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HEMODYNAMIC EFFECTS OF NITROGLYCERIN OINTMENT IN EMERGENCY DEPARTMENT PATIENTS

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□ **Abstract—Background: Nitroglycerin ointment is commonly used in the treatment of emergency department (ED) patients with suspected acute heart failure (AHF) or suspected acute coronary syndrome (ACS), but its hemodynamic effects in this population are not well described. Objective: Our objective was to assess the effect of nitroglycerin ointment on mean arterial pressure (MAP) and systemic vascular resistance (SVR) in ED patients receiving nitroglycerin. We hypothesized that nitroglycerin ointment would result in a reduction of MAP and SVR in the acute treatment of patients. Methods: We conducted a prospective, observational pilot study in a convenience sample of adult patients from a single ED who were treated with nitroglycerin ointment. Impedance cardiography was used to measure MAP, SVR, cardiac output (CO), stroke volume (SV), and thoracic fluid content (TFC) at baseline and at 30, 60, and 120 min after application of nitroglycerin ointment. Mixed effects regression models with random slope and random intercept were used to analyze changes in hemodynamic parameters from baseline to 30, 60, and 120 min after adjusting for age, sex, and final ED diagnosis of AHF. Results: Sixty-four subjects with mean age of 55 years (interquartile range, 48–67 years) were enrolled; 59% were male. In the adjusted analysis, MAP and TFC decreased after application of nitroglycerin ointment ($p = 0.001$ and $p = 0.043$, respectively). Cardiac index, CO, SVR, and SV showed no change ($p = 0.113$, $p = 0.085$, $p = 0.570$, and $p = 0.076$, respectively) over time. Conclusions: Among ED patients who are treated with nitroglycerin ointment, MAP and TFC decrease over time. However, other hemodynamic parameters do not change after application of nitroglycerin ointment in these patients.** © **2014 Elsevier Inc.**

□ **Keywords—heart failure; nitroglycerin; impedance cardiography**

INTRODUCTION

Coronary artery disease is the leading cause of death in the United States (US), and heart failure (HF) contributes to one of every eight deaths in the US (1,2). Together, HF and acute coronary syndrome (ACS) lead to > 2.5 million hospitalizations each year, with the majority of these patients receiving initial treatment in the emergency department (ED) (3).

The American Heart Association (AHA), the European Society of Cardiology, and the Heart Failure Society of America advocate the use of intravenous vasodilators, including nitroglycerin, nitroprusside, or nesiritide, in addition to diuretic therapy in patients with

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acute heart failure (AHF) (4–6). Similarly, the American College of Cardiology (ACC) and AHA recommend the use of sublingual or intravenous nitroglycerin in patients with ACS (1). These agents cause venous and arterial dilatation by increasing levels of cyclic guanosine monophosphate, which in turn decreases intracellular calcium and relaxes smooth muscle. At lower doses, nitroglycerin causes primarily venodilatation; at higher doses, it also causes arterial dilatation (7). Intravenous nitroglycerin has been shown to decrease blood pressure, pulmonary capillary wedge pressure, right atrial pressure, systemic vascular resistance, and pulmonary vascular resistance, while increasing cardiac output in patients with AHF (8). In acute myocardial infarction, sublingual nitroglycerin has been shown to decrease mean arterial pressure (MAP), cardiac index (CI), and stroke volume (SV) (9).

Nitroglycerin ointment is commonly used in US EDs (10). Nitroglycerin ointment exerts its effects in 15–60 min, with peak action at 30–120 min and an overall duration of action of 3–8 h (11). Limited data suggest that nitroglycerin ointment has good bioavailability and substantial hemodynamic benefits in chronic HF and stable angina (12–14). However, its effectiveness in the ED management of AHF and ACS has not been well studied. To better understand its effectiveness in the ED setting, data describing acute effects are needed.

Our overall goal in this study was to determine the hemodynamic effects of nitroglycerin ointment on MAP, systemic vascular resistance (SVR), cardiac output (CO), and SV in the acute time period of treatment. Using noninvasive impedance cardiography to measure these parameters, we hypothesized that nitroglycerin ointment would result in a reduction in MAP and SVR.

METHODS

Study Design

We conducted a prospective observational study at a single urban, academic ED with an annual adult census of approximately 60,000 patients. This study was approved by our Institutional Review Board.

Setting and Population

We enrolled a convenience sample of patients aged 18 years and older who presented to the ED between December 1, 2009, and November 30, 2010 during the hours of 8 AM to 5 PM, and in whom the attending emergency physician suspected AHF or ACS and ordered nitroglycerin ointment for treatment. We excluded dialysis patients and those with a systolic blood pressure < 90 mm Hg at time of enrollment. Patients who were unable to provide informed consent were also excluded.

Study Protocol

After providing informed consent, impedance cardiography (BioZ® Dx Diagnostic System, Sonosite, Inc., Bothell, WA) was used to measure CI, CO, MAP, SV, SVR, and thoracic fluid content (TFC). Impedance cardiography is a noninvasive diagnostic test that gathers data from four dual sensors to calculate the resistance encountered by a current as it travels through the aorta. Dual sensors were placed bilaterally at the base of neck beneath the ear and on the chest wall, in mid-axillary line at the level of the xiphoid. Eight impedance cardiography lead wires were attached to the sensors and an oscillometric blood pressure cuff was applied to the patient's arm. Impedance cardiography measurements have been shown to correlate with Swan-Ganz catheter values (15). A 5-min impedance cardiography recording was performed at each time point, and hemodynamic parameters were calculated by the BioZ® Dx Diagnostic System. The system's noninvasive blood pressure measurements were taken using a pneumatic cuff placed over the upper arm. Impedance cardiography electrodes remained on the patient between recordings, and all recordings were taken with the patient lying in approximately the same position with the head of the bed elevated at 45° when possible.

Nitroglycerin 2% ointment was applied by the ED nurse to the left anterior chest wall in accordance with standard hospital procedures. Nitroglycerin usage and dose was at the discretion of the treating ED physician. Standard order sets used at the time of the study included doses of 1 inch and 2 inches. Patients who received sublingual nitroglycerin before ED arrival were eligible for inclusion; patients did not receive nitrates via alternative routes (sublingual, intravenous) in the ED.

Measurements

Baseline SVR, CI, CO, MAP, SV, and TFC measurements were taken before the application of nitroglycerin ointment, as well as at 30 min, 60 min, and 120 min after application of nitroglycerin ointment.

Outcomes

Primary outcomes were change in MAP and SVR over time after application of nitroglycerin ointment. Our sample size provided 79% power to detect a 10% change in SVR from baseline to 120 min after nitroglycerin application and > 80% power to detect a 4% change in MAP from baseline to 120 min. Secondary outcomes were