Rev Bras Anestesiol. 2016;66(4):383–387

REVISTA BRASILEIRA DE ANESTESIOLOGIA
Publicação Oficial da Sociedade Brasileira de Anestesiologia
www.sba.com.br

SCIENTIFIC ARTICLE

The effect of pheniramine on fentanyl-induced cough: a randomized, double blinded, placebo controlled clinical study

Zakir Arslan[a,*], **Eyup Serhat Çalık**[b], **Bekir Kaplan**[a], **Elif Oral Ahiskalioglu**[a]

[a] *Regional Training and Research Hospital, Department of Anesthesiology and Intensive Care, Erzurum, Turkey*
[b] *Regional Training and Research Hospital, Department of Cardiac Surgery, Erzurum, Turkey*

Received 28 October 2014; accepted 26 November 2014
Available online 22 December 2015

KEYWORDS
Fentanyl;
Cough;
Pheniramine maleat;
Anesthesia

Abstract
Background and objectives: There are many studies conducted on reducing the frequency and severity of fentayl-induced cough during anesthesia induction. We propose that pheniramine maleate, an antihistaminic, may suppress this cough. We aim to observe the effect of pheniramine on fentanyl-induced cough during anesthesia induction.
Methods: This is a double-blinded, prospective, three-arm parallel, randomized clinical trial of 120 patients with ASA (American Society of Anesthesiologists) physical status III and IV who aged ≥18 and scheduled for elective open heart surgery during general anesthesia. Patients were randomly assigned to three groups of 40 patients, using computer-generated random numbers: placebo group, pheniramine group, and lidocaine group.
Results: Cough incidence differed significantly between groups. In the placebo group, 37.5% of patients had cough, whereas the frequency was significantly decreased in pheniramine group (5%) and lidocaine group (15%) (Fischer exact test, $p = 0.0007$ and $p = 0.0188$, respectively). There was no significant change in cough incidence between pheniramine group (5%) and lidocaine group (15%) (Fischer exact test, $p = 0.4325$). Cough severity did also change between groups. Post Hoc tests with Bonferroni showed that mean cough severity in placebo differed significantly than that of pheniramine group and lidocaine group ($p < 0.0001$ and $p = 0.009$, respectively). There was no significant change in cough severity between pheniramine group and lidocaine group ($p = 0.856$).
Conclusion: Intravenous pheniramine is as effective as lidocaine in preventing fentayl-induced cough. Our results emphasize that pheniramine is a convenient drug to decrease this cough.

* Corresponding author.
E-mail: zakir-arslan@hotmail.com (Z. Arslan).

http://dx.doi.org/10.1016/j.bjane.2014.11.018

PALAVRAS-CHAVE
Fentanil;
Tosse;
Maleato de feniramina;
Anesthesia

Efeito de feniramina sobre a tosse induzida por fentanil: estudo clínico, randômico, duplo-cego e controlado com placebo

Resumo
Justificativa e objetivos: Há muitos estudos sobre a redução da frequência e gravidade da tosse induzida por fentanil durante a indução da anestesia. Propomos que maleato de feniramina, um anti-histamínico, pode suprimir essa tosse. Nosso objetivo foi observar o efeito de feniramina sobre a tosse induzida por fentanil durante a indução da anestesia.
Métodos: Este é um estudo clínico prospectivo, de três braços paralelos, randômico e duplo-cego, de 120 pacientes com estado físico ASA III e IV (de acordo com a Sociedade Americana de Anestesiologistas), com idades ≥ 18 anos e programados para cirurgia cardíaca aberta eletiva sob anestesia geral. Os pacientes foram divididos aleatoriamente em três grupos de 40 pacientes cada, usando números aleatórios gerados por computador: grupo placebo, grupo feniramina e grupo lidocaína.
Resultados: A incidência de tosse diferiu significativamente entre os grupos. No grupo placebo, 37,5% dos pacientes apresentaram tosse, enquanto que a frequência foi significativamente reduzida no grupo feniramina (5%) e no grupo lidocaína (15%) (teste exato de Fischer, $p = 0{,}0007$ e $p = 0{,}0188$, respectivamente). Não houve alteração significativa na incidência de tosse entre os grupos feniramina (5%) e lidocaína (15%) (teste exato de Fischer, $p = 0{,}4325$). A gravidade da tosse também alterou entre os grupos. Testes *post hoc* com Bonferroni mostraramu que a média da gravidade da tosse no grupo placebo diferiu significativamente das médias dos grupos feniramina e lidocaína ($p < 0{,}0001$ e $p = 0{,}009$, respectivamente). Não houve alteração significativa na gravidade da tosse entre o grupo feniramina e grupo lidocaína ($p = 0{,}856$).
Conclusão: Feniramina por via intravenosa possui a mesma eficácia que lidocaína na prevenção da tosse induzida por fentanil. Os resultados enfatizam que feniramina é um medicamento conveniente para diminuir essa tosse.

Introduction

Intravenous fentanyl which is used mainly for induction of anesthesia frequently causes an irritating cough in the patient.[1] The prevalence of fentanyl-induced cough ranges from 21.6% to 74%.[2–5] It is generally transitory and limited, but it can be harmful in cases with increased intracranial, intraocular or intra-abdominal pressure; cerebral aneurysm, brain trauma and hernia, dissecting aortic aneurysm, pneumothorax or reactive airway disease.[4–7] Although the mechanism of fentanyl-induced cough has not been fully clarified, it is thought that allergic mediators such as histamine may cause it.[8] Various medicaments and methods have been used with varying degrees of success to hinder or relieve this side-effect.[2] One study reported that lidocaine 2 mg/kg iv given one minute before fentanyl decreased the prevalence of cough from 65% (according to the control group) to 14%.[6] Another study reported that iv fentanyl administered in diluted form or more slowly markedly hindered cough.[9]

Many solutions have been proposed for this cough of unidentified origin. We wanted to investigate the effect of pheniramine on fentanyl-induced cough. The purpose of this study was to compare the effect of the antihistaminic *pheniramine maleate* and lidocaine on fentanyl-induced cough.

Method

Design

This is a double-blinded, prospective, three-arm parallel, randomized clinical trial conducted in a research hospital between September 2013 and April 2014. The approval of the Ethics Committee of our hospital and informed consent forms were taken from all patients participating in the study (Decision n° 2013/13). One hundred and twenty ASA (American Society of Anesthesiologists) physical status III and IV patients aged ≥18 and scheduled for elective open heart surgery during general anesthesia, were randomly assigned to one of three groups of 40 patients each, using computer-generated random numbers: placebo group, pheniramine group, and lidocaine group. Dr. ZA was responsible for drug preparation and the allocation sequences (contained in a set of sealed envelopes). The observers and all the patients involved in the study were blinded.

Inclusion criteria

Consecutive patients planned for open heart surgery (coronary artery by-pass, mitral and aortic valve replacement), receiving no premedication, and in the ASA-III and IV class were included.