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Suppression of fentanyl-induced cough. A priming dose of intravenous dexmedetomidine–magnesium sulfate: A double blind, randomized, controlled study

Enas Abd El Motlb *

Department of Anesthesiology and Surgical ICU, Faculty of Medicine, Mansoura University, Oncology Center, Egypt

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KEYWORDS

Fentanyl induced cough;
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Abstract *Introduction:* Fentanyl induced cough (FIC) often follows bolus fentanyl administration in 18% up to 65% of cases. Several researches have been done to reduce such side effect. Our hypothesis is that pretreatment with intravenous dexmedetomidine–magnesium sulfate could effectively suppress fentanyl induced cough.

Patients and methods: 200 patients of (ASA) I and I aged 18–60 years, weighting from 40 to 90 kg, undergoing elective surgeries, were randomized into four groups using sealed envelope system. Patients belong to (D) group received DEX 0.5 μg/kg. Patients belong to group (M) received magnesium sulfate 20 mg/kg, and those of group (D + M) received DEX 0.5 μg/kg + magnesium sulfate 20 mg/kg. The above preparations were reconstructed by saline to reach a volume of 20 ml. Patients belong to group (S) received 20 ml normal saline. Patients of each group received their cross bonding drug one minute before fentanyl bolus injection (2 μg/kg within 5 s). The primary end points were the onset time, frequency and severity of cough from time of fentanyl injection till 1 min. According to four point scale, severity of cough was graded as follows: grade 0 = no cough; grade 1 = single cough; grade 2 = more than one attack of non- sustained cough; grade 3 = repeated and sustained cough with head lift.

Results: Nineteen (38%) cases had cough in group (S), 8(16%) in group (D) and 14(28%) cases in group (M). No patients in group (D + M) experienced any cough. Patients of groups (D) and (D + M) showed a significantly lower incidence of cough compared with group (S) ($P < 0.05$). There was no significant difference regarding the onset time or severity of cough between groups.

Conclusion: Pretreatment with dexmedetomidine–magnesium sulfate could effectively suppress fentanyl induced cough following injection of 2 μg/kg fentanyl injected within 5 s.

* Address: Department of Anesthesia and Surgical Intensive Care, Mansoura University Hospital, Egypt. Mobile: +20 1005401236.
E-mail address: sevo2006@gmail.com

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1. Introduction

Due to some sympathetic and psychological side effects that may occur during induction of general anesthesia, opioids and particularly fentanyl are used for analgesia and to relieve anxiety [1,2]. Fentanyl is characterized by the rapid onset, short duration, effective analgesia, less histamine release, no negative inotropic action plus it can be titrated easily [3]. However, fentanyl induced cough (FIC) often follows bolus fentanyl administration in 18% up to 65% of cases [4]. Several researches have been done to reduce such side effect which is a critical issue in those suffering from intracranial hypertension, cerebral or aortic aneurysm, increased intra-abdominal or intraocular pressure, pneumothorax or hyperactive air way diseases [5,6]. FIC may be simple or may be severe enough to cause upper air way obstruction that necessitates immediate intervention [6]. Bronchoconstriction was expected to be the engine of this cough reflex, so bronchodilators (selective β2 agonist) inhalation was used. Others such as lidocaine, N-methyl-D-aspartate (NMDA) receptor antagonists, atropine, propofol, midazolam and slow administration of fentanyl were tried [7,8]. Dexmedetomidine (DEX) is a specific α2-receptor agonist, used to reduce anxiety and tension and to promote relaxation and sedation with hemodynamic stability [9]. Magnesium (Mg) is a major cation in the human body that antagonizes calcium influx into the cell through a noncompetitive mechanism at N-methyl-D-aspartate (NMDA) receptor [10] and helps to increase flaccidity [11], as well; it inhibits contraction of smooth muscle and may be helpful in treatment of asthma [12]. This study aims to investigate the efficacy of DEX–Mg SO_4 to prevent or suppress FIC. The hypothesis of this study is that DEX–Mg SO_4 complex is a powerful and effective regimen for suppression of FIC.

2. Patients and methods

This prospective, randomized, double blind, controlled study took approval of Mansoura Medical Research Ethics Committee. The study was conducted in Mansoura University Hospital (Oncology center) and after obtaining written informed consent. 200 American Society of Anesthesiologists (ASA) physical status I and I patients with age range from 18 to 60 years and body weight from 40 to 90 kg who were undergoing general anesthesia for different elective surgeries were included in our study. Patients suffering from hyperactive airway, upper respiratory tract infection, expected difficult airway, hepatic or renal impairment, uncontrolled hypertension, coronary artery disease, and diabetes and those receiving anesthetic premedication were excluded from the study. Patients were randomly assigned to one of the four following groups using sealed envelope system: Group S (control group), Group D (DEX group), Group M (magnesium sulfate group) and Group D-M (DEX–magnesium sulfate group). I used sealed envelope system through prepared randomly generated treatment allocations within sealed envelopes. Once a patient has consented to enter the trial an envelope is opened and the patient is offered the allocated treatment regimen. The anesthetics were prepared by an anesthesiologist, who was no further involved in data collection. Patients included in this study didn't receive any premedication before surgery. On arrival to the operating room, pressure cuff, pulse oximetry probe and ECG electrodes were connected to the patient. An intravenous access (20 G cannula) was inserted. Patients belong to (D) group received DEX 0.5 μg/kg + normal saline to reach a volume of 20 ml. Patients belong to group (M) received magnesium sulfate 20 mg/kg + normal saline to reach a volume of 20 ml, and those of group (S) received normal saline of 20 ml volume. Patients belong to group (D-M) received DEX 0.5 μg/kg + magnesium sulfate 20 mg/kg + normal saline to reach a volume of 20 ml. Patients of each group received their cross bonding drug by steady rate over 10 min-one minute before fentanyl bolus injection (2 μg/kg within 5 s).

The primary end points were the onset time (time from end of bolus injection of fentanyl till beginning of cough), frequency and severity of cough. These parameters were recorded by an anesthesiologist blind to group assignment, from time of fentanyl injection till 1 min. According to four point scale, severity of cough was graded as follows: grade 0 = no cough; grade 1 = single cough; grade 2 = more than one attack of non-sustained cough; grade 3 = repeated and sustained cough with head lift. Later, by 1–2 mg propofol, anesthesia was induced and maintained with inhalational agent and/or propofol infusion plus air/oxygen mixtures.

Statistical analysis

Data were analyzed using SPSS (Statistical Package for Social Sciences) version 22.0. Qualitative data were presented as number, proportion or percentage. Comparison between groups was done by Chi-square test or Fisher's exact test with Bonferroni correction. Quantitative data were tested for normality by Kolmogrov–Smirnov test. Normally distributed data were presented as mean ± SD. F test (ANOVA) was used to compare between groups. $P \leqslant 0.05$ was considered to be statistically significant.

Post hoc power analysis was done using G power program (version 3.0.10) to calculate the power of this study. Chi-square (χ^2) test (contagency tables) was used with effect size = 0.3 (medium), α error = 0.05, total sample size = 200 and degree of freedom = 3. Calculated power was 0.95.

Table 1 Demographic data in four groups. Values are in means ± SD.

Demographics	Group S (n = 50)	Group D (n = 50)	Group M (n = 50)	Group D + M (n = 50)	P
Age (years)	40.3 ± 11.1	39.8 ± 12.3	40.9 ± 10.9	38.6 ± 14.1	0.63
Gender male/female	27/23	26/24	22/28	24/26	0.75
Weight (kg)	80.9 ± 8.4	78.5 ± 5.3	79.3 ± 1.2	80.6 ± 4.3	0.76
Height (cm)	161.8 ± 7.2	165.6 ± 5.5	162.4 ± 8.1	164.3 ± 4.6	0.81
ASA class I/II	46/4	43/7	42/8	47/3	0.32

No significant difference was detected in this table.