinically important to prevent FIC. Various interventions, including lidocaine, *N*-methyl-D-aspartate (NMDA) receptor antagonists, propofol, α_2 agonists, β_2 agonists, atropine, benzodiazepines, priming, and slow injection, have been used to reduce the incidence of FIC. (Lin et al, 2004; Pandey et al, 2004; Horng et al, 2007; Yeh et al, 2007; Lui et al, 1996; Hung et al, 2010; Phua et al, 1991; Tang et al, 2010) However, the prophylactic efficacy of these measures remains controversial, and to date, no meta-analysis has been performed to evaluate their efficacy in preventing FIC. The purpose of this meta-analysis of randomized trials was to analyze the efficacy of pharmacological and non-pharmacological interventions to reduce the incidence of FIC.

Ⅱ. MATERIALS AND METHODS

This study followed the guidelines recommended in the Cochrane Handbook for Systematic Reviews of Interventions, (Higgins and Green, 2009) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. (Moher at al, 2009) We searched PubMed, Embase, and Cochrane Library databases using the following terms: ‘‘fentanyl’’ AND (‘‘cough’’ OR ‘‘coughing’’). For gathering all available evidence, we hand-searched the references cited in selected articles for additional studies. The language of publication was not restricted. The last database search date was March 2013.

We searched for clinical and randomized controlled trials that compared pharmacological or non-pharmacological interventions with controls, the latter receiving no treatment to prevent FIC. Reviews, abstracts, correspondences, letters, were excluded. The title and abstract of each identified article were read by a single primary investigator (JHK) who completed the screening process. When an article met our selection criteria, its quality was assessed and data were extracted by two independent reviewers (JHK, JYK). Any conflicting results were resolved by discussion between the two reviewers. Extracted data included patient characteristics, dose, timing, route of prophylactic agent administration, intervention technique, and fentanyl dose and injection speed. The primary outcome was the number of patients coughing during IV fentanyl administration.

Statistical analysis

Review Manager 5.1 software (RevMan 5.1, The Cochrane Collaboration, Oxford, UK) was used for statistical analysis. Results are expressed as odds ratio (OR) (95% confidence interval), I^2, and P value for heterogeneity. Analysis of FIC incidence was performed using the OR computed with the Mantel–Haenszel method (fixed or random effect models). Forest plots were used to graphically represent and evaluate treatment effect. OR represents the likelihood of FIC in the treatment group compared with the control group. A 95% CI for the OR < 1 was considered to represent statistical significance, and it indicates efficacy in FIC prevention. Statistical heterogeneity was assessed with the I^2 value; $I^2 > 40\%$

and a P value of < 0.1 were considered the threshold for heterogeneity, and a random effects model was applied. If the data were homogeneous ($P \geq 0.1$), a fixed effect model was applied. For investigating heterogeneity, subgroup analysis was performed according to the dose of intervention drug, speed of fentanyl administration, or timing modalities, whichever was appropriate. To reduce the issues related to the unit of analysis in studies with more than two intervention groups, the number of patients in the control group and the FIC count were divided into more than two control groups within each meta-analysis. Bias related to unpublished studies was assessed using the funnel plot if at least ten studies of each intervention were included. However, we were not able to create a funnel plot due to the small number of studies in our meta-analysis. To evaluate relative efficacy of interventions, statistical testing of indirect comparison was carried out. For indirect comparison of individually significant interventions including three or more studies, mixed effects metaregression was performed using R metafor package, (Viechtbauer, 2010) and summary statistic values were presented as the relative risk (RR) (95% confidence interval).

Ⅲ. RESULTS

A total of 879 articles were found with the search criteria, and 36 articles were considered as being potential clinical trials that could be included. The selection process is summarized in Figure 1. The meta-analysis finally included 28 articles (5,660 patients in the intervention groups and 3,188 patients in the control groups).

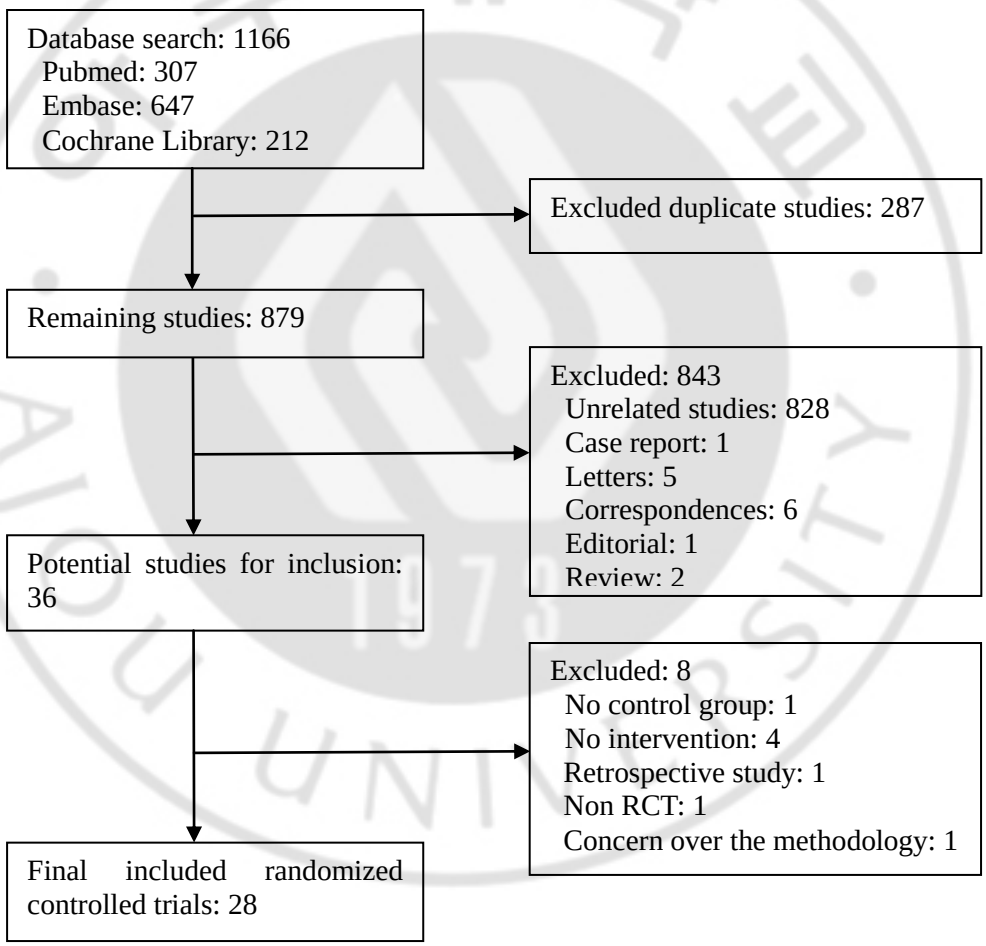

Fig. 1. Flow diagram of the study.

Interventions used to prevent FIC were as follows: administration of lidocaine, NMDA receptor antagonists (ketamine, dextromethorphan), propofol, α_2 agonists (clonidine, dexmedetomidine), β_2 agonists (terbutaline, salbutamol), atropine, benzodiazepines (midazolam, temazepam), fentanyl (for priming), beclomethasone, sodium chromoglycate, morphine, pentazocine, dezocine, ephedrine, rocuronium, slow injection method, dilution, and huffing maneuver. (Table 1) Beclomethasone, sodium chromoglycate, morphine, pentazocine, dezocine, ephedrine, rocuronium, dilution, and huffing maneuver were used in single studies and not included in the meta-analysis.

Table 1. Characteristics of randomized controlled studies.

Study (author, year)	Sample size (*n*)	Number of coughing patients in the control group (%)	Intervention	Incidence of cough (%)	Fentanyl dose	Fentanyl injection speed	Age (years)
Pandey, 2004	502	86/251 (34)	Saline	34	3 μg/kg	5 s	18-60
			Lidocaine 1.5 mg/kg	13*			
Pandey, 2005	320	28/80 (35)	Saline	35	3 μg/kg	5 s	18-60
			Lidocaine 0.5 mg/kg	14*			
			Lidocaine 1 mg/kg	15*			
			Lidocaine 1.5 mg/kg	14*			
Lin, 2004	118	20/31 (65)	Saline	65	2.5 μg/kg	2 s	18-65
			Lidocaine 2 mg/kg	14*			
			Propofol 0.6 mg/kg	37			
			Ephedrine 5 mg	21*			
Guler, 2010	300	23/100 (23)	Saline	23	1.5 μg/kg	2 s	18-65
			Lidocaine 1 mg/kg	11*			
			Ketamine 0.5 mg/kg	0*			

Table 1. continued.

Study (author, year)	Sample size (*n*)	Number of coughing patients in the control group	Intervention	Incidence of cough (%)	Fentanyl dose	Fentanyl injection speed	Age (years)
Horng, 2007	300	58/150 (39)	Saline	39	2 μg/kg	2 s	18-80
			Clinidine 2 μg/kg	17*			
He, 2012	300	61/100 (61)	Saline	61	4 μg/kg	2 s	18-60
			Dexmedetomidine 0.5 μg/kg	40*			
			Dexmedetomidine 1 μg/kg	18*			
Yu, 2012	440	45/110 (41)	Saline	41	3 μg/kg	2 s	18-65
			Midazolam 0.06 mg/kg	64*			
			Dexmedetomidine 0.6 μg/kg	2*			
			Dexmedetomidine 0.6 μg/kg + midazolam 0.06 mg/kg	0*			
Yeh, 2007	360	39/180 (22)	Saline	22	1.5 μg/kg	5 s	18-65
			Ketamine 0.15 mg/kg	7*			

Table 1. continued.

Study (author, year)	Sample size (*n*)	Number of coughing patients in the control group	Intervention	Incidence of cough (%)	Fentanyl dose	Fentanyl injection speed	Age (years)
Tang, 2010	120	24/30 (80)	Intralipid	80	2.5 μg/kg	2 s	25-60
			Propofol 1 mg/kg	40*			
			Propofol 1.5 mg/kg	7*			
			Propofol 2 mg/kg	3*			
Phua, 1991	250	14/50 (28)	None	28	1.5 μg/kg	Not mentioned	Not mentioned
			Atropine 0.01 mg/kg	30			
			Midazolam 7.5 mg (po)	40			
			Morphine 0.2 mg/kg (IM)	6*			
Lui, 1996	131	13/30 (43)	Saline	43	5 μg/kg	5 s	16-45
			Terbutaline 5 mg (inhalation)	3*			
			Atropine 0.01 mg/kg	46			

Table 1. continued.

Study (author, year)	Sample size (*n*)	Number of coughing patients in the control group (%)	Intervention	Incidence of cough (%)	Fentanyl dose	Fentanyl injection speed	Age (years)
Hung, 2010	600	37/200 (19)	Saline	19	150 μg	Not mentioned	18-75
			Fentanyl 25 μg	4*	125 μg		
			Fentanyl 25 μg	8*	150 μg		
Jung, 2011	800	34/200 (17)	None	17	2.0 μg/kg	3-5 s	18-75
			Fentanyl 0.5 μg/kg 1min	10	1.5 μg/kg		
			Fentanyl 0.5 μg/kg 2min	13	1.5 μg/kg		
			Fentanyl 0.5 μg/kg 3min	12	1.5 μg/kg		
Gu, 2012	400	68/100 (68)	Saline	68	2.5 μg/kg	5 s	22-70
			Fentanyl 0.5 μg/kg	5*	2.0		
			Fentanyl 1 μg/kg	40*	1.5		
			Fentanyl 1.5 μg/kg	64	1.0		
Shrestha, 2012	150	15/50 (30)	Saline	30	150 μg	Not mentioned	18-75
			Fentanyl 25 μg	8*	125 μg		
			Fentanyl 25 μg	14*	150 μg		

Table 1. continued.

Study (author, year)	Sample size (*n*)	Number of coughing patients in the control group	Intervention	Incidence of cough (%)	Fentanyl dose	Fentanyl injection speed	Age (years)
Agarwal, 2003	200	14/50 (28)	None	28	2 μg/kg	5 s	18-60
			Salbutamol (inhalation)	6*			
			Beclomethasone (inhalation)	0*			
			Sodium chromoglycate	4			
Dimitriou, 2006	50	6/26 (23)	None	23	2-3 μg/kg	Not mentione	Not mentioned
			Temazepam 20 mg (po)	21			
Ai, 2010	277	21//93 (23)	Saline	23	2 μg/kg	2 s	19-63
			Pentazocine 0.5 mg/kg	4*			
Sun, 2011	120	42/60 (70)	Saline	70	5 μg/kg	2 s	20-60
			Dezocine 0.1 mg/kg	0*			
Horng, 2012	260	30/130 (23)	Saline	23	1.5 μg/kg	2 s	18-80
			Rocuronium 0.06 mg/kg	9*			
Mukherjee, 2012	320	91/152 (60)	Antacid (po)	60	2 μg/kg	2 s	18-60
			Dextromethorphan 40 mg (po)	4*			

Table 1. continued.

Study (author, year)	Sample size (*n*)	Number of coughing patients in the control group (%)	Intervention	Incidence of cough (%)	Fentanyl dose	Fentanyl injection speed	Age (years)
Elmenesy, 2011	60	11/30 (36)	Water (po) Dextromethorphan 60 mg (po)	37 13*	2 μg/kg	2 s	Not mentioned
Ambesh, 2009	300	48/150 (32)	Normal breathing Huffing maneuver	32 4*	2.5 μg/kg	5 s	18-60
Lin, 2005	450	27/150 (18)	Injection over 2 s Injection over 15 s Injection over 30 s	18 8* 1*	<70 kg;100 μg, >70 kg; 150 μg	2, 15, 30 s	18-80
Schäpermeier, 2008	464	4/117 (3)	Saline injection over 2 s Injection over 2 s Injection over 5 s Injection over 10 s	2 3 6 3	1.5 μg/kg	2, 5, 10 s	Not mentioned

Injection means fentanyl injection..

Table 1. continued.

Study (author, year)	Sample size (*n*)	Number of coughing patients in the control group	Intervention	Incidence of cough (%)	Fentanyl dose	Fentanyl injection speed	Age (years)
Yu, 2007	200	16/50 (32)	Injection over 5 s (50 μg/ml)	32	3 μg/kg	5, 30 s	18-65
			Injection over 5 s (25 μg/ml)	16			
			Injection over 5 s (10 μg/ml)	12*			
			Injection over 30 s (10 μg/ml)	2*			
Chen, 2009	75	11/25 (44)	Injection over 2 s	44	4 μg/kg	2, 15 s	18-70
			Injection over 2 s (into the lower leg vein)	52			
			Injection over 15 s	8*			
Yakici, 2013	981	114/493 (23)	Injection over 5 s	23	2 μg/kg	5, 30 s	18-65
			Injection over 30 s	4*			

Injection means fentanyl injection.
All interventions were administered IV except for the above-mentioned interventions (e.g., PO, IM, inhalation)
PO per os, *IM* intramuscular
* $P < 0.05$ vs. control group in each study

Overall incidence of FIC in the control group was approximately 31.4%. Efficacy of each intervention is summarized in Table 2.

Table 2. Summary of interventions.

	No. of studies and references	No. of patients	Odds ratio (95% CI)	Heterogeneity I^2%, *P* value
Atropine	2 (7,9)	165	1.10 (0.58, 2.11)	0, 1.00
α_2 agonists	3 (5,16,17)	820	0.32 (0.21, 0.48)	45, 0.14
β_2 agonists	2 (7,21)	164	0.10 (0.03, 0.30)	21, 0.26
Benzodiazepines	3 (9,17,22)	370	2.04 (1.33, 3.13)	12, 0.32
Fentanyl priming	4 (8,18−20)	1950	0.33 (0.19, 0.56)	73, 0.0001
Lidocaine	4 (1,4,14,15)	1082	0.29 (0.21, 0.39)	0, 0.51
NMDA receptor antagonists	4 (6,15,26,27)	924	0.09 (0.02, 0.42)	86, < 0.001
Propofol	2 (1,11)	181	0.07 (0.01, 0.36)	72, 0.01
Speed of injection	5 (10,29−32)	1929	0.25 (0.11, 0.58)	69, 0.004

NMDA means *N*-methyl-D-aspartate: CI means confidence interval.

Intravenous lidocaine was effective in suppressing FIC [OR = 0.29, 95% CI 0.21 − 0.39, I^2 = 0%, *P* = 0.51]. (Figure 2) Subgroup analysis according to lidocaine dosage (0.5 − 1.0 mg/kg, 1.5 − 2.0 mg/kg) showed it was effective in preventing FIC irrespective of dosage (OR = 0.37, 95% CI 0.22 − 0.63, I^2 = 0%, *P* = 0.89; OR = 0.26, 95% CI 0.17 − 0.38, I^2 = 32%, *P* = 0.23, respectively).

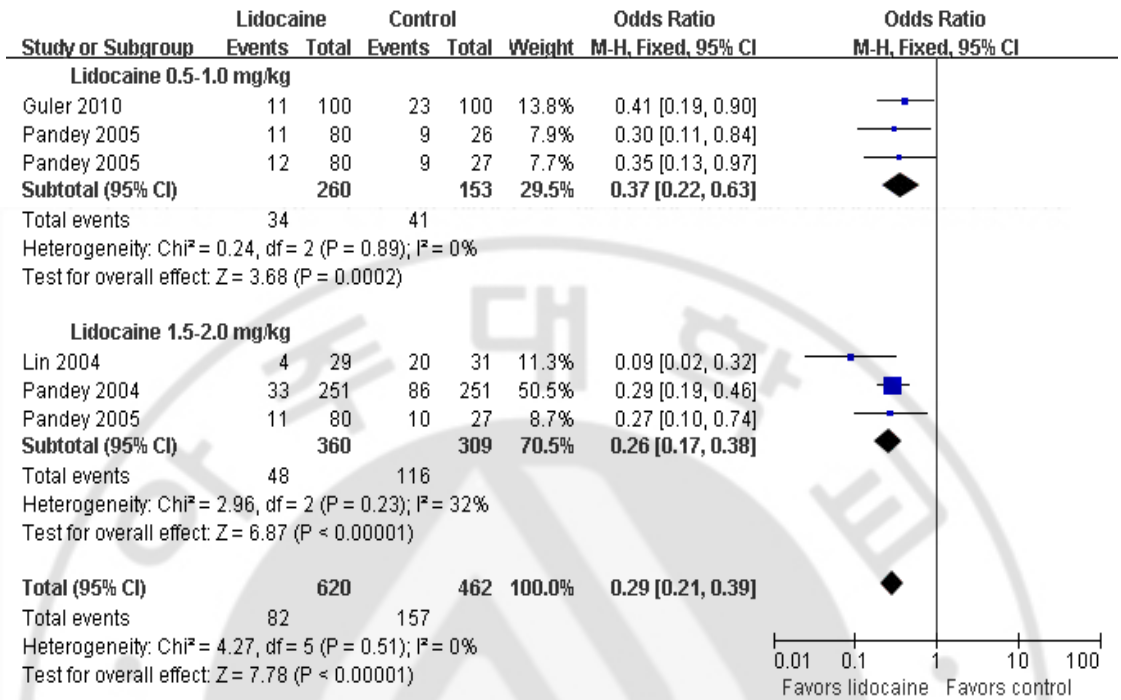

Fig. 2. Forest plot for the effect of lidocaine on fentanyl-induced cough.

Intravenous administration of α_2 agonists decreased the incidence of FIC (OR = 0.32, 95% CI 0.21 − 0.48, I^2 = 45 %, P = 0.14). When subgroup analysis was performed according to the type of α_2 agonists (clonidine, dexmedetomidine), heterogeneity was not corrected. Except in one sub-study using a high dose of dexmedetomidine (1.0 μg/kg), the heterogeneity was within acceptable ranges (OR = 0.38, 95% CI 0.27 − 0.65, I^2 = 0 %, P = 0.81]. Slow injection speed during fentanyl administration decreased the incidence of FIC (OR = 0.25, 95% CI 0.11 − 0.58, I^2 = 69%, P = 0.004). (Figure 3) Heterogeneity was assessed by injection speed during administration. Injection of fentanyl for a period of less than 15 s was not effective in preventing FIC (OR = 0.50, 95% CI 0.18 − 1.43, I^2 = 55%, P = 0.08); however, injection over a 30-s period was effective in preventing FIC (OR = 0.11, 95% CI 0.07 − 0.19, I^2 = 0%, P = 0.73).

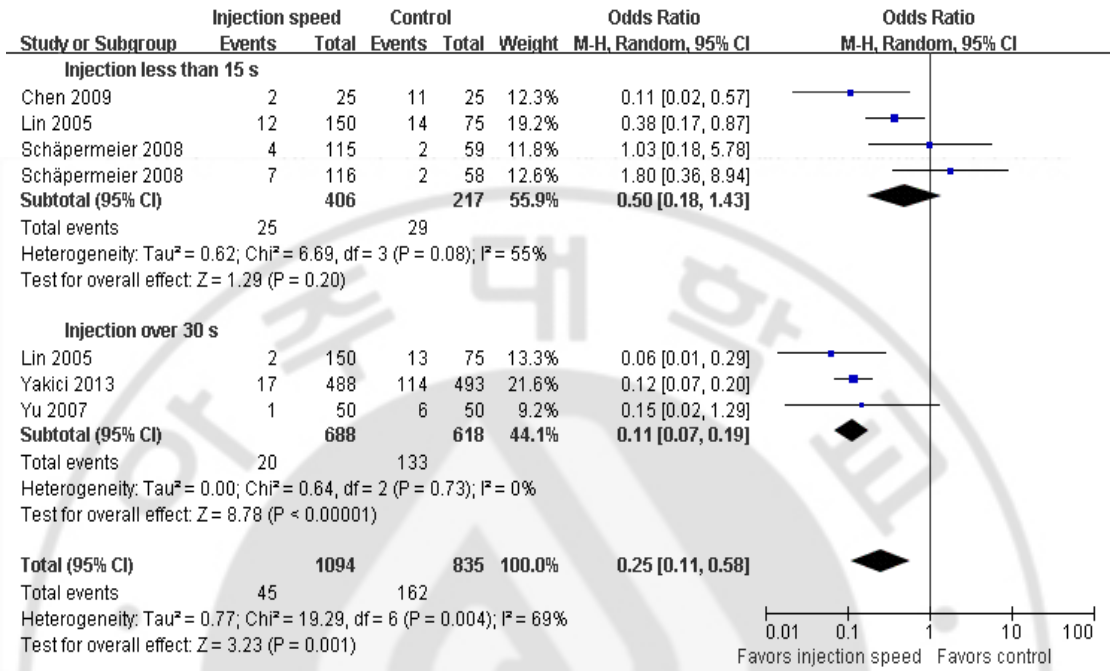

Fig. 3. Forest plot for the effect of injection speed on fentanyl-induced cough.

Propofol was effective in attenuating FIC (OR = 0.07, 95% CI 0.01 − 0.36, I^2= 72%, P = 0.01). Subgroup analysis according to propofol dosage (≤ 1.0 mg/kg, ≥ 1.5 mg/kg) caused a decrease in heterogeneity, in which both doses of propofol were effective in attenuating FIC (OR = 0.26, 95% CI 0.11 − 0.64, I^2 = 0%, P = 0.53; OR = 0.01, 95% CI 0.00 − 0.07, I^2 = 0%, P = 0.66, respectively). Inhalation of β_2 agonists (terbutaline, salbutamol) was also effective in suppressing FIC (OR = 0.10, 95% CI 0.03 − 0.30, I^2 = 21%, P = 0.26). Priming low-dose of fentanyl decreased the incidence of FIC (OR = 0.33, 95% CI 0.19 − 0.56, I^2 = 73%, P = 0.0001). Although heterogeneity was explored using the priming dose, heterogeneity was not corrected using the main fentanyl dose and interval of priming time. NMDA receptor antagonists (ketamine, dextromethorphan) could effectively suppress FIC (OR = 0.09, 95% CI 0.02 − 0.42, I^2 = 86%, P < 0.001). Heterogeneity was not decreased by

analyzing the studies according to the dose and type of antagonists and fentanyl dose.

Atropine and benzodiazepines were ineffective in preventing FIC (OR = 1.10, 95% CI 0.58 − 2.11, I^2 = 0%, P = 1.00; OR = 2.04, 95% CI 1.33− 3.13, I^2 = 21%, P = 0.26, respectively). Indirect comparisons were carried out for five statistically significant interventions: RR (95% CI) of NMDA receptor antagonists, slow injection, lidocaine, priming dose of fentanyl, and α_2 agonists were OR 0.21, 95% CI 0.08 – 0.53, OR 0.33, 95% CI 0.16 – 0.66, OR 0.46, 95% CI 0.36 – 0.59, OR 0.51, 95% CI 0.35 – 0.74, and OR 0.59, 95% CI 0.46 – 0.74, respectively. RR of NMDA receptor antagonists was lower than those of fentanyl priming dose and α_2 agonists (P = 0.019 and 0.016, respectively). RR of slow injection was lower than that of α_2 agonists (P = 0.043).

Ⅳ. DISCUSSION

This meta-analysis demonstrated that lidocaine, NMDA receptor antagonists, propofol, α_2 agonists, β_2 agonists, and priming dose of fentanyl were all effective in preventing FIC, but atropine and benzodiazepines were not. Slow injection of fentanyl seems to be effective in preventing FIC, but it depends on the speed of administration (> 30 s).

Although various mechanisms responsible for FIC have been proposed, the exact mechanism of FIC is unclear. Fentnayl could inhibit central sympathetic outflow, therefore activating the vagus nerve. This enhancement of vagal activity was reported as a possible cause of cough and reflex bronchoconstriction. (Lui et al, 1996; Agarwal et al, 2003) Other possible mechanisms included a pulmonary chemoreflex mediated by rapidly adapting receptors (irritant receptors) or vagal C-fiber receptors located in proximity to pulmonary vessels, (Böhrer et al, 1990) and stimulation of the irritant receptors in the upper pulmonary mucosa secondary to fentanyl-induced tracheal smooth muscle constriction. (Yasuda et a, 1978) A recent study suggested that fentanyl enhances the excitability of rapidly adapting receptors to cause cough. (Kamei et al, 2013) Ketamine, propofol, and β_2 agonists have bronchodilatory effects on airway smooth muscles. (Cheng et al, 1996) The result of our analysis that β_2 agonists, NMDA receptor antagonists and propofol reduce the incidence of FIC supports the possible role of bronchoconstriction in FIC.

In this analysis, α_2 agonists (clonidine, dexmedetomidine) were effective in preventing FIC. Although actual mechanisms are unknown, the reduction in fentanyl-induced muscle rigidity via central effect of α_2 agonists may be a possible explanation. (Hung, 2009) Lidocaine was effective in suppressing FIC, irrespective of the dosage. However, pretreatment with a high dose of lidocaine could not be justified because lidocaine may have arrhythmogenic effects, and its vasodilatory effect could augment the cardiovascular depression caused by induction agents. (Schlimp and Wiedermann, 2005) The mechanism by which lidocaine suppress cough reflex induced by mechanically and chemically remains unknown, but depression of brain-stem function was suggested to be one of the possibility. (Poulton and James, 1979) Atropine did not suppress FIC, suggesting that vagal efferent pathways, via muscarinic receptors, may not be involved in FIC. Although, midazolam has

bronchorelaxant effects on airway smooth muscles, benzodiazepine premedication could not reduce the incidence of FIC in this analysis. Therefore, FIC may be caused by multiple mechanisms and may be affected by several confounding factors.

Priming with a small dose of fentanyl and slow injection of fentanyl over a period of 30 s could effectively suppress FIC. From a pharmacologic viewpoint, the occurrence of cough is likely to be related to the balance between the time course of the drug's plasma concentration and the effect-site concentration. In the remifentanil study, episodes of cough tended to occur when drug plasma concentration was maintained above its effect-site concentration, but no episodes of cough were induced when the difference between the plasma concentration of and effect-site concentration decreased or during the steady equilibrium state. (Kim et al, 2012) In this respect, priming with a small bolus dose of fentanyl, that is insufficient to trigger an episode of cough while passing through the pulmonary circulation and then entering the systemic circulation, may mean that the effect-site concentration of the drug could be raised without triggering an episode of cough. In addition, fentanyl injection speed is an important factor in preventing FIC, as drug infusion time can affect peak plasma concentration. With prolonged infusion time, peak plasma concentration is reduced. The threshold for FIC is reached more easily at a high peak plasma concentration. If fentanyl is injected over a period of 30 s, the possibility of reaching the threshold of plasma concentration for coughing will be reduced because the mean FIC onset time was 15 s. This suggests that the threshold of fentanyl plasma concentration to induce an episode of cough may be reached within 15 s. (Yeh et al, 2007) Therefore, prolonging the infusion time can decrease the incidence of FIC. In our meta-analysis, when fentanyl was administrated over a period < 15 s, the injection speed did not reduce the incidence of FIC. Therefore, fentanyl should be administered slowly − at least over a period > 15 s in a routine clinical setting.

There are some limitations to this study. With respect to heterogeneity among the included studies, subgroup analyses were performed to decrease the heterogeneity and identify factors that influence the results. However, despite performing subgroup analyses, acceptable statistical heterogeneity was not reached in several interventions (NMDA receptor antagonists, fentanyl priming). Although the value of investigating heterogeneity when there are very few studies is questionable; statistical heterogeneity between the studies limits

direct comparisons of efficacy. In addition, publication bias cannot be excluded. We did not test for publication bias with funnel plots or other statistical tests, as these are unreliable in analyses of a small number of studies, as was the case in our review. (Terrin et al, 2005; Thornton and Lee, 2000) Publication bias towards a small number of trials with positive results does not allow us to draw firm conclusions, and hence, larger observational studies are required. Lastly, besides a list of significant and non-significant results from various interventions, comparison in terms of adverse reactions and cost effectiveness are considered to be indispensable in the meta-analysis. However, such data were not mentioned in most original articles, so we could not extract relevant data from selected studies.

Ⅴ. CONCLUSION

In conclusion, this meta-analysis suggests that lidocaine, NMDA receptor antagonists, propofol, α_2 agonists, β_2 agonists, priming with fentanyl, and slow injection of fentanyl effectively suppress FIC.

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– 국문요약 –

펜타닐 유도성 기침의 예방을 위한 약물적 혹은 비약물적 중재법: 메타분석

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펜타닐 유도성 기침은 마취 유도시에 펜타닐을 일회 정주한 후 종종 관찰된다. 본 메타분석에서는 펜타닐 유도성 기침의 발생률을 줄이기 위해 시행되는 약물적 혹은 비약물적 중재법들의 효능을 평가하였다. 펜타닐 유도성 기침 예방을 위하여 대조군과 약물적 혹은 비약물적 중재법들을 비교한 무작위대조군연구들을 대상으로 하였다. Pub-Med, Embase, Cochrane Library 을 기반으로 하여 총 28 개의 연구들이 분석되었다. 펜타닐 유도성 기침의 전반적인 발생률은 31% 이었다. 리도카인 [odds ratio (OR) = 0.29, 95% confidence interval (CI) 0.21 – 0.39], N-methyl-D-aspartate (NMDA) 수용체 길항제 [OR = 0.09, 95% CI 0.02 – 0.42], 프로포폴 [OR = 0.07, 95% CI 0.01 – 0.36], 알파2 작용제 [OR = 0.32, 95% CI 0.21 – 0.48], 베타2 작용제 [OR = 0.10, 95% CI 0.03 – 0.30], 펜타닐 예비정주 [OR = 0.33, 95% CI 0.19 – 0.56], 그리고 펜타닐의 저속 주입 [OR = 0.25, 95% CI 0.11 – 0.58]들은 펜타닐 유도성 기침의 발생 감소에 효과적이었다. 반면 아트로핀 [OR = 1.10, 95% CI 0.58 – 2.11]과 벤조다이아제핀 [OR = 2.04, 95% CI 1.33 – 3.13] 계열들은 효과가 없었다. 본 연구에서 리도카인, NMDA 수용체 길항제, 프로포폴,

알파2 작용제, 베타2 작용제, 펜타닐 예비정주, 및 펜타닐의 저속 주입은 펜타닐 유도성 기침 예방에 효과가 있고, 아트로핀과 벤조다이아제핀은 효과가 없음이 밝혀졌다. 펜타닐 저속 주입은 펜타닐 유도성 기침의 예방에 효과가 있으나, 이는 주입 속도에 따라 결과가 달랐다.

핵심어: 마취, 펜타닐 유도성 기침, 메타분석, 예방