Isopropyl Alcohol Nasal Inhalation for Nausea in the Emergency Department: A Randomized Controlled Trial

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Study objective: We compare nasal inhalation of isopropyl alcohol versus placebo in treating nausea among emergency department (ED) patients.

Methods: A convenience sample of adults with chief complaints of nausea or vomiting was enrolled in a randomized, double-blind, placebo-controlled trial conducted in an urban tertiary care ED. Patients were randomized to nasally inhaled isopropyl alcohol versus nasally inhaled normal saline solution. Patient nausea and pain were measured with previously published 11-point verbal numeric response scale scores; patient satisfaction was measured by a 5-point Likert scale. The primary outcome was reduction in nausea 10 minutes poststart. Secondary outcomes included patient satisfaction and pain reduction measured at 10 minutes poststart.

Results: Of 84 recruited patients, 80 (95.2%) completed the study. Thirty-seven (46.3%) received nasally inhaled isopropyl alcohol and 43 (53.8%) received nasally inhaled normal saline solution. At 10 minutes postintervention, median nausea verbal numeric response scale score was 3 in the isopropyl alcohol arm versus 6 in the placebo arm, for an effect size of 3 (95% confidence interval 2 to 4). Median satisfaction score was 4 in the isopropyl alcohol arm versus 2 in the placebo arm, for an effect size of 2 (95% confidence interval 2 to 2). There were no significant differences between the 2 arms in median pain verbal numeric response scale scores or subsequent receipt of rescue antiemetics.

Conclusion: We found that nasally inhaled isopropyl alcohol achieves increased nausea relief compared with placebo during a 10-minute period. [Ann Emerg Med. 2015; -:1-9.]

Please see page XX for the Editor’s Capsule Summary of this article.

INTRODUCTION

Background

Isopropyl alcohol nasal inhalation has been demonstrated by meta-analysis of multiple trials to be more effective than saline solution in treating postoperative nausea and vomiting. This therapy is inexpensive and has been demonstrated to be safe in animal models. None of the human studies of this therapy in the postoperative setting have reported any adverse events. Given that previous studies have been isolated to postoperative settings, it is not yet established whether isopropyl alcohol effectively treats all patients with nausea or only those patients in whom nausea is attributable to anesthetic agents. To our knowledge, there have been no investigations of this therapy in the emergency department (ED) or in patients with undifferentiated nausea or vomiting.

Importance

Nausea or vomiting is a common chief complaint, accounting for approximately 4.8 million ED visits within the United States each year. Commonly used antiemetics, including ondansetron, promethazine, and metoclopramide, have demonstrated efficacy in specific patient populations (eg, ondansetron in chemotherapy patients). However, multiple randomized trials comparing these agents with placebo among undifferentiated ED patients with nausea or vomiting have not demonstrated superiority.

Identification of an antiemetic medication whose therapeutic benefit outperforms placebo in this population would be of great benefit to the ED provider.

Goals of This Investigation

The aim of this study is to compare the efficacy of nasally inhaled isopropyl alcohol to nasally inhaled saline...
solution in alleviating nausea among patients presenting to the ED with a chief complaint of nausea.

MATERIALS AND METHODS

Study Design and Setting
A randomized controlled trial was conducted at San Antonio Military Medical Center. This facility is an urban tertiary care hospital serving active-duty military personnel, retirees, and beneficiaries in the San Antonio metropolitan area. The annual ED census is approximately 80,000 patients. The trial was approved by the Brooke Army Medical Center institutional review board.

Selection of Participants
A convenience sample of potential study subjects was identified by nursing staff at ED triage. Nursing staff were advised to identify every patient meeting inclusion criteria without exclusion criteria, to include patients with signs of active vomiting or discomfort who presented during the periods when study investigators were available to enroll subjects. Nursing staff were further advised not to administer any antiemetic therapy (including nasally inhaled isopropyl alcohol) to these patients while they awaited evaluation by research personnel.

Inclusion criteria included adults (aged 18 to 65 years) presenting to the ED with a chief complaint of nausea or vomiting at a level of 3 or greater on a verbal numeric response scale (0 to 10). Exclusion criteria included known allergy to isopropyl alcohol, inability to inhale through the nares (including recent upper respiratory infection), inability to read or write in English, and altered mental status (including intoxication). No concerted efforts were taken within the department during the study period to discourage or prevent providers from treating nauseated patients in the ED with isopropyl alcohol. However, patients were further excluded if they reported receipt within the past 24 hours (including while in ED triage) of an antiemetic (including nasally inhaled isopropyl alcohol) or psychoactive drug or a medication known to potentially produce nausea when exposed to alcohol (eg, disulfiram, metronidazole, cefoperazone).

Patients were approached by study investigators (K.L.B., A.R.H., and C.J.H.) while in the waiting room or shortly after arrival to their assigned ED room before arrival of their treating physician. Study investigators (physician assistant and physicians) were responsible for obtaining written consent, applying the study intervention, and measuring outcomes. Periods when investigators were available for patient recruitment included daytime, nighttime, and weekends. Consent forms disclosed that the patients would be randomized to inhaling one of 2 unspecified substances from preparation pads. Patients were advised that both substances were believed safe but were otherwise not provided any information about the identity of these substances. By design, all study interventions and patient-reported outcomes were completed before patient evaluation and treatment by treating providers. Therefore, treating physicians were unable to remove patients from the trial. Patient flow was documented and recorded in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement (Figure 1).9

![Figure 1. CONSORT diagram of patient enrollment, allocation, follow-up, and analysis.](image-url)
**Interventions**

The study intervention comprised subject nasal inhalation from a commercially prepared medical preparation pad. Pads were saturated with either isopropyl alcohol (Professional Disposables International, Inc., Orangeburg, NY) or normal saline solution (Hygea Holdings Corp., Doral, FL). Both sets of pads were maintained in their original commercial packaging, which was identical except for label. Subject blinding was achieved by obscuring the individual pad package labels with opaque brown tape labeled with a unique pad identification number generated for each study participant (1 to 80). This tape tore open together with the packing, making the label indiscernible both before and after opening (Figure 2).

A simple randomization sequence was generated by computer. After screening, consent, and enrollment, successive patients were assigned their unique subject identification number and allocated to study arm according to the randomization sequence by a nonstudy individual. This individual then provided study investigators with the appropriate pad with obscured label for each subject. Only this nonstudy individual had access to the study key linking pad contents (normal saline solution versus isopropyl alcohol) to unique pad study identification number and unique subject study identification number.

Investigator blinding was maintained by instructing patients to open the pads. If patients were unwilling or unable to open the pads, the investigator opened the pad at arm’s length to avoid detecting the pad’s scent. Additionally, investigators instructed subjects to avoid behaviors that might indicate pad contents, including describing pad scent to either investigators or any other subsequent providers during the ED visit. Treatment allocations were revealed to study investigators only after all subject-reported outcome measurements had been completed and recorded.

Study investigators instructed subjects to nasally inhale from their assigned pad at study start, 2 minutes, and 4 minutes. At each of these 3 points, subjects were instructed to take deep inhalations for no more than 60 seconds through their nose. During these deep inhalations, subjects were instructed to hold their pad 2.5 cm from their nose. If at any time subjects’ nausea became completely relieved, they were instructed not to take further deep inhalations. No subjects were permitted any inhalation therapy after the 4-minute period. Subjects reporting no improvement in

![Image of study pads both unblinded (A) and blinded (B).](image-url)
their nausea by study completion (10 minutes postintervention) were permitted rescue antiemetic drugs in accordance with the treating ED provider’s preference.

Methods of Measurement

Investigators used hard copy case report forms to record patient self-reported pain and nausea, for which the investigators were blinded to subject intervention allocation. These were both measured at study start and then again at 2, 4, 6, and 10 minutes postintervention. Furthermore, at 10 minutes poststart patients answered a question soliciting their satisfaction on a 5-point Likert scale. Demographic data including age (years) and sex were also recorded for each patient, according to registration data.

After study completion and unblinding, all subject charts were reviewed by a study investigator (S.L.L.). All charts were handwritten. Data were abstracted about receipt of poststudy rescue antiemetics, clinical impressions, and mortality in the ED. A second investigator (A.R.H.) repeated data entry for a random selection of charts comprising 10% of the data set, and measures of interrater reliability (κ coefficient for categorical variables; intraclass correlation coefficient for continuous variables) were calculated for all variables.

Outcome Measures

Pain and nausea outcomes were self-rated on an 11-point verbal numeric response scale ranging from 0 to 10. The nausea scale was labeled “no nausea” at the left end (0) and “worst nausea imaginable” at the right end (10). The pain scale was labeled “no pain” at the left end (0) and “worst pain imaginable” at the right end (10). The satisfaction scale for the survey administered at study completion 10 minutes postintervention was a 5-point Likert scale. Demographic data including age (years) and sex were also recorded for each patient, according to registration data.

After study completion and unblinding, all subject charts were reviewed by a study investigator (S.L.L.). All charts were handwritten. Data were abstracted about receipt of poststudy rescue antiemetics, clinical impressions, and mortality in the ED. A second investigator (A.R.H.) repeated data entry for a random selection of charts comprising 10% of the data set, and measures of interrater reliability (κ coefficient for categorical variables; intraclass correlation coefficient for continuous variables) were calculated for all variables.

Primary Data Analysis

Sample size calculations were based on the assumption that 11-point nausea verbal numeric response scale values and distributions approximated those from visual analog scale measurements. The minimally clinically significant difference was assumed to be 2 points on the 11-point scale. SD was anticipated to reach 3 points. For α=.05 and β=.20 with 2-sided testing, sample size required was 36 patients per arm.

Printed case report forms and chart review abstracted data were entered into a secure Excel database (version 14.0.7159.5000; Microsoft, Redmond, WA). Forms were double entered by study investigators (K.L.B. and A.R.H.). All data were subsequently exported to SPSS (version 22; IBM, Armonk, NY), with which all statistical analyses were performed.

All analyses were intention to treat. Patient baseline characteristics were summarized with descriptive statistics. Given that the primary outcome of nausea verbal numeric response scale score is an ordinal outcome without a normal distribution, scores were compared between treatment arms with nonparametric statistical testing (Wilcoxon rank sum testing). For secondary outcomes, pain and satisfaction scores were also compared between treatment arms with Wilcoxon rank sum testing. Ordinal data median differences were calculated directly for point estimates, whereas confidence intervals were calculated with a Hodges-Lehmann estimator. Ordinal data were further depicted across study periods with box plots. Receipt of rescue antiemetic drugs was compared with Fisher’s exact test. The number of rescue antiemetic drugs received was compared with a 2-tailed independent-samples t test.

RESULTS

Characteristics of Study Subjects

Eighty-four patients were screened for study inclusion by the study investigators with use of an exclusion checklist. All 84 screened patients were eligible for study inclusion. Of these, 4 patients declined to participate once their treating physician became available. All 80 remaining patients (95.2%) were ultimately enrolled. All enrolled patients underwent randomization (37 to nasally inhaled isopropyl alcohol, 43 to nasally inhaled saline solution) and completed the study (Figure 1). Baseline patient characteristics were similar across the 2 treatment arms (Table 1). The only characteristic for which a substantive difference was noted was initial pain verbal numeric response scale score (median 7 with interquartile range 6 to 8 in the isopropyl alcohol arm versus median 6 with interquartile range 2 to 8 in the placebo arm).

Main Results

In regard to primary outcome, patients allocated to the isopropyl alcohol arm reported lower verbal numeric...
Table 1. Patient baseline characteristics for each treatment group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Isopropyl Alcohol (37)</th>
<th>Placebo (43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>32.0 (12.1)</td>
<td>35.7 (14.2)</td>
</tr>
<tr>
<td>Female sex (95% confidence interval), %</td>
<td>62.2 (46.1–76.0)</td>
<td>76.7 (62.1–87.0)</td>
</tr>
<tr>
<td>Symptom severity (IQR), scale 0–10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial nausea median VNRS</td>
<td>6 (4–8)</td>
<td>6 (5–8)</td>
</tr>
<tr>
<td>Initial pain median VNRS</td>
<td>7 (6–8)</td>
<td>6 (2–8)</td>
</tr>
<tr>
<td>Associated symptom frequency (95% confidence interval), %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>35.1 (21.8–51.3)</td>
<td>25.6 (14.8–40.4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>32.4 (19.6–48.6)</td>
<td>39.5 (26.3–54.4)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>16.2 (7.3–31.5)</td>
<td>18.6 (9.5–32.9)</td>
</tr>
<tr>
<td>Headache</td>
<td>16.2 (7.3–31.5)</td>
<td>14 (4.5–33.1)</td>
</tr>
</tbody>
</table>

VNRS, Verbal numeric response scale; IQR, interquartile range.

Figure 3. Patient nausea verbal numeric rating scale (VNRS) scores from 0 to 10 minutes after intervention for each study arm. The horizontal axis separates data for each patient, with the central line demarcating data for patients receiving placebo (left) versus isopropyl alcohol (right). The vertical axis represents the patient-reported nausea VNRS score (0 to 10). Each circle represents the initial nausea VNRS score for each patient. Associated vertical lines represent changes in nausea from study start (0 minutes) to time of final outcome measure (10 minutes). Circles without lines represent patients reporting no changes in nausea VNRS. The box plots on the figure margins represent summary statistics, with the central lines representing medians, boxes representing interquartile ranges, and outermost plots representing maximum and minimum nausea VNRS values for the samples composing each study arm. Median nausea VNRS scores at 10 minutes postintervention were lower by 3 (Hodges-Lehmann estimator 95% confidence interval 2 to 4) in the isopropyl alcohol arm compared with the placebo arm (P<.001 by Wilcoxon rank sum test).

LIMITATIONS

This study had several limitations. The prospective evaluation period was limited to 10 minutes. This study was unlikely to identify adverse events attributable to isopropyl alcohol outside of this window. The subsequent chart review component of the study demonstrated no patient deaths and no clinical impressions indicative of complications related to isopropyl alcohol. Nevertheless, the retrospective nature of this chart review may have limited ascertainment of adverse events after study completion at 10 minutes postintervention.

The 10-minute study period also provided limited information about duration of symptom relief. There were no statistically significant differences in the proportions of patients receiving antiemetics between the 2 study arms. This finding suggests that although the antinausea effect of isopropyl alcohol may last 10 minutes, it may not last the duration of a typical ED stay. Similarly, although patients allocated to the isopropyl alcohol arm reported increased...
satisfaction at 10 minutes compared with those allocated to the placebo arm, it is unclear whether this difference would persist at patient disposition from the ED.

Selection bias was a potential issue, given recruitment of a convenience sample. We attempted to limit the potential for such bias by making study personnel available for patient recruitment during a broad range of times, including daytime, nighttime, and weekends. Furthermore, we emphasized to nursing staff identifying eligible patients at triage to notify study personnel of every one of these patients presenting to the ED with nausea during these periods, to include patients with signs of active vomiting or discomfort. Nevertheless, it is impossible to quantify the extent to which these efforts controlled for selection bias because we collected no data characterizing those patients presenting to our ED with nausea who were not recruited into the study. By extension, it is difficult to know how generalizable our results are to other ED patients with undifferentiated nausea and vomiting.

Blinding patients and investigators to scent is challenging, and we cannot prove perfect blinding in our study. Our study design included several measures to ensure effective double blinding. These included pad label obscuration (Figure 2), investigators maintaining physical distance (arm’s length or more) from patients during pad inhalation, investigator instructions to patients to not describe pad scent, and lack of disclosure to patients of the potential pad contents (eg, normal saline solution versus isopropyl alcohol) to which they were being exposed. Nevertheless, it is conceivable that the lack of significant olfactory stimulation from normal saline solution may have compromised effective blinding of patients allocated to the placebo arm. Because patients were not informed of their potential allocation to placebo, no effort was made to query them in regard to their beliefs about which arm they were allocated to to prove effective blinding.

Our choice of primary outcome measure may complicate comparison of our results with those of other studies of antiemetics in the ED. The 11-point nausea verbal numeric response scale was chosen because of its widespread use in the anesthesia literature previously studying isopropyl alcohol. Although this scale has been used in ED studies, much of the previous literature on the treatment of nausea has instead used a continuous visual analog scale measurement tool. Nevertheless, these comparisons are likely to be meaningful, given recent work suggesting substantial correlation between verbal numeric response scale and visual analog scale nausea measurements.

Our choice of primary outcome measure is further limited in that it is subjective. Advantages associated with this choice include an outcome important to patients and low likelihood of measurement bias. However, many alternative objective measures potentially important to patients are not captured by this study. Examples include numbers of vomiting episodes, length of ED stay, patient disposition, and duration of nausea symptoms. The absence of other objective outcome measures limits our ability to fully establish the clinical relevance of our findings.

Table 2. Patient outcomes for each treatment group.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Placebo (43)</th>
<th>Isopropyl Alcohol (37)</th>
<th>Effect Size (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-min nausea median VNRS, 0–10</td>
<td>6</td>
<td>3</td>
<td>3 (2 to 4)</td>
</tr>
<tr>
<td>10-min pain median VNRS, 0–10</td>
<td>6</td>
<td>6</td>
<td>0 (-1 to 2)</td>
</tr>
<tr>
<td>10-min satisfaction score, 1–5</td>
<td>2</td>
<td>4</td>
<td>2 (2 to 2)</td>
</tr>
<tr>
<td>Antiemetic receipt, %</td>
<td>72.1</td>
<td>89.2</td>
<td>17.1 (-0.5 to 34.8)</td>
</tr>
<tr>
<td>Antiemetic doses, No.</td>
<td>1.2</td>
<td>1.2</td>
<td>0 (-0.2 to 0.3)</td>
</tr>
</tbody>
</table>

Figure 4. Patient pain verbal numeric rating scale (VNRS) scores from 0 to 10 minutes after intervention for each study arm. The horizontal axis separates data for each patient, with the central line demarcating data for patients receiving placebo (left) versus patients receiving isopropyl alcohol (right). The vertical axis represents the patient-reported pain VNRS score (0 to 10). Each circle represents the initial pain VNRS score for each patient. Associated vertical lines represent changes in pain from study start (0 minutes) to time of final outcome measure (10 minutes). Circles without lines represent patients reporting no changes in pain VNRS. The box plots on the figure margins represent summary statistics, with the central lines representing medians, boxes representing interquartile ranges, and outermost plots representing maximum and minimum pain VNRS values for the samples composing each study arm. Median pain VNRS scores at 10 minutes postintervention were comparable in the two arms with a difference of 0 (Hodges-Lehmann estimator 95% confidence interval -1 to 2).
Our objective secondary outcome measure of rescue antiemetic receipt also had limitations. These data were collected retrospectively by chart review. All such retrospective data are subject to potential issues of missing data and ascertainment bias. Rescue antiemetic receipt was based on the handwritten order sheet for each patient, with nursing notations confirming medication delivery. There were few missing entries, and we expect these data to be robust. We further double entered 10% of charts to ensure data accuracy, and our statistical measures of intrarater reliability suggest excellent agreement.

An additional limitation to the rescue antiemetic receipt outcome measure is that treating physicians, although blinded to treatment arm allocation, were not blinded to subject trial participation. Although treating physicians were not actively informed of the participation of their patients in the trial, we cannot exclude the possibility that these providers were aware of subject participation and that this knowledge affected their subsequent decisions to treat with antiemetics. We attempted to minimize the likelihood that investigators or treating physicians would be aware of subject treatment arm allocation through instructions to all patients to not describe to any providers the scent of the pad from which they nasally inhaled.

DISCUSSION

Nausea is a frequent symptom for patients presenting to the ED. Identification of an effective agent that outperforms placebo would be of significant value. Isopropyl alcohol is a simple and inexpensive agent previously demonstrated to be effective in treating postoperative nausea. It has not previously been examined in undifferentiated patients presenting to the ED, to our knowledge. Our randomized, double-blind, placebo-controlled trial demonstrated decreased self-reported nausea by patients allocated to receive nasally inhaled isopropyl alcohol compared with placebo during 10 minutes.

Our finding that isopropyl alcohol outperforms placebo in treating nausea among ED patients makes this agent unique. Antiemetics have been demonstrated by randomized trials to outperform placebo in the treatment of postoperative and postchemotherapy nausea and vomiting. Yet commonly prescribed antiemetics including ondansetron, metoclopramide, and promethazine have not outperformed placebo in randomized trials of patients with nausea who present to the ED. Although our results provide data only during a limited 10-minute period, our potential identification of an agent outperforming placebo may provide a useful tool for treating nausea in this undifferentiated patient population.

The difference in effect size in nausea alleviation noted in our study versus that in previous randomized trials of commonly prescribed antiemetics in the ED may be due in large part to differences in placebo effect. Previous ED studies of traditional antiemetics in which patients were allocated to placebo reported marked improvement in their nausea. This placebo effect likely contributes to the inability of these studies to demonstrate efficacy in treating nausea with traditional antiemetics. Conversely, subjects allocated to our placebo arm exhibited essentially no improvement in their nausea. The lack of placebo effect noted in our study may be due to limitations in blinding patients to aromatherapy as discussed above. Alternatively, the placebo effect reported by previous ED trials may be due to the significant volumes of normal saline solution administered in all arms of these studies, which may itself significantly reduce nausea. Future ED trials of antiemetics will need to carefully account for intravenous fluid resuscitation to better clarify the effect of fluid resuscitation on patient nausea.

Although isopropyl alcohol is generally accepted to be effective in treating postoperative nausea, previous studies have yielded variable results. Three anesthesia studies demonstrated a reduction in nausea when patients inhaled isopropyl alcohol compared with placebo. Yet additional anesthesia studies found isopropyl alcohol to have similar or inferior antinausea effects compared with placebo. Potential explanations for those studies whose results align with the null hypothesis include questionable blinding, focus on longer (>6 hours postintervention) periods, or use of a 4-point verbal numeric response scale, which may have had inadequate gradations to demonstrate efficacy. Also, although the balance of evidence as summarized by meta-analysis suggests isopropyl alcohol has efficacy in treating postoperative nausea compared with placebo, this effect has not been shown to decrease need for rescue antiemetics, similar to the results of our study.

Comparison of the effect size estimated by this study to that estimated by previous anesthesia studies is difficult, given heterogeneity in outcome measures and statistical methods. Most studies using an 11-point verbal numeric response scale used time to 50% nausea score reduction as a primary outcome measure. These estimates ranged from 6.5 to 15.0 minutes. These times are slightly longer than those in our results, which suggests a peak effect realized by 4 minutes postinhalation. The single study reporting specific verbal numeric response scale values associated with isopropyl alcohol use noted a mean value of 5.7 preinhalation to 2.7 postinhalation, which is broadly consistent with our findings of a transition from median values of 6 to 3.
The mechanism of isopropyl alcohol’s antinausea effect is unclear. This effect may be related to olfactory distraction. Support for this hypothesis comes from multiple studies demonstrating that nasally inhaled scented oils achieve equivalent or superior nausea alleviation compared with nasally inhaled isopropyl alcohol. Although not statistically significant, the pain alleviation among our patients receiving isopropyl alcohol compared with placebo supports this explanation. Another posited explanation relates to the controlled breathing because of the inhalation instructions rather than a pharmacologic effect. Further research will be necessary to elucidate this agent’s mechanism of action.

Multiple studies have noted rapid onset of nausea alleviation with isopropyl alcohol but high incidence of symptom recurrence, particularly over periods beyond 6 hours postintervention. Longer study periods in ED settings are necessary to clarify the duration of antinausea effect. Study of alternative aromatherapies (eg, peppermint oil) in the ED may be high yield because they have shown efficacy in the anesthesia literature.

Perhaps most important will be studies directly comparing nasally inhaled isopropyl alcohol with standard therapies in the ED such as ondansetron. Such comparisons in the anesthesia literature focusing on time to nausea relief as a primary outcome have noted more rapid symptom alleviation with isopropyl alcohol. However, aromatherapy has generally failed to outperform conventional intravenous antiemetics in studies examining longer periods. Indeed, a meta-analysis of trials examining aromatherapy trials concluded no superiority in nausea alleviation with isopropyl alcohol compared with ondansetron or promethazine. There is reason to suspect that similar trials conducted in an ED would have different outcomes: whereas intravenous antiemetics have demonstrated efficacy in the postoperative setting, this is not true for ED studies, in which these agents have not outperformed placebo.

This study suggests that nasally inhaled isopropyl alcohol outperforms placebo in treating nausea in the undifferentiated ED patient during a 10-minute period. Although to our knowledge this is the first such study in the emergency medicine literature, this finding reinforces the results of multiple studies in the anesthesia literature that isopropyl alcohol has efficacy in treating nausea. This agent appears rapid in onset and safe, with no adverse events reported. Future research is necessary to better inform the duration of effect and performance in comparison with traditional antiemetics. Nevertheless, emergency medicine providers should consider incorporation of this agent into their clinical practice. The available evidence suggests this agent may provide a potent tool over short periods for alleviating nausea and improving satisfaction among patients presenting to the ED.

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Author contributions: KLB, SLL, and CJH conceived the study and designed the protocol. KLB, ARH, and CJH undertook patient recruitment, data collection, and data management. MDA contributed data analysis and interpretation. All authors substantively contributed to article preparation and revision. KLB takes responsibility for the paper as a whole.

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The views expressed herein are those of the authors and do not reflect the official policy or position of Brooke Army Medical Center, the US Army Medical Department, the US Army Office of the Surgeon General, the Department of the Army, the Department of the Air Force and Department of Defense, or the US government.

REFERENCES

Figure E1. Box plot of patient nausea verbal numeric rating scale scores from 0 to 10 minutes after intervention for each study arm. Patients receiving isopropyl alcohol had significantly lower nausea score distributions at every interval after study start.

Table E1. Rescue antiemetic doses administered (n=64).

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Placebo (43)</th>
<th>Isopropyl Alcohol (37)</th>
<th>Mean Dose Size Difference (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rescue medication 1, n</td>
<td>31</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Ondansetron, n</td>
<td>24</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Mean dose size, mg</td>
<td>5.7</td>
<td>5.3</td>
<td>0.4 (–0.7 to 1.5)</td>
</tr>
<tr>
<td>Promethazine, n</td>
<td>3</td>
<td>0</td>
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<tr>
<td>Mean dose size, mg</td>
<td>12.5</td>
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<td>N/A</td>
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<tr>
<td>Metoclopramide, n</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Mean dose size, mg</td>
<td>10</td>
<td>10</td>
<td>0</td>
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<tr>
<td>Rescue medication 2, n</td>
<td>5</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Ondansetron, n</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mean dose size, mg</td>
<td>6</td>
<td>4</td>
<td>2.0 (–42.0 to 46.0)</td>
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<tr>
<td>Promethazine, n</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mean dose size, mg</td>
<td>16.7</td>
<td>12.5</td>
<td>4.2 (–31.7 to 40.0)</td>
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<tr>
<td>Metoclopramide, n</td>
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<tr>
<td>Mean dose size, mg</td>
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<td>N/A</td>
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<tr>
<td>Rescue medication 3, n</td>
<td>1</td>
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<td></td>
</tr>
<tr>
<td>Ondansetron, n</td>
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<td>0</td>
<td></td>
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<tr>
<td>Mean dose size, mg</td>
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<td>N/A</td>
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<td>Promethazine, n</td>
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<td></td>
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<tr>
<td>Mean dose size, mg</td>
<td>N/A</td>
<td>12.5</td>
<td>4.2 (–31.7 to 40.0)</td>
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</table>

N/A, Not applicable.

Figure E2. Box plot of patient pain verbal numeric rating scale scores from 0 to 10 minutes after intervention for each study arm. There were no significant differences in scores at any interval after study start.