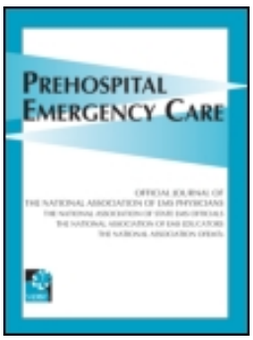

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ORIGINAL ARTICLES

EFFECTS OF PREHOSPITAL NITROGLYCERIN ON HEMODYNAMICS AND CHEST PAIN INTENSITY

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ABSTRACT

Objective. To assess the effects of prehospital nitroglycerin (NTG) on vital signs and chest pain intensity. **Methods.** A retrospective review of advanced life support (ALS) run sheets was performed in a suburban volunteer emergency medical services (EMS) system receiving 8,000 annual ALS calls. All consecutive patients who were administered NTG by EMS were included. Standardized forms were used to collect data on patient demographics, history, and physical exam. Patients assessed their chest pain (CP) before and after NTG on a verbal numeric scale of 0–10 from least to most severe. The presence of syncope, dysrhythmias, or profound hypotension [loss of peripheral pulses, a systolic blood pressure (SBP) of <90 mm Hg after NTG, or a drop of >100 mm Hg in BP] was noted. **Results.** One thousand six hundred sixty-two patients received NTG over 18 months, their mean age was 66 years, and 48% were female. Indications for NTG included CP (83%), dyspnea (45%), and congestive heart failure (20%). After NTG administration, the CP score decreased from 6.9 to 4.4 (mean difference = 2.6; 95% CI = 2.4 to 2.8). The CP completely resolved in 10% of the patients. Mean decreases in SBPs and diastolic BPs were 11.8 mm Hg (95% CI = 10.7 to 13.0) and 4.0 mm Hg (95% CI = 2.9 to 5.1). The mean pulse rate increased by 2.7 beats/min (95% CI = 0.6 to 4.9). There were 12 patients with adverse events [0.7% (95% CI = 0.4% to 1.3%)], including profound bradycardia and hypotension (1), transient drop in SBP of 100 mm Hg responding to fluids (6), post-NTG SBP <90 mm Hg (4), and syncope (1). There were no deaths in the prehospital setting. **Conclusions.** Use of prehospital NTG appears safe. While NTG reduces CP, most patients have residual pain. **Key words:** organic nitrates; nitroglycerin; chest pain; prehospital; EMS.

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Nitroglycerin (NTG) is one of the most important medications used to treat ischemic heart disease in both the prehospital and inpatient settings.[1,2] Initially described in 1879,[3] its vasodilatory effects were first noted by Sir Thomas Lewis in 1933.[1]

Since administration of NTG may be associated with a decrease in blood pressure, many prehospital systems (as well as emergency departments) have protocols requiring the insertion of an intravenous (IV) catheter prior to the administration of NTG. For example, New York State Emergency Medical Services (EMS) protocols,[4] New York City protocols,[5] and Suffolk County protocols[6] all require establishment of IV access prior to administration of NTG. In addition, NTG is usually contraindicated in the presence of a low systolic blood pressure (SBP), usually defined as an SBP of less than 100–120 mm Hg.[7]

Other common adverse effects associated with the administration of sublingual NTG include nausea, headache, vomiting, lightheadedness, flushing, palpitations, and reflex tachycardia.[8] Syncope, hypotension with bradyarrhythmias, and even asystole have been less frequently described.[9] Despite these potential adverse events, many patients self-administer NTG on a daily basis without the need for IV access. As a result, we questioned the need for establishing IV access in all patients prior to administering NTG in the prehospital setting.

The objectives of the current study were to assess the incidence of adverse events associated with use of sublingual NTG in the prehospital setting and to evaluate the effectiveness of NTG in reducing the intensity of chest pain (CP).

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METHODS

Study Design

A retrospective review of advanced life support (ALS) run sheets was performed to assess the incidence of adverse events associated with administration of NTG in the prehospital setting. In our EMS system, ALS run sheets are completed on all ALS calls to medical control and entered daily into a computerized database. The study was approved by the University Hospital and Medical Center at Stony Brook Institutional Review Board.

Study Setting

The study was conducted within the Suffolk County EMS System, which is a multi-tiered system, and included patients transported to any one of 12 hospitals by an ALS ambulance. Suffolk County, New York, is a suburban/rural county on eastern Long Island. The county covers 932 square miles and has a population of 1.5 million. The Suffolk County Department of Health Services administers the EMS system, which provides both basic and ALS care. Fire, rescue, and emergency medical services throughout the region are provided on an all-volunteer basis by 111 fire departments (of whom 63 provide ambulance service) and 31 volunteer ambulance corps. Seventy-five of these services provide ALS-level care to all or part of their service areas. Advanced life support crews consist of at least one critical care emergency medical technician (EMT) or paramedic. The emergency ambulance services in the county respond to more than 80,000 calls each year, of which approximately 8,000 involve ALS care.

The Department of Emergency Medicine of the University Medical Center at Stony Brook serves as the sole online medical control facility for all 12 ambulance-receiving hospitals in Suffolk County. Providers performing ALS services must contact medical control, where care is directed by one of 19 emergency physicians certified as base-station medical control physicians. The ALS protocols for all services are reviewed and approved by the county EMS medical director.

All patients who were administered NTG by prehospital providers in the Suffolk County EMS system between January 1993 and June 1994 were included in the study. All patients received a single dose of 0.4 mg sublingual NTG. During the study period all patients were routinely transported to one of 12 receiving hospitals in the county for continuing treatment. Indications for administering NTG in the prehospital setting include the presence of CP of suspected cardiac origin and/or the presence of signs or symptoms consistent with congestive heart failure (CHF). Morphine sulfate is not routinely administered to patients with CP or CHF.

Measurements

A structured closed-question data instrument was used to collect demographic and clinical data for all patients. Data collection was performed by certified medical control operators specifically trained in the use of the Suffolk County EMS ALS run sheet. Data collected included chief complaint, past medical history, medication and allergy history (including prior use of NTG and self-administration of NTG prior to EMS arrival), vital signs, and physical examination findings. Repeated measurements of vital signs and physical findings were performed approximately every 3–5 minutes. Patients assessed their CP intensity before and after NTG using a verbal numeric scale of 0–10 from least to most severe[10] and this information was recorded on the run sheet. Complete relief of pain was considered to be present if the post-NTG pain score was 0. The presence of syncope, dysrhythmias, or profound hypotension (arbitrarily defined as a loss of peripheral pulses, a drop of >100 mm Hg in SBP, or a post-NTG SBP of less than 90 mm Hg) was noted.

Data Analysis

Data were entered into Access 97 (Microsoft, Inc., Redmond, WA) and imported into SPSS 8.0 for Windows (SPSS Inc., Chicago, IL) for statistical analysis. The incidence of adverse events is presented as frequency of occurrence with 95% confidence intervals (CIs). The effect of NTG on the intensity of CP was assessed by subtracting the post-NTG verbal numeric score from the pre-NTG score. Descriptive statistics were used to analyze blood pressures and heart rates before and after administration of NTG.

RESULTS

During the study period there were 8,255 patients treated in the Suffolk County EMS system, of whom 1,662 (20%) received sublingual NTG. The mean age of the patients who were administered NTG was 66 ± 15 years (range = 16–99 years); 48% were female. The indications for administering NTG in the prehospital setting were CP (901), respiratory distress consistent with CHF (251), or a combination of CP and respiratory distress (510). Of all patients, 265 (16%) had self-administered NTG immediately prior to ALS arrival and administration of NTG by an ALS provider.

The mean pre-NTG SBP and diastolic blood pressure (DBP) were 157.6 mm Hg (95% CI = 155.2 to 158.9) and 90.0 mm Hg (95% CI = 88.8 to 91.3), respectively. The mean pre-NTG heart rate was 93.2 beats/min (95% CI = 90.9 to 91.6). After administering NTG, the mean decrease in SBP was 11.8 mm Hg (95% CI = 10.7 to 13.0). The mean decrease in DBP was 4.0 mm Hg (95% CI = 2.9 to 5.1). The mean increase in heart rate was 2.7 beats/min (95% CI = 0.6 to 4.9).

There were 12 adverse events associated with prehospital NTG administration, including profound bradycardia and hypotension (1), a transient drop in SBP of 100 mm Hg responding to IV fluids or leg elevation (6), a post-NTG SBP of less than 90 mm Hg (4), and syncope (1). All patients in whom the SBP dropped at least 100 mm Hg had an SBP greater than 210 mm Hg prior to administration of NTG. There were no deaths reported. Thus, the estimated incidence of adverse events was 0.7% (95% CI = 0.4% to 1.3%). None of the adverse events noted above occurred in patients who had self-administered NTG prior to receiving NTG from an ALS provider.

Both pre- and post-NTG verbal numeric rating pain scores were available for 779 patients (47%). The mean pre-NTG pain score was 6.9 (95% CI = 6.8 to 7.1). The mean decrease in pain scores after administration of NTG was 2.6 (95% CI = 2.4 to 2.8). After administration of NTG, the CP completely resolved in only 80 patients (10%).

DISCUSSION

The results of the current study indicate that the overall rate of serious adverse events associated with prehospital administration of NTG is small, with an upper 95% CI of less than 1.5%. Also, the occurrence of adverse events was not associated with self-administration of NTG immediately prior to receiving NTG from ALS providers. Importantly, no deaths were associated with use of prehospital NTG. Thus, our results (as well as common sense) suggest that use of prehospital NTG is safe and may not necessitate the establishment of IV access prior to administration. However, since all patients in our study had IV access, it is unclear what if any consequences these adverse events would have had without such access. For example, several patients who developed a 100-mm Hg decline in the SBP were successfully treated with IV fluid. We can only speculate on what the outcome may have been had these patients not received immediate fluid resuscitation if IV access could not have been established.

Requiring routine establishment of IV access in all patients prior to administering NTG could potentially prolong the time spent at the scene by prehospital providers, delaying patient transport to the hospital for definitive care. Furthermore, establishment of IV access (especially during transport) may be difficult or impossible, which would delay or prevent patients with ischemia or CHF from receiving NTG in the prehospital setting, denying them the clinical benefits of nitrates.[11]

Our results are in agreement with those of prior reports. For example, Wuerz et al. found that of 300 patients receiving NTG in the prehospital setting, only four (1.3%) developed adverse effects.[12] Similarly, in a series of 815 patients who received prehospital NTG, Brice et al. noted hypotension (SBP < 100 mm Hg) in only 37 patients (3.6%) with very few other adverse events.[13] While relatively safe, use of NTG has been associated with significant adverse events such as bradycardia, hypotension, and even asystole.[9] Nemerovski and Shaw reviewed 17 cases of patients who developed hypotensive bradycardia after administration of sublingual NTG. Unfortunately, they were unable to identify any clinical factors that would allow physicians to predict which patients would develop a hypotensive bradycardic reaction after NTG.[14] Ferguson et al. found that hypotension after NTG was more frequent in patients who subsequently were diagnosed as having right ventricular myocardial infarctions.[15] However, they were unable to identify any other risk factor for adverse events after NTG administration. Finally, Cheng found that hypotensive bradycardia developed in 5% of 3,000 patients undergoing cardiac catheterization who also received sublingual NTG.[16] Whether these results can be generalized to the prehospital setting is questionable. While we recognize the potential for serious adverse events after NTG, the rarity of such events should not prevent administration of NTG to patients in the prehospital setting in whom IV establishment is delayed or not possible. Furthermore, since nitrates have been shown to reduce the odds of death after acute myocardial infarction (AMI),[11] withholding such therapy may be detrimental. Finally, the American College of Cardiology and the American Heart Association recommend sublingual NTG every 5 minutes at home, where IV access is almost never established.[3] Therefore, withholding such therapy in an ambulance does not make sense.

Few studies have addressed the effect of NTG on CP intensity. In a study comparing sublingual nifedipine and NTG in 13 patients who developed CP during diagnostic exercise stress testing, complete pain relief was noted in five of seven patients (71%) who received NTG.[17] In a study evaluating the effectiveness of IV boluses of NTG in emergency department patients who failed to experience pain relief after one to two sublingual doses, Nashed et al. noted complete relief in two of five patients with AMI and nine of 11 patients with unstable angina.[18] Previous reports examining continuous IV NTG infusions in patients with unstable angina have yielded rates of complete pain relief ranging from 0% to 81%.[19–22] We are unaware of any prior studies that specifically evaluated the changes in CP intensity after administration of a single dose of sublingual NTG in the prehospital or hospital setting. In the current study prehospital administration of a single dose of NTG resulted in a mean decrease of 2.6 units on the verbal numeric pain score (or a relative reduction of approximately 40%)

from 6.9 to 4.4. While a difference in visual analog scale (VAS) pain scores of this magnitude is considered to be of clinical significance,[23] pain relief was complete in only 10% of patients. Thus, most patients continued to experience pain in the ambulance. While prior studies indicate that most patients get relief from NTG, in many of these studies patients received more than one dose of NTG. Furthermore, in many such studies, relief of CP was defined as complete or partial relief of pain. In contrast, we defined pain relief as a post-NTG pain score of 0. Finally, many of our patients may not have had ischemic heart disease as the cause of their pain, limiting extrapolation of our results to patients with ischemic heart disease who develop chest pain.

LIMITATIONS AND FUTURE QUESTIONS

Our study has several limitations that merit further discussion. The first and foremost limitation of this study was that we did not obtain any information regarding final diagnoses. Thus, we cannot comment on the safety and effectiveness of sublingual NTG specifically for patients with ischemic heart disease. Similarly, without a final diagnosis, we cannot comment on the safety of NTG for subsets of ischemic heart disease, such as right-sided myocardial infarctions, in which one would expect a higher rate of adverse events after administration of NTG. However, in reality, rarely can this determination be made in the prehospital setting. Second, complete data collection was not available in all patients. This may have led to either underestimation or overestimation of NTG's safety and effectiveness.

CONCLUSIONS

The results of our study indicate that administration of sublingual NTG to patients presenting with CP of suspected cardiac origin or CHF in the prehospital setting is safe. Although rapid establishment of IV access is recommended in all patients with suspected chest pain of ischemic origin or CHF, we do not feel that withholding sublingual NTG in patients without IV access is justified. While significantly reducing pain, a single dose of sublingual NTG does not result in complete CP relief in most patients in the prehospital setting.

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