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AN EVALUATION OF ONDANSETRON FOR UNDIFFERENTIATED NAUSEA AND VOMITING IN THE PREHOSPITAL AND INTERFACILITY TRANSFER SETTING

Report to the California Commission on EMS

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1. Acknowledgements

This ondansetron trial study was made possible through extensive cooperation from four (4) EMS Agencies covering eight (8) California counties. We wish to express our appreciation and gratitude to the following individuals who helped make this study possible through their support and participation in the project.

Santa Barbara County		
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Iris Pena, RN	Nurse Specialist	Inland Counties EMS
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2. Abstract

Objectives: The primary objective was to evaluate the safety and efficacy of ondansetron in the out-of-hospital treatment of undifferentiated nausea or vomiting. The secondary objective was to explore the utility of an online database in the coordination of a multi-site study group.

Methods: EMS patients in eight California counties with severe nausea or intractable vomiting were treated with intravenous, intramuscular, or oral ondansetron, without online medical control. Data were collected prospectively for a 6-month period using an online database. Outcome measures were: 1) efficacy as measured by a verbal quantitative nausea scale and 2) incidence of adverse effects. There were no control or placebo groups.

Results: Ondansetron was administered to 2071 patients (~3.1% of all patients transported during the study period). Overall the mean decrease in nausea score was 3.99 on a 10 point scale. After medication administration, four patients had mild hypotension, one had hypertension, two had itching or rash, and one had a brief episode of supraventricular tachycardia that resolved spontaneously. The online database system was effective in allowing for universal accessibility, ease of data entry, and availability for monitoring and analysis, and enabled a uniform and consistent quality improvement process.

Conclusions: Ondansetron is safe and effective in the out-of-hospital treatment of nausea and vomiting. Given the prevalence and degree of discomfort of this condition, ondansetron should be added to the statewide paramedic scope of practice and its use widely encouraged. The online database method of data collection and analysis was highly effective and its expanded use should be facilitated by the EMS Authority to support other statewide EMS CQI projects, studies, and data collection.

3. Introduction

Nausea and vomiting are common patient complaints in emergency medical services systems, both prehospital and during interfacility transfers. Though not well-studied, one report found that 5% of prehospital patients required treatment.[1] Nausea is often a significant concern, and many patients consider nausea to be a more uncomfortable symptom than pain.[2] In California, the paramedic scope of practice does not address this well. Diphenhydramine may be used as an antiemetic, but is rarely used for that purpose in the emergency department, and causes drowsiness. A previous California EMS trial study on the treatment of motion sickness with diphenhydramine (Benadryl®) or metoclopramide (Reglan®) was terminated in 2008, and with a limited number of enrolled patients no addition to the paramedic scope of practice was recommended.

Ondansetron (Zofran®) is a widely used antiemetic agent in the hospital and in outpatient settings. It has been used safely and effectively for the treatment of undifferentiated nausea and vomiting in emergency department and emergency medical services settings.[1,3-8] It is used in a number of EMS jurisdictions outside California. As the cost of the medication has declined to less than $1.00 per dose, ondansetron is an attractive option in prehospital and interfacility transfer care.

On 21 August, 2008, the Santa Barbara County Emergency Medical Services (EMS) Agency submitted a Trial Study request with the California EMS Authority to evaluate the utilization, safety, and efficacy of ondansetron in the out-of-hospital setting. On 20 October, 2008, Dr. Tharratt approved the trial study for a period of eighteen (18) months. Coastal Valleys EMS Agency, Inland Counties EMS Agency (ICEMA), and El Dorado County EMS Agency were also approved to participate. Approval and EMS Commission dates are listed in Table 1.

Table 1: Participating EMS Agencies and Counties

EMS Agency	County(ies)	Approval Date	EMS Commission Notification
Santa Barbara	Santa Barbara	10/20/08	12/3/08
Coastal Valleys	Napa Sonoma Mendocino	10/20/08	12/3/08
Inland Counties	San Bernardino Inyo Mono	10/21/08	12/3/08
El Dorado	El Dorado	3/25/08	3/25/09

Interim trial results were presented to the EMDAC Scope of Practice Committee and Dr. Tharratt on March 24, 2009. Based on that discussion it was agreed that sufficient data would be available before the 18 month approval period was complete and that the trial results would be presented for analysis and action at the June 2009 EMDAC Scope of Practice and EMS Commission meetings.

4. Methods

Study Design

This was a prospective, observational study with the objective of evaluating the utilization, safety and efficacy of the out-of-hospital administration of intravenous, intramuscular, and oral ondansetron in the treatment of undifferentiated nausea or vomiting. There were no control or placebo groups. Paramedic treatment protocols were modified so that all patients without a contraindication who met clinical criteria were candidates to receive the medication.

Setting

The trial study took place simultaneously in four EMS Agencies comprising 8 counties: Santa Barbara County, Inland Counties EMS Agency (ICEMA - San Bernardino, Inyo, and Mono Counties), Coastal Valleys EMS Agency (CVEMSA - Napa, Sonoma and Mendocino Counties) and El Dorado County. Populations and annual call volume are listed in Table 2 below:

Table 2: Participating Counties - Demographics

County	Population[1]	Size (sq mi)[1]	EMS (ALS & BLS)[2]	IFT[2]
Santa Barbara	425,710	2737	30,500	4500
San Bernardino	2,015,355	20,052	165,478	53,554
Inyo	17,136	10,203	1823	187
Mono	12,774	3044	1429	45
Napa	133,433	754	5,492	n/a
Sonoma	466,741	1576	30,639	n/a
Mendocino	86,221	3509	5,041	n/a
El Dorado	176,075	1711	12,417	1705

1: Source; US Census Bureau, 2008 Estimate

2: Source: Local EMS Agency for respective county

Experimental Protocol

The trial study began in Santa Barbara County on December 15, 2008 and by mid-March 2009 all jurisdictions were participating.

Paramedics were provided a 90-minute training program, facilitated by their local service provider's education program (or base hospital), consisting of a PowerPoint® presentation, demonstration, skill competency and written examination. The curriculum included drug pharmacology, patient selection, and the nausea scale. (Appendix A)

A standardized protocol was implemented that allowed paramedics to administer ondansetron without online medical control (Appendix B). Inclusion criteria were: 1) age 4 years or greater, and 2) severe nausea or intractable vomiting. Exclusion criteria (contraindications) were known sensitivity to drugs of the same class as ondansetron (5-HT3 antagonists). The preferential route was intravenous. Patients without an IV were given the medication IM or PO (oral-dissolving tablet – ODT). Route was selected by the paramedic with assistance of the base hospital where local protocol required. The dose was 4 mg IV/IM/PO for all ages (4 years or greater). A single repeat dose was allowed in the protocol under standing orders or with online medical control. A third dose required online medical control orders.

Outcome Measures

The primary outcome measures were the change in nausea as reported by the patient and any adverse effect experienced by the patient after administration of ondansetron. A 10-point verbal quantitative scale was prepared (*Figure 1*) and used before and after each dose of the medication. The verbal scale was taken from the work of Craig Warden, MD (personal communication, [1])

The special nausea visual analog scale (VAS) was developed to evaluate patient comfort and status prior to and following every ondansetron administration. This 10-point scale was used by paramedics and their patients to quantitatively evaluate the patient's level of distress and track any improvement in the patient's status. All patients with adverse or untoward effects were identified by both the treating paramedic and during the clinical review of each case. All possible adverse reactions were reviewed by the provider medical director and these data were entered into the online data tool.

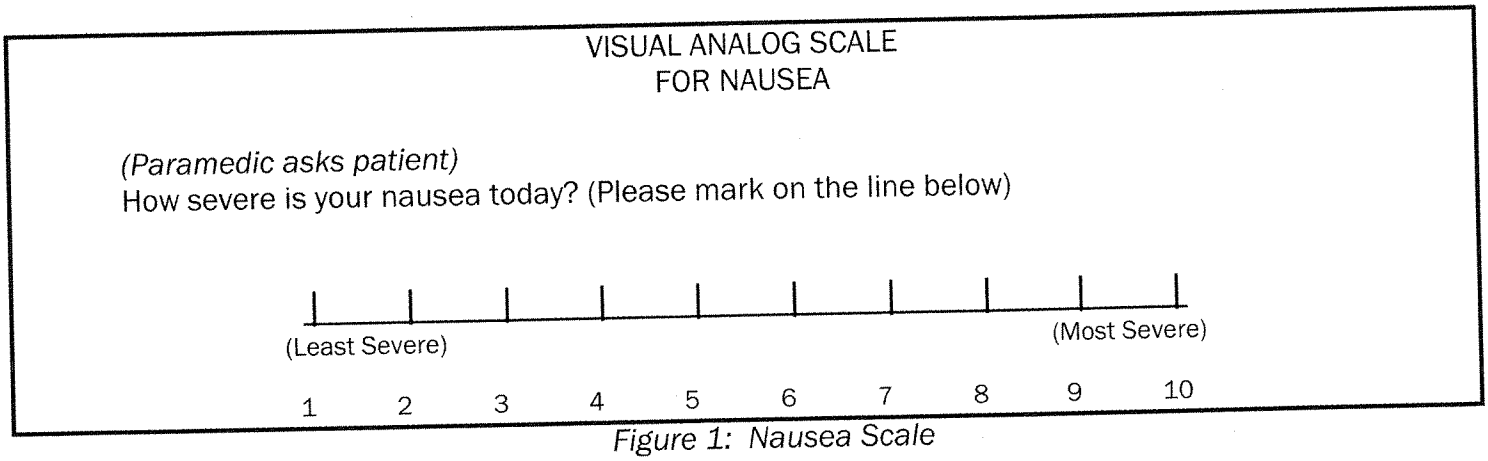

Figure 1: Nausea Scale

Medical Oversight

Paramedics were required to successfully complete a training session and pass a post-course examination before being authorized to administer the medication. A quality improvement /data collection form was completed after all uses (Appendix C), and these were reviewed by a quality improvement coordinator. All unusual events were reviewed by the medical directors of the ALS provider and LEMSA.

Data Collection

Data was collected using a structured data collection form designed by the investigators. After each patient contact in which ondansetron was administered, the treating paramedic completed a data collection form and/or electronic patient care record (PCR). These forms were reviewed by the provider CQI coordinator and verified against the PCR. If discrepancies were present, the prehospital care report was used. After verification, deidentified data from the forms were entered by CQI coordinators into an online electronic database, SurveyMonkey.com (www.surveymonkey.com). See Appendix D.

Data from the electronic online database was downloaded as an Excel spreadsheet (Microsoft, Inc., Redmond WA) and imported into STATA/IC 10.1(STATA Corporation, College Station, TX) for analysis.

Statistical Methods

Exact confidence intervals for the mean change in nausea score were calculated and P-values for the changes were calculated using the Wilcoxan sign rank test. Differences in improvement of nausea scores by route of administration were compared by multivariate regression.

5. Results

All eligible patients transported between December 15, 2008 and May 15, 2009 were included. Data were submitted for 2072 subjects. All 2072 records had complete premedication and postmedication nausea scores. The intent to treat analysis included 2001 subjects who received one dose, 70 subjects who received two doses and one subject who did not receive any medication. Subjects with an initial nausea score of zero (cases in which ondansetron was given prophylactically) were excluded from the effectiveness analysis but were included in analysis of adverse events.

Subject ages ranged from 2 years old (out of protocol, interfacility transfer with physician order) to 100 years old. 66 subjects were less than 18 years old, 17 less than 13 years old, and three were 6 years old and younger. The full age fractal analysis is show in Figure 2 below. 64% of subjects were female and 36% were male (*Figure 3*)

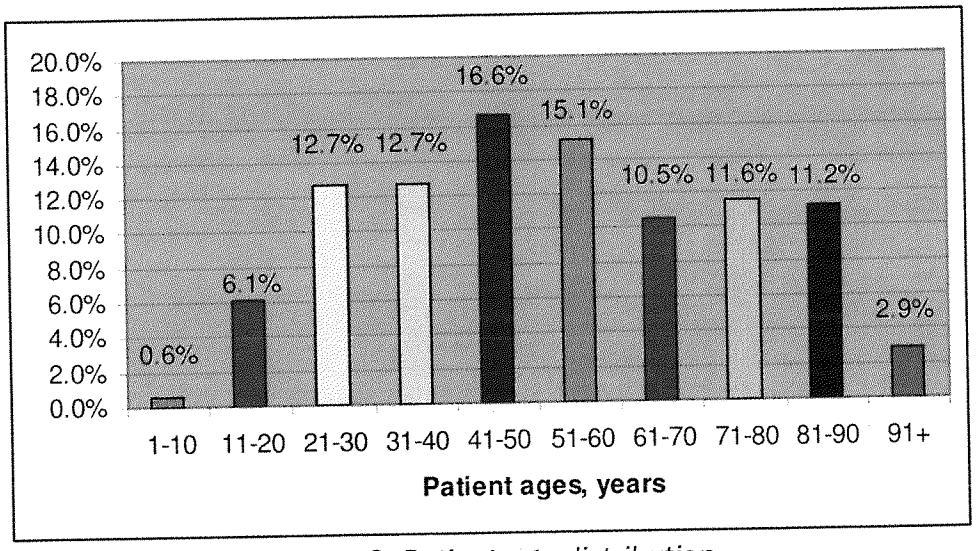

Figure 2: Patient age distribution

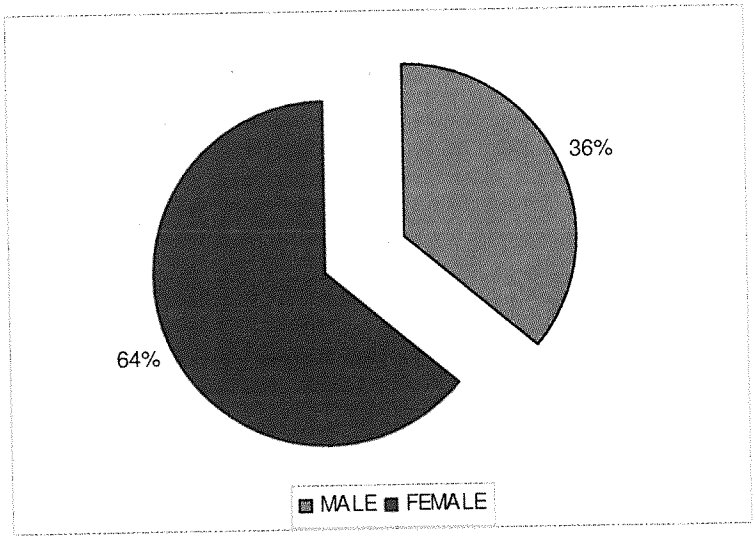

Figure 3: Gender distribution