Clinical Practice Statement

Should Antiemetics be Given Prophylactically with Intravenous Opioids While Treating Acute Pain in the Emergency Department? (Reviewed/Updated from 2010)

Co-Chairs: Steve Rosenbaum, MD FAAEM
Michael Abraham, MD FAAEM
Authors: Kristin D. Rowland, MD (AAEM/RSA)
Justin Fuehrer, DO (AAEM/Fellow-in-Training)
Sergey M. Motov, MD FAAEM

The authors disclosed no commercial relationships or conflicts of interest.

Reviewers: Eric Bruno, MD FAAEM
Robert Sherwin, MD FAAEM

Reviewed and approved by AAEM Board of Directors. (6/7/2019)

Recommendation

Antiemetics are not indicated for routine use with intravenous opioids in treating acute pain in the ED. The potential benefit from administering prophylactic antiemetics to all patients receiving opioids is small at best, and this benefit is outweighed by potentially undesirable additive sedation and extrapyramidal side effects.

Introduction

Parenteral opioids are the most common analgesics used in the emergency department (ED) for relief of acute pain. Gastrointestinal side effects such as nausea and vomiting are common following opioid analgesia in long-term therapy for malignant and chronic pain and are considered a limiting factor in effective pain therapy.[1] Despite the lack of clear and supporting evidence, it has been common practice to prophylactically use antiemetics when administering intravenous opioids in treating acute pain in the ED. The recent literature is challenging this concept and advocating against the prophylactic administration of antiemetics in the ED, as the incidence of vomiting associated with opioid administration for acute pain is low. Given concerns for the additive sedative and extrapyramidal effects of many anti-emetics when co-administered with opioids, the routine use of prophylactic antiemetics likely causes far more adverse effects

relative to episodes of vomiting prevented.[2-4] The existing research is limited in terms of the antiemetics used (mostly metoclopramide), however more recent studies have evaluated ondansetron as well. Other studies have found certain risk factors that are associated with a higher incidence of nausea and vomiting after opioid administration. The overwhelming evidence shows a low incidence of nausea and vomiting after administration of opioid analgesics in the ED.

Executive Summary

A structured review was performed of the medical literature using PubMed. Based on this review, 13 unique articles were identified.

Talbot et al. evaluated the incidence of nausea and vomiting after morphine and pethidine (meperidine) analgesia in a prospective, randomized, double-blind, placebo-controlled trial. Patients were further randomized to receive either metoclopramide or normal saline in addition to either morphine or pethidine. Out of 122 patients, 7 patients (5.7%) experienced nausea and 1 patient (0.8%) had vomiting. There was no statistical significance in incidence of nausea and vomiting between treatment groups. However, of those receiving metoclopramide, 7.9% had side effects unrelated to nausea and vomiting versus 3.4% in the normal saline group. These findings showed metoclopramide administration increased adverse effects, such as dystonic reaction, vertigo, dizziness, restlessness, and drowsiness, without affecting the rate of nausea and vomiting.[5]

Paoloni et al designed a prospective observational study in 205 ED patients in an effort to evaluate the rate of vomiting before and after administration an intravenous opiate analgesia at 30 and 60 minutes. The results showed a cumulative incidence of vomiting of 1.5% at 30 minutes and 2.4% at 60 minutes.[6]

Bradshaw and colleagues conducted a randomized controlled trial comparing the incidence of nausea and vomiting in 259 patients with acute pain treated with morphine along with prophylactic metoclopramide or placebo. The results showed the overall incidence of nausea and vomiting was 2.7% in the whole study population, 1.6% in the metoclopramide group, and 3.7% in the placebo group without statistical significance.[7]

Yeoh and colleagues evaluated the value of an educational initiative designed to reduce the prophylactic use of metoclopramide with initial morphine dose by conducting a pre-and post-intervention trial. The results showed a significant reduction of the proportion of patients receiving metoclopramide from 22.6% to 4.1% ($P<0.001$), although incidence of nausea and vomiting after receiving morphine was not recorded. [8]

Culver and colleagues conducted a prospective observational study to evaluate the efficacy of IV ondansetron in preventing nausea and vomiting after opioid administration in the ED. The study evaluated nausea levels at baseline, 5 minutes, and 30 minutes after opioid administration with and without ondansetron. Out of 133 patients, incidence of nausea after 30 minutes was 15.9% in in the ondansetron and opioid group, and 4.6% in the opioid only group ($p = 0.047$).[9]

Bounes and colleagues conducted a prospective, observational, pharmaco-epidemiological international cohort study to identify potential risk factors for adverse effects after morphine administration in 1128 patients. The results showed that morphine-related nausea and vomiting was seen more often in patients with a history of travel illness (adjusted OR 1.7, CI 1.01-2.86) and in patients with a history of morphine-induced nausea or vomiting (adjusted OR 3.86, CI 2.29-6.51).[10]

Ishihara and colleagues conducted a multi-institutional retrospective study on 619 hospitalized patients receiving oral opioid analgesics and analyzed the incidence of opioid-induced side effects. This included looking at the incidence of side effects when premedicated with dopamine D2 blockers such as metoclopramide, promethazine, and prochlorperazine. Results showed that premedication with dopamine D2 blockers was not sufficient to prevent nausea or vomiting.[11]

Giusti and colleagues conducted a web-based cross-sectional national survey comprised of an 11 item survey asking specific questions regarding the prophylactic use of antiemetics for prevention of opioid-induced nausea and vomiting. Results showed that 45% of physicians prescribed prophylactic antiemetics at the beginning of opioid prescription, while 81% prescribed antiemetics at the occurrence of opioid-induced nausea or vomiting.[12]

Nicholson wrote a review paper regarding the incidence of opioid induced nausea and/or vomiting as well as recommendations regarding the possible use of prophylactic antiemetics to prevent opioid-induced nausea and/or vomiting. In this article, it was recommended that prophylactic antiemetics only be used in those at high risk for opioid-induced nausea and/or vomiting.[13]

Conclusion

Antiemetics are not indicated for routine use with intravenous opioids in treating acute pain in the ED. The potential benefit from administering prophylactic antiemetics to all patients receiving opioids is small at best, and this benefit is outweighed by potentially undesirable additive sedation and extrapyramidal side

effects. Nausea and vomiting are infrequent after opioid use, however there is a slightly higher incidence of these adverse effects in patients with a history of nausea and vomiting after opioid administration and in patients with a history of travel sickness.[7] Therefore, questioning patients regarding any history of nausea and vomiting after opioid administration, or history of travel sickness, is indicated and prophylactic antiemetics considered in patients with these risk factors.

References

1. Porrecca F, Ossipov MH. Nausea and Vomiting Side Effects with Opioid Analgesics during Treatment of Chronic Pain: Mechanism, Implications, and Management Options. Pain Medicine. 2009; Vol 10(4): 654-662

2. Benyamin R, Trescot AM, Datta S, Buenaventura R, Adlaka R, Sehgal N, Glaser SE, Vallejo R. Opioid Complications and Side Effects. Pain Physician. 2008 Mar; 11 (2 Suppl): S105-120.

3. National Institute of Health. MedlinePlus. Metoclopramide. https://medlineplus.gov/druginfo/meds/a684035.html. Accessed 4/5/2019.

4. National Institute of Health. MedlinePlus. Ondansetron. https://medlineplus.gov/druginfo/meds/a601209.html. Accessed 4/5/2019.

5. Talbot-Stern J, Paoloni R. Prophylactic metoclopramide is unnecessary with intravenous analgesia in the ED. Am J Emerg Med. 2000 Oct;18(6):653-7.

6. Paoloni R, Talbot-Stern J. Low incidence of nausea and vomiting with intravenous opiate analgesia in the ED. Am J Emerg Med. 2002 Nov;20(7):604-8.

7. Bradshaw M, Sen A. Use of a prophylactic antiemetic with morphine in acute pain: randomised controlled trial. Emerg Med J. 2006 Mar; 23(3):210-3.

8. Yeoh BS, Taylor DM, Taylor SE. Education initiative improves the evidence-based use of metoclopramide following morphine administration in the emergency department. Emerg Med Australas. 2009 Jun; 21(3):178-83.

9. Culver MA, Richards EC, Jarrell DH, Edwards CJ. Use of prophylactic ondansetron with intravenous opioids in emergency department patients: a prospective observational pilot study. J Emerg Med. 2017 Nov; 53(5): 629-634.

10. Bounes V, Charriton-Dadone B, Levraut J, Delangue C, Carpentier F, Mary-Chalon S, Houze-Cerfon V, Sommet A, Houze-Cherfon CH, Ganetsky M. Predicting morphine related side effect in the ED: An international cohort study. Am J Emerg Med. 2017 Apr; 35(4): 531-535.

11. Ishihara M, Ikesue H, Matsunaga H, Suemaru K, Kitaichi K, Suetsugu K, Oishi R, Sendo T, Araki H, Itoh Y. A Multi-institutional Study Analyzing Effect of Prophylactic Medication for Prevention of Opioid-induced Gastrointestinal Dysfunction. Clin J Pain. 2012 Jun; 28(5): 373-381.

12. Giusti R, Mazzotta M, Filetti M, Daniele G, Tsukuura H, Ficorella C, Porzio G, Marchetti P, Verna L. Prophylactic use of antiemetics for prevention of opioid-induced nausea and vomiting: a survey about Italian physicians' practice. Supportive Care in Cancer. 2019 Jan: 1-5.

13. Nicholson B. Economic and clinical burden of opioid-induced nausea and vomiting. Postgraduate Medicine. 2016 Oct; 129(1): 111-117.