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Evaluation of the Effect of Pheniramine Maleate on Fentanyl-induced Cough (FIC) in Opium Addicts

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ABSTRACT

Background: Fentanyl is a synthetic opioid used to induce anesthesia. Intravenous bolus injection can cause coughing during induction of anesthesia and intracranial, intraocular, and intra-abdominal hypertension. This cough is often temporary and self-limiting, but can be harmful in some patients. pheniramine maleate is a first-generation antihistamine that is used to control allergies. Thus, this study evaluated the effect of pheniramine maleate on this type of cough in opium addicts.

Material and Methods: This randomized, double-blind clinical trial was performed on opium addicts admitted to Imam Reza Hospital in Mashhad, Iran in 2019. After obtaining informed consent, opium addicts who underwent elective surgery for more than half an hour were divided into two groups. Patients were routinely monitored. Serum infusion was started for all patients. In the control group, 2 ml of normal saline 0.9% and in the patient group, 2-3 ml of pheniramine maleate iv bolus was injected. After 90 seconds, fentanyl was injected for 3 seconds at a dose of 2 µ/kg to induce anesthesia. 90 seconds after fentanyl injection, cough intensity was divided into three groups including mild (1 to 2), moderate (3 to 5) and severe (more than 5) depending on the number of coughs observed and vital signs parameters were recorded. Induction of anesthesia was completed with propofol and atracurium. All data were analyzed using Spss software version 23.

Results: In the evaluation of 86 opioid patients who underwent elective surgery, it was observed that 7 patients (16.3%) and 1 patient (2.3%) had coughs in the control and intervention groups, respectively. This difference was statistically significant (P = 0.029). Additionally, cough severity was mild in 4 patients (9.3%) in the control group, followed by moderate (2 patients, 4.7%) and severe (1 patient, 2.3%). In the intervention group, the severity of cough in a person was only mild, which this difference was statistically significant (P = 0.025). In the control group, the duration of cough in patients (7 patients) who had a cough was 5.7 ± 3.1 seconds, while this amount was 4 seconds for a person in the intervention group, which this difference was statistically significant (P = 0.026).

Conclusion: Pheniramine maleate reduces the incidence and duration of fentanyl-induced cough in opium-addicted patients, therefore, it can be used to improve the condition of fentanyl-induced cough in patients with opium addiction.

KEYWORDS

Pheniramine Maleate, Cough, Fentanyl, Opium.

Introduction

Cough is an innate primitive reflex of the body to respiratory stimuli, air pollution, or as a result of increased mucous secretions during illness. The mechanism of cough is the rapid expiration of exhaled air due to the contraction of the respiratory muscles (1). Cough is an explosive and sudden passage of air through the throat that cleans the bronchi, trachea and larynx from mucus or other substances (3, 2). Side effects of coughing during anesthesia include increased intracranial, intraocular, and intra-abdominal hypertension. These complications are harmful in patients with cerebral aneurysms, brain trauma, aortic aneurysms, and pneumothorax, as well as in patients with pre-existing intracranial, intraocular, and intra-abdominal hypertension (4). Fentanyl is a synthetic opioid used to induce anesthesia. Although opioids have an antitussive effect, but intravenous bolus injections can induce coughing during induction of anesthesia (5). The incidence of this cough is seen in 26.1% to 74% of patients. This cough is often temporary and self-limiting, but can cause serious side effects in some patients, thus prompt action is necessary for its control (6). Fentanyl-induced cough (FIC) can be caused by several mechanisms, including the release of allergic mediators such as histamine, supraglottic obstruction by soft tissue, and adduction of the vocal cord muscles due to opioid-induced muscle stiffness (7). Many solutions have been suggested for the treatment of cough of unknown cause, including intravenous lidocaine injection, pheniramine malate, fentanyl priming, propofol, magnesium sulfate, and dexmedetomidine. Pheniramine is a first-generation antihistamine (3). It is a derivative of alkylamine and is a

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sedative antihistamine with moderate muscarinic and sedative activities that is used in the treatment of allergic rhinitis and conjunctivitis (6). This drug reduces the allergic response by affecting the blood vessels, gastrointestinal tract and respiratory tract through competing with histamine (5). Its most common side effects include dizziness, drowsiness, unbalanced movements, fatigue, anxiety, euphoria, dizziness, wheezing, anemia, dry mouth, nausea, anorexia, diarrhea, photosensitivity, urinary retention, urinary burning and blurred vision (8). The most common side effects of this drug are lethargy and drowsiness. Anorexia, vomiting and diarrhea may also occur (9). It is contraindicated in asthma, lower respiratory tract diseases and lactation. Its effect time starts from one hour after consumption and reaches its peak effect after two hours, and its renal clearance time is after six hours (10). Its concomitant use with phenytoin may increase the pharmacological effects of phenytoin. Furthermore, concomitant use with alcohol and sedatives weakens the body's nervous system (11). Therefore, the aim of this study was to evaluate the effect pheniramine maleate on fentanyl-induced cough in opium addicts.

Materials and Methods

This randomized, double-blind clinical trial was performed on opium addicts admitted to Imam Reza Hospital in Mashhad, Iran in 2019. Patients who had inclusion and exclusion criteria in the intervention and control groups were studied and compared. A checklist was used to collect information.

Inclusion criteria: 1- Opium addicted patients, 2- Age between 18 to 65 years, 3- ASA class I and II, 4- Elective surgery more than half an hour. Exclusion criteria: 1- Receiving premedication before pheniramine injection, 2- History of chronic cough, 3- History of pharyngitis three weeks before surgery, 4- Consumption of Angiotensin-converting-enzyme inhibitors, 5- Drug allergy, 6- History of asthma or Chronic obstructive pulmonary disease, 7- History of bronchodilator or steroid treatment in the past month, 8- Neuromuscular diseases.

Sample Size

We considered an incidence of 5% and 37% for cough in the intervention and placebo groups. The sample size was calculated as 43 people in each group by considering β of 0.1 and α = 0.01. Finally, 86 patients were included in the study.

Two Independent Proportions (Null Case) Power Analysis

Numeric Results of Tests Based on the Difference: P1 - P2

H0: P1-P2=0. H1: P1-P2=D1<>0. Test Statistic: Z test with pooled variance

		Prop	Prop|H1		Sample	Sample
	Diff	Diff		Grp 2 or	Grp 1 or	Size	Size
Actual		Target	if H1	if H0	Control	Trtmnt	Grp 2	Grp 1
Beta	Alpha	Alpha	D1	D0	P2	P1	N2	N1	Power
0.0959	0.0013	0.0100	0.3200	0.0000	0.0500	0.3700	43	43	0.9041

Procedure

After obtaining informed consent, patients admitted to Imam Reza hospital, who underwent elective surgery for more than half an hour patients were divided into two groups based on randomization software. Patients and administrators had no information about the control and intervention groups. After dividing the patients, placebo and drugs were injected blindly and the administrators were not aware of the patient group or control and the type of drug. Patients underwent routine monitoring including pulse oximetry, non-invasive blood pressure and ECG. Serum infusion was started for all patients. In the control group, 2 ml of normal saline of 0.9% was injected and, pheniramine maleate 2-3 ml iv bolus was injected in the patient group. After 90 seconds, fentanyl was injected for 3 seconds at a dose of μ/kg to induce anesthesia. 90 seconds after fentanyl injection, cough intensity was divided into three groups including mild (1 to 2), moderate (3 to 5) and severe (more than 5) depending on the number of coughs observed and vital signs parameters were recorded. Induction of anesthesia was completed with propofol and atracurium.

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Translation Types

Data Analysis

All data were analyzed using Spss software version 23. Tables, graphs, mean indices, standard deviation, median and range of changes were used for description of data. Quantitative variables, frequency indices and percentages were also applied for qualitative variables. To analyze the quantitative variables, normality was first determined by Kolmogorov-Smirnov test. Two-group independent sample t-test was used for intergroup comparisons and paired t-test was used for intra-group comparisons if the data were normal. If the data were not normal, Mann–Whitney–Wilcoxon tests were used for intergroup and intragroup comparisons, respectively. Chi-square test or Fisher's exact test was applied to compare qualitative variables in groups. Analysis of covariance was used to control confounding variables. $P < 0.05$ was also considered to be significant in all analyzes.

Ethical Considerations

In this study, the names and details of the subjects were kept confidential. No cost was imposed to the patient's family and hospital. Completing the form and giving training to patients was done with their consent. Written consent was obtained from patients. At all stages of the research, researchers were required to comply with the ethics of research approved by the Ministry of Health and the Helsinki Declaration. The present study has been approved with the ethics code: IRCT20191204045603N1.

Results

A total of 86 opium addicts underwent elective surgery. In the intervention group, 29 men (67.4%) and 14 women (32.6%) were included. There were 32 men (74.4%) and 11 women (25.6%) in the control group. According to the results, there was no statistically significant difference between the two groups (P = 0.476). On the other hand, 46.5% of people in the control group were between 18 and 40 years old, followed by 27.9% in the age group of 41 to 55 years and 25.6% in the age group of 56 years and older. The intervention group, the majority of people were in the age group of 18 to 40 years (37.2%), followed by 41 to 55 years (34.9%) and over 55 years of age (27.9%). No significant difference was found between the mean ages in the two groups (P = 0.692).

According to the body mass index in both groups, half of the people were in normal condition, where 34.9% and 32.6% of the people in the control and intervention groups were overweight, respectively. Based on the results, there was no significant difference between the two groups in terms of body mass index (P = 0.694).

As shown in Table 1, the majority of people in the two groups had undergraduate education (control group: 53.5% and intervention: 39.5%). No statistically significant difference was found between the frequency distribution of education in the two groups (P = 0.165).

Table 1. Distribution of education frequency in two groups of intervention and control

		Control number (%)	**Intervention number (%)**	**P-value***
education	illiterate	1 (2.3%)	6 (14%)	0.165
	Under diploma	23 (53.5%)	17 (39.5%)	
	Diploma	12 (27.9%)	15 (34.9%)	
	High diploma	7 (16.3%)	5 (11.6%)	
	Total	43 (100%)	43 (100%)	

*Fisher test

According to the Table 2, the frequency of self-employed people in the intervention and control groups was 41.9%, which make up the majority of individuals in the two groups. Also, Fisher's exact test showed no statistically significant difference between the two groups (P = 0.615).

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Table 2. Distribution of job frequency in intervention and control groups

		Control number (%)	Intervention number (%)	P-value*
Job	Farmer	3 (7%)	4 (9.3%)	0.615
	manual worker	8 (18.6%)	5 (11.6%)	
	housewife	8 (18.6%)	11 (25.6%)	
	Employee	2 (4.7%)	4 (9.3%)	
	student	4 (9.3%)	1 (2.3%)	
	Employer	18 (41.9%)	18 (41.9%)	
	Total	43 (100%)	43 (100%)	

*Fisher test

According to Table 3, there was no significant difference between the two groups in terms of disease type (P = 0.258).

Table 3. Frequency distribution of disease type in intervention and control groups

		Control number (%)	Intervention number (%)	P-value*
Disease type	No disease	25 (58.1%)	24 (55.8%)	0.258
	Diabetic	1 (2.3%)	5 (11.6%)	
	hypertension	7 (16.3%)	4 (9.3%)	
	thyroid	1 (2.3%)	1 (2.3%)	
	Hemato	3 (7%)	0	
	Cardiac	0	1 (2.3%)	
	Renal	2 (4.7%)	0	
	GI	1 (2.3%)	3 (7%)	
	Diabetic and hypertension	1 (2.3%)	2 (4.7%)	
	Diabetic and cardiact	1 (2.3%)	0	
	Hypertension and cardiac	1 (2.3%)	2 (4.7%)	
	Other	0	1 (2.3%)	
	Total	43 (100%)	43 (100%)	

*Fisher test

As shown in Table 4, the majority of surgeries in the control group were related to urological surgery (48.8%) and abdomen (27.9%). In the intervention group, the majority of surgeries belonged to orthopedics (37.2%) and abdomen (34.9%). According to the results of Fisher test, a statistically significant difference was found between the types of surgery in the two groups (P = 0.006).

Table 4. Frequency distribution of surgery in the intervention and control groups

		Control number (%)	Intervention number (%)	P-value*
Surgery type	Orthopedic	5 (11.6%)	16 (37.2%)	0.006
	Urology	21 (48.8%)	7 (16.3%)	
	Abdominal	12 (27.9%)	15 (34.9%)	
	Gynecology	2 (4.7%)	2 (4.7%)	
	Other	3 (7%)	3 (7%)	
	Total	43 (100%)	43 (100%)	

*Fisher test

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According to Fisher's exact test (Table 5), no significant difference was observed between the distribution of opium consumption in the two groups (P = 0.3).

Table 5. Frequency distribution of opium consumption in the intervention and control groups

		Control number (%)	Intervention number (%)	P-value*
opium consumption	Opium	27 (62.8%)	21 (48.8%)	0.3
	Sap	10 (23.3%)	9 (20.9%)	
	Methadone	2 (4.7%)	3 (7%)	
	Crystal	1 (2.3%)	1 (2.3%)	
	Heroin	0	3 (7%)	
	Tramadol	1 (2.3%)	0	
	Sap and opium	2 (4.7%)	6 (14%)	
	Total	43 (100%)	43 (100%)	

Fisher test *

The frequency distribution of the type of consumption was examined in the intervention and control groups. In the control group, 18 patients (41.9%) had oral substance abuse, followed by inhalation (20; 46.5%), injection/inhalation (1; 2.3%), injection (3; 7%) orally/inhalation. In the intervention group, substance abuse in 23 patients (53.5%) was oral, followed by inhalation (13 patients; 30.2%), oral-injectable form (1 patient; 2.3%), injectable-inhalation (1 patient) and orally-inhalation (5 people; 11.6%). This distribution was not found to be statistically significant in both groups (P = 0.416).

The distribution of opium consumption time in the intervention and control groups was examined. The mean duration of use was 11.7±8.8 years in the control group and 14±10.8 years in the intervention group. In both groups, the minimum duration of opium use was 1 year. The maximum duration of use was 40 in the control group and 38 years in the intervention.

As indicated in Figure 1, the majority of individuals (46.5%) in the control group were between 6 and 15 years old, while 37.2% were less than 5 years old in the intervention group and 37.2% had more than 15 years of opium use history.

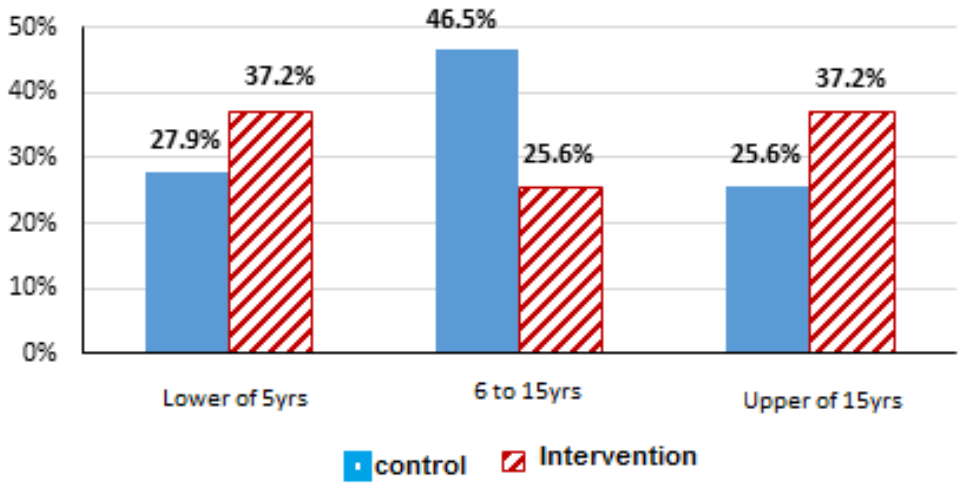

Figure 1. Frequency distribution of opium consumption time in intervention and control groups

The mean number of opium use in the intervention (1.8 ± 0.8) and control (1.6 ± 0.7) groups during the day was not

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statistically significant between the two groups (P = 0.177).
According to Table 6, the pulse rate before and after the intervention was not significantly different between the two groups (P> 0.05). Furthermore, the rate of increase in pulse rate in the control and intervention groups was 5.2 ± 5.8 and 6 ± 6.5, respectively, which was not significantly different (P = 0.509). On the other hand, the rate of increase in pulse rate after the intervention was significant in both groups (P <0.001).

Table 6. Pulse rate distribution

		Control		**Intervention**		**P-value***
		Mean±SD	**Middle (variation range)**	**Mean±SD**	**Middle (variation range)**	
Pulse rate	Before the intervention	78.3±14.1	(48-115) 80	79±16.8	(50-110) 80	0.841
	After intervention	83.5±14.4	(49-120) 85	85±16.9	(55-120) 85	0.647
	Differences before and after the intervention	5.2±5.8	(-20-15) 5	6±6.5	(-8-23) 5	0.509
P-value**		<0.001		<0.001		

* Two-group independent t-test to compare the two groups ** From paired t-test to compare two times

As shown in Table 7, the rate of respiration per minute before and after the intervention in the control group was significantly higher than the intervention group (P <0.05), but this rate was not significantly different between the two groups after the intervention (P> 0.05). Additionally, the rate of increase in respiration in the control and intervention groups was 0.25 ± 1.0 and -0.16 ± 1.0, respectively, which was not significantly different (P = 0.16). On the other hand, changes in respiration rate after the intervention were not significant in both groups (P> 0.05).

Table 7. Distribution of respiration rate per minute in intervention and control groups

		control		intervention		P-value*
		Mean±SD	Middle (variation range)	Mean±SD	Middle (variation range)	
respiration rate	Before the intervention	17.6±2.9	(14-25) 18	16.3±2.9	(10-25) 16	0.047
	After intervention	17.9±2.9	(14-25) 18	16.2±2.8	(10-25) 16	0.006
	Differences before and after the intervention	0.25±1.0	(-2-3) 0	-0.16±1.0	(-4-20) 0	0.16
P-value**		0.133		0.377		

* From the Mann-Whitney test to compare the two groups ** From the Wilcoxon test to compare two times

Systolic blood pressure was also assessed in the intervention and control groups. According to Mann-Whitney test, systolic blood pressure in the control group before the intervention was 124.7 ± 20.4 while it was found to be 126.5 ± 17.7 in the intervention group, but no statistically significant difference was between the two groups (P = 0.413). After the intervention, systolic blood pressure was determined in the control and intervention groups to be 127.3 ± 17.3 and 132.3 ± 17.5, respectively; There was no statistically significant difference between the two groups in terms of systolic blood pressure (P = 0.132). According to Wilcoxon test, the difference between systolic blood pressure after the was significant intervention in both groups (P <0.01).

Mann-Whitney test showed that the mean diastolic blood pressure before the intervention in the control and

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 8343 - 8352
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intervention groups was 72.1 ± 8.4 and 78.7 ± 7.8, respectively, which was statistically significant (P = 0.001). After the intervention, diastolic blood pressure was in the control and intervention groups 73.1± 6.7 and 79.4± 8.3, respectively, which was statistically significant (P <0.001). However, Wilcoxon test showed that diastolic blood pressure was not statistically significant in the control group (P = 0.446) and the intervention group (P = 0.41) before and after the intervention.

According to Table 8, body temperature before and after the intervention was not found to be significantly different between the two groups (P> 0.05). In addition, the rate of decrease in body temperature in the control group (-0.1 ± 0.7) and in the intervention group (0 ± 0.04) was not significantly different (P = 0.743). On the other hand, in both groups, the rate of decrease in body temperature after the intervention was not significant according to Wilcoxon test (P> 0.05).

Table 8. Body temperature distribution in intervention and control groups

		control		intervention		P-value*
		Mean±SD	Middle (variation range)	Mean±SD	Middle (variation range)	
Body temperature	Before the intervention	37±0.07	(36.9-37.3) 37	37±0.1	(36.8-37.5) 37	0.087
	After intervention	36.9±0.8	(32-37.3) 37	37±0.1	(36.8-37.5) 37	0.201
	Differences before and after the intervention	-0.1±0.7	(-5-0.2) 0	0±0.04	(-0.1-0.2) 0	0.743
P-value**		0.726		0.705		

* Mann-Whitney test to compare the two groups ** Wilcoxon test to compare two times

Our findings revealed that 36 (83.7%) and 42 patients (97.7%) had no cough in the control and intervention groups, respectively. In the control group, 7 patients (16.3%) had a cough, of which 4 (9.3%) had a mild cough, 2 (4.7%) had a moderate cough, and 1 (2.3%) had a severe cough. In the intervention group, 1 patient (2.3%) showed a mild cough. According to Fisher test, the difference between the two groups was statistically significant in terms of cough (P = 0.029) and severity of cough (P = 0.025) between the two groups (Figure 2).

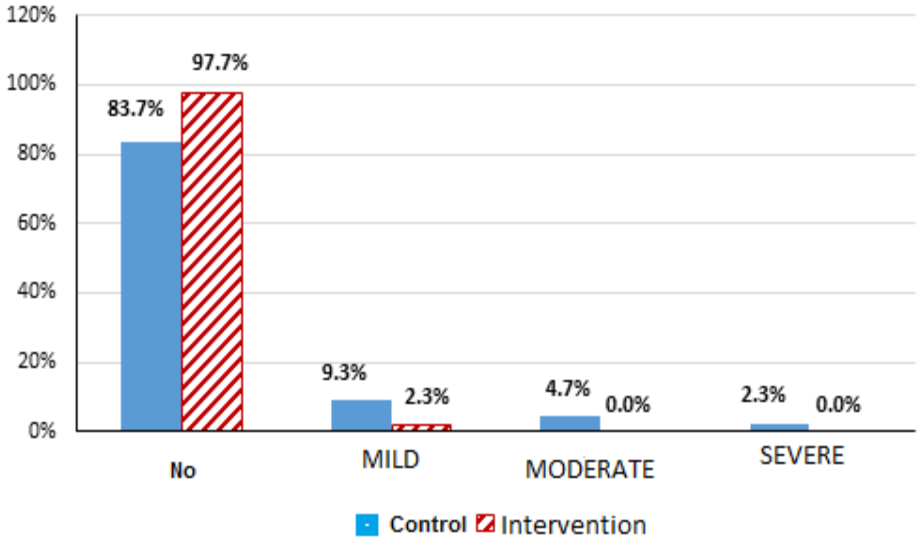

Figure 2. Frequency distribution of cough severity in intervention and control groups

As shown in Table 9, no significant difference was found in the frequency of cough between the control (9.4%) and

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intervention (3.4%) groups in men (P = 0.614). However, the frequency of cough in women in the control group was significantly higher than women in the intervention group (P = 0.026).

Table 9. Frequency distribution of cough in intervention and control groups by gender

Sex			Control number(%)	Intervention number(%)	P-value*
Male	cough	NO	29 (90.6%)	28 (96.6%)	0.614
		YES	3 (9.4%)	1 (3.4%)	
		TOTAL	32 (100%)	29 (100%)	
Female	cough	NO	7 (63.6%)	14 (100%)	0.026
		YES	4 (36.4%)	0	
		TOTAL	11 (100%)	14 (100%)	

* Fisher test

The duration of cough in 5 patients (11.6%) was 4 seconds, followed by 8 seconds (2.3%, 4 patients) and 12 seconds (2.3%, 1 patient). In the intervention group, the duration of cough in a person who had a cough was 4 seconds, this difference was found to be statistically significant among both groups (P = 0.026).

Discussion

In the evaluation of 86 patients with opium addiction, it was observed that 7 patients in the control group (16.3%) and 1 patient (2.3%) in the intervention group had a cough after the intervention, which was statistically significant (P = 0.029). Additionally, cough severity was mild in 4 patients (9.3%) in the control group, followed by moderate (2 patients, 4.7%) and severe (1 patient, 2.3%). In the intervention group, the severity of cough in a person who had a mild cough was mild; this difference was statistically significant (P = 0.025).

Various studies have been conducted in this regard. A study by Ozmen et al. on the efficacy of pheniramine maleate in fentanyl-induced cough found that 8 patients (25%) in group C (Normal Saline) had fentanyl-induced cough, while three patients (7.5%) in group L (Lidocaine) and one patient (2.5%) in group F (PM) had this condition. They also reported a statistically significant difference between groups F and C (P <0.05). However, the difference between group L and C or group F and group L was not found to be statistically significant (P> 0.05) (6), therefore this was consistent with the results observed in the recent study. The observed difference was also due to the differences in the methods used in the two study, where different doses of the drug were applied.

In a study by Arslan et al., the effect of Pheniramine maleate on fentanyl-induced cough was evaluated, where the incidence of cough varied significantly between groups. They reported that 37.5% of patients had a cough in the placebo group, while the frequency in the phenirami*n*e (5%) and lidocaine (15%) groups was significantly reduced (Fisher's exact test, P = 0.0007 and 0.01858). They also found no significant difference in the incidence of cough between the Pheniramine group (5%) and the lidocaine group (15%) (Fisher's exact test, P = 0.4325). They also stated that the mean of cough in placebo group, Pheniramine group and lidocaine was significantly different by Post Hoc test (P = 0.0001 and P = 0.009, respectively). But no significant difference in cough severity was observed between Pheniramine group and lidocaine group (P = 0.856) (5). Accordingly, these results were consistent with those observed in the recent evaluation and the limited difference was due to differences in the evaluated groups in the two studies.

Kolahdouzan et al. also evaluated the effect of intravenous lidocaine on cough status in patients and observed that out of 63 patients who received intravenous lidocaine before fentanyl administration, 55 patients did not cough while this amount was found to be 38 in the control group. This difference was statistically significant (P <0.0002). They also stated that no side effects of lidocaine were observed, which is consistent with the results observed in our evaluation, indicating the importance of new treatments in these patients (12).

Rafiei et al. Also evaluated the effect of clonidine on cough in patients treated with fentanyl in a 2013 study and observed that the frequency of cough following fentanyl injection in the control group was significantly higher than

clonidine (36.1% vs. 15.6) (P <0.01). They also stated that the severity of cough was not significantly different between the two groups (P> 0.05), which was different from the results observed in the current study. This difference could be due to differences in the drugs used in the two evaluations (13).

Shoja et al. also evaluated the effect of lidocaine on fentanyl-induced cough and observed that the incidence of cough was 2.5% in groups 1 and 9.2% and 22.5% in groups II and III, respectively. In group III, the incidence of cough was significantly higher (P <0.001). The incidence of cough in patients under 18 years of age in all three groups was higher than in patients over 18 years of age (P <0.01) (14), which was also largely similar to the findings presented herein and the observed difference was due to differences in medication used in two study.

On the other hand, no significant difference was found between the two groups in terms of the type of diseases of individuals (P = 0.258), distribution of type and manner of opium use (P = 0.3), duration of use (P = 0.432), average frequency of opium use (P = 0.177), last time of use Opium (P = 0.972), pulse rate before and after the intervention (P = 0.509), rate of change in respiration per minute, before and after the intervention (P = 0.509) and systolic and diastolic blood pressure) before and after the intervention (After removing the confounder effect).

Regarding hemodynamic changes in patients in other studies, Yang et al. observed that the prevalence of systolic blood pressure, with an increase of more than 30% in baseline, was significantly higher in the fentanyl group than in the R group during the study period. However, the prevalence of systolic blood pressure was significantly lower in the fentanyl group than in the remifentanil group with a decrease of> 30% in baseline values (15). Casati also did not observe a clear difference in systolic blood pressure between the remifentanil and sufentanil groups (16). In a study by Zhang et al., it was observed that the decrease in heart rate after induction of anesthesia was greater in the remifentanil group than the fentanyl and sufentanil groups (17). Regarding hemodynamic changes, Rafiei et al. reported that systolic and diastolic blood pressure decreased significantly in the clonidine group (P <0.05) (13). No difference was observed in the Observer Assessment of Alertness/Sedation (OAA/S) classification criteria between the two groups (P> 0.05).

Importantly, the effect of pheniramine maleate on fentanyl-induced cough in opium addicts has not been studied to date, and only a few studies have examined the effect of pheniramine maleate on fentanyl-induced cough (6, 5).

Conclusion

Pheniramine is capable of reducing the incidence and duration of fentanyl-induced cough in opium-addicted patients. It acts like lidocaine and has no side effects on the patient's vital signs. It can be used as an effective cough medicine instead of other medicines because of its cheapness and availability. Based on data presented herein, it can be used to improve the cough condition caused by fentanyl in patients with opium addiction.

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Imam Reza Clinical Research Development Center.

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