The Use of Neuromuscular Blockers and Advanced Sedation by Field EMT-Paramedics to Promote More Effective Airway Management in Adult Trauma Patients With Glasgow Coma Scale of 8 or Less

Succinylcholine
Rocuronium
Midazolam

EMT-P Trial Study Proposal
County of San Diego Department of Health Services
Division of Emergency Medical Services

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Overview

The San Diego County Division of Emergency Medical Services proposes to undertake a prospective, matched cohort study of the effectiveness of two neuromuscular blocking (NMB) agents and a single amnesic/sedative in promoting increased effectiveness of field airway management among certain adult trauma patients. These pharmaceuticals would be used in implementing advanced airway techniques, such as rapid sequence intubation (RSI) and hyperventilation by EMT-Paramedics (EMT-Ps) in the field. This proposal involves an 18 month study period, with an anticipated 18 month continuation.

Specifically, the Division of EMS proposes to study the following hypothesis:

> "The use of neuromuscular blockers and advanced sedation by EMT-Paramedics can improve airway management in the field and decrease hypoxia-mediated brain injury in adult (age ≥ 18 years) Trauma Center Candidates with a Glasgow Coma Scale ≤8."

The medications to be evaluated are:

1. Succinylcholine
2. Rocuronium (Zemuron™)
3. Midazolam (Versed™)

In San Diego County, prehospital RSI (which requires neuromuscular blockade) has been available to patients only through the involvement of the County's advanced life support air medical provider(s). These providers, which have used registered nurses or flight physicians to provide this treatment intervention, serve as flight crews for on-scene air medical support. Because neuromuscular blockers are not included in the California Scope of Practice for EMT-Paramedics (nor have they been formally evaluated for possible inclusion into the California EMT-P Scope of Practice), they have not been available to patients receiving care and transport in paramedic ground ambulances.

An airway management study, undertaken by the County's Prehospital Audit Committee (which advises the EMS Medical Director on issues relating to prehospital care) and the Base Station Physicians Committee, has identified that the care of adult trauma center candidates with a Glasgow Coma Score of 8 or less might be improved through more aggressive advanced airway management. Up to 50% of this patient population does not arrive at the receiving hospital's emergency department with an endotracheal tube. Generally, the primary reasons for non-intubation of these patients (no attempt or unsuccessful attempt) were (1) the patient's gag reflex, (2) clenched teeth, (3) management difficulties, and (4) short ETA to receiving trauma

center. It is thought that the addition the drugs and skills proposed will allow paramedics to quickly obtain control of the patients' airways and thereby improve oxygenation and outcomes.(See Fig.1.)

Figure 1 **San Diego County**
Intubation success on trauma patients, based on Glasgow Coma Score (GCS). 1/1/95 through 6/30/95

Glasgow Coma Score	Number of cases	Intubations Successful	Unsuccessful	No attempt	% Successful
8	11	1	1	9	9%
7	17	3	5	9	18%
6	8	3	0	5	38%
5	4	2	1	1	50%
4	6	1	4	1	17%
3	71	44	14	13	50%

(Note: In GCS=3, the patients who were dead on scene were excluded in the above numbers. These included 10 successful intubations, 2 unsuccessful intubations, 13 not attempted.)

This population is almost universally intubated immediately upon delivery to a trauma center, yet current San Diego County data demonstrate only 50% arrive at a trauma center with an endotracheal tube. Medical literature supports intubation of these patients such that the damaging effects of hypercarbia and hypoxia may be minimized. Indeed, hyperventilation is still a field intervention expected of head injured patients with altered level of consciousness (LOC).

1. A description of the procedure(s) or medication(s) proposed, the medical conditions for which they can be utilized, and the study population that will benefit.

The County of San Diego proposes to implement an 18 month (with an anticipated 18 month continuation), prospective, matched cohort trial study to evaluate the effectiveness of three medications (currently not within the Scope of Practice for EMT-Paramedics) in improving the airway management efforts in certain patients in the field. These medications are:

1. Succinylcholine
2. Rocuronium
3. Midazolam

These medications will be used to facilitate the insertion of an endotracheal tube for airway management prior to delivery of the patient to the receiving trauma center.

The population to be included in this study will include adult (18 years or greater) trauma patients who present to the 9-1-1 system with a Glasgow Coma Scale of 8 or less.

2. A compendium of studies and material from the medical literature

The classes of medications proposed in the study are not new to emergency medicine and are well described in the literature. Benzodiazepines (midazolam) and neuromuscular blockers (succinylcholine, rocuronium) are well known among emergency department physicians and anesthesiologists. Their value in assisting emergency physicians, anesthesiologists, and air medical providers in gaining and maintaining of critical patients' respiratory status is unquestioned.

Rationale for immediate control of patient's respiratory status (trauma patients with GCS 8 or less)

"Head injury is the leading cause of all trauma-related deaths."[1]

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[1]McGinnis, Trauma Nursing, WB Saunders Company, 1988, p365.

"Hypoxia and hypotension [are] independently associated with significant increases in morbidity and mortality from severe head injury.[2]"

"A controlled rapid sequence intubation is the best method of simultaneously establishing an airway and protecting the patient from potentially harmful effects of increased ICP.[3]"

Almost half (46%) of this population will experience some sort of hypoxia during the early post-traumatic period.[4]

Discussion - rationale for testing the three medications to be evaluated

Succinylcholine (Anectine™) is an ultra short-acting depolarizing-type, skeletal muscle relaxant for intravenous administration. Its onset of flaccid paralysis is rapid (within 1 minute of intravenous administration), and with single administration lasts approximately 4-6 minutes[5]. The ultra short period of activity makes this the neuromuscular blocker of choice in the field. Its short duration of action allows the field paramedic to quickly gain control of the patient's airway, but allows for rapid recovery of the patient from neuromuscular blockade in case airway interventions are unsuccessful.

Rocuronium (Zemuron™) is a non-depolarizing neuromuscular blocking agent with a rapid to intermediate onset (1-2 minutes to maximum block after intravenous administration) and a duration of action of approximately 33 minutes.[6] The proposed study protocols allow rocuronium to be used on patients who have been successfully intubated to facilitate transport without frequent re-bolusing of succinylcholine. This should minimize the increase in ICP

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[2]Chesnut, Marshall, et al, "The Role of Secondary Brain Injury in Determining Outcome from Severe Head Injury", Journal of Trauma, Vol. 32, No. 2, p. 216.

[3]Olshaker, JS, *et al*: Head Trauma Emergency Medicine Clinics of North America - Advances in Trauma, Vol. 11, Number 1, Feb 93, p 169.

[4]Chesnut, Marshall, et al. p 220.

[5] Product Insert, Succinylcholine Chloride, Organon Inc, June 1991.

[6]Product Information Insert, Zemuron, Organon, Inc., December, 1994.

associated with the neuromuscular blocker wearing off prior to delivery to a trauma center.

Midazolam (Versed™) is a short-acting benzodiazepine central nervous system depressant. Sedation after IV injection is achieved within 3 - 5 minutes. Full recovery from IV midazolam sedation generally is seen 2 hours after IV administration.[7] Midazolam is commonly used in the hospital setting because of its minimal impact on respiratory drive. The administration of an amnesic/sedative prior to NMB is a common practice in the emergency department, and is provided as a humanitarian effort to limit the patients' experience of NMB.

Additional references from the medical literature are presented in the attachments to this document.

3. A description of the proposed study design including the scope and method of evaluation the effectiveness of the procedure(s) or medication(s) and the expected outcome.

As proposed for the San Diego County trial study, succinylcholine, rocuronium and midazolam will be incorporated into the treatment protocols for certain adult trauma center candidates such that rapid sequence intubation may become available to the field paramedic. Paramedics will document their justification to implement these medications and skills as opposed to intubation without NMB. These justifications include:

1. initial attempts at intubation without neuromuscular blockers fail, or
2. the patient is exhibiting signs that indicate endotracheal intubation without NMB would be difficult (agitation, uncooperative, etc.), or
3. the patient is clenching teeth such that no ET attempt can be made without NMB, or
4. the intubated patient becomes unmanageable for transport.

By definition, the medications will be used only upon patients in severe crisis when any delay in airway management might pose a threat to the patient, therefore, these medications will be

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[7]1992 Physicians' Desk Reference, Roche Labs, Versed, p 1924.

used by participating paramedics upon "standing order" to optimize airway control and scene time.

Provider agency eligibility to participate in study

The personnel to be included in this study will include personnel from any ALS provider agency that meets the following criteria:

1. Pulse oximetry capability.
2. Ability to enter study data directly into the County's computerized Quality Assurance Network.
3. Commitment to comply with medication storage requirements and procedures.
4. Commitment to support personnel training activities.
5. Commitment to cooperate in the investigation of incidents with EMS agency and base hospital personnel.
6. Commitment to provide ancillary equipment (such as in-line colormetric end-tidal CO2 detectors).

Field Personnel to participate in study

Any licensed and locally accredited EMT-Paramedic who successfully completes the prescribed training program, agrees to comply with study requirements, and is working for a participating ALS provider agency may participate in the study.

Data Collection

The San Diego County Quality Assurance Network (QA-Net) provides real time, on-line communication among virtually all base hospitals, receiving hospitals, dispatch centers, many ALS provider agencies, and the EMS office. Among the capabilities of the QA-Net is the capacity for EMT-Paramedics and Mobile Intensive Care Nurses (MICNs) to generate a computerized patient record, immediately following service, in a paperless environment. The QA-Net can be configured to accept additional data from the paramedic directly on its "research screens." Additionally, the paramedic will be required to complete a NMB/RSI Study worksheet (see attachments) to record additional data points, and additional data will be collected from the San Diego County Trauma Registry.

Patients enrolled in the study will be matched with cases found in the San Diego Trauma Registry to serve as the control group.

Evaluation

Evaluation of data collected will be coordinated by the San Diego Division of Emergency Medical Services, and will include the following components:

Concurrent:

1. Immediate notification and review of each individual case by the EMS Medical Director as each study participant is enrolled by field personnel.

2. Ongoing collection and trending of field data by EMS bio-statistical and clinical personnel.

Retrospective:
The evaluation of the study will focus on the following questions.

Study Question	Evaluation Data Points
1. Compared to baseline data on the intubation rate for adult patients with a GCS≤8 within the San Diego County EMS system, does the use of neuromuscular blockers increase the rate that these patients arrive to the ED successfully intubated?	Successful ET field intubation Number of intubation attempts Number of attempts prior to NMB Use of NMB after ET insertion? Arrive ED with tube?
2. For all patients enrolled in the study, does pulse oximetry demonstrate an improved oxygen saturation upon delivery to the ED in those patients intubated, versus those not intubated, using NMB?	O2 Saturation as measured before initial NMB O2 saturation measured within 5 minutes of initial NMB O2 saturation measured in ambulance upon arrival to ED
3. Are scene times prolonged when neuromuscular blockers are initiated in the field? Is this significant to patient care??	Arrive Scene time / Depart scene time NMB attempted Successful intubation achieved in field Tube still in place at ED
4. Is there increased morbidity or mortality associated with the use of neuromuscular blockade in the field?	ED Outcome Trauma Registry Complication List Discharge outcome

5.	Is there an improved discharge functional capacity among patients treated in the field with NMB (versus those in the matched case controls).	Trauma Registry

If, during the study period, increased morbidity or mortality is demonstrated (as compared to baseline data), the study will be immediately suspended and continuation of the study will be re-evaluated by the EMS Medical Director. It is recognized that this group of patients is, by nature, extremely unstable, and that some of the patients enrolled in the study will have poor outcomes regardless of the field use of NMB. We will attempt to evaluate the exact cause of any morbidity or mortality seen to determine if study protocols and training efforts remain appropriate.

4. Recommended policies and procedures to be instituted by the local EMS agency regarding the use of medical control of the procedure(s) or medication(s) used in the study.

The medical control issues regarding the study are outlined completely in Attachment I of this document. This attachment includes:

Study Protocol Summary
Master Study Research Protocol (for submission to Trauma Center Investigative Review Boards)
Standing Orders for Field Treatment
EMT-Paramedic data collection worksheet

5. A description of the training and competency testing required to implement the study

The proper training and testing of field paramedics in the medications and skills proposed is recognized as the key to the implementation of a successful study. Therefore, significant

efforts have been made to ensure the highest quality of prehospital education for the field personnel participating.

The training curriculum will focus on the following topics:

1. Assessment - EMT-Paramedics, as an essential component of their job, are continually asked and expected to assess patients with compromise to their respiratory system. This training includes the ability to assess the effectiveness of spontaneous respirations, the need for external respiratory support, the effectiveness of respiratory support, circulatory status, etc. All paramedics participating in the trial study will have received additional, specialized instruction in the use and interpretation of oxygen saturation monitors (pulse oximetry), indeed, most paramedics in San Diego County have already incorporated pulse oximetry into their assessment procedures. Base hospital radio personnel routinely use field oximetry data to refine the prehospital treatment plan for individual patients.

   System wide quality assurance/improvement monitoring has not demonstrated significant deficiencies in this area of monitoring.

   As proposed in the trial study, the decision as to which patients should receive NMB will be partly dependant on the field paramedics' ability to correctly calculate a Glasgow Coma Score (GCS) in the field. Paramedics are trained in a general manner to understand GCS calculations, but will require additional, specific training before the trial study to become proficient in this assessment. The training modules attached to this document include a proposed training module to increase the proficiency of EMT-Paramedics to correctly make an accurate and consistent GCS determination using a video presentation (using standardized patient scenarios) and skills demonstrations.

2. Patient treatment skills

   A. Venous access

   RSI requires that prehospital personnel have established a secure venous access for the patient. This fundamental skill is mandated within the California Scope of Practice for EMT-Paramedics.

   B. Hyper-oxygenation

   Hyper oxygenation with 100% oxygen via bag/valve/mask apparatus, or through the use of high flow mask is a skill already in use by EMT-Paramedics and EMT-1s throughout the prehospital care system. This is a basic skill for all prehospital certificate/license holders.

3. Medication administration.

All licensed paramedics demonstrate competency in calculating correct dosages of many medications based on weight, size, or standard criteria developed by the local EMS agency through the state's licensure process.

To minimize dosage errors, patients will be classified in the field by paramedics as either "Small" (35-63 Kg.), "Medium (64Kg-100Kg) or "Large"(>100Kg. Standardized dosages have been calculated for each of these approximate weight ranges (see field treatment protocol).

5. Endotracheal Tube placement (adult)
This skill is included in the State Scope of Practice for Paramedics. This skill has undergone intense scrutiny and quality improvement analysis, and paramedics continue to demonstrate that they can perform this procedure on the appropriate patients with reliability and skill.

Training will be designed and coordinated by the directors of the two approved EMT-P training agencies in San Diego County. The content, presentation and testing of necessary information will be developed by the training agencies and a field Advisory Committee, and shall be approved by the local EMS Medical Director.

Training modules and tests are still under development pending approval for the study, but outlines of proposed content are included in an attachment to this document. The behavioral objectives to be attained include the following:

1. The participant will demonstrate knowledge of the purpose, scope, ethics and EMT-P responsibilities involved in the study, as demonstrated verbally to an instructor and upon written examination.

2. The participant will demonstrate a thorough clinical knowledge of the medications used in the study (succinylcholine, rocuronium, midazolam), as demonstrated via written examination.

3. The participant will demonstrate, through written examination, awareness of proper storage measures and administration precautions to be taken for the medications used in the study.

4. The participant will demonstrate ability to calculate Glasgow Coma Score measurements by correctly calculating the score given standardized patient situations (perhaps via video)

5. The participant will be able to verbalize all components of the treatment protocol that will be utilized during the study.

6. The participant will demonstrate appropriate skill and judgement capabilities by successfully negotiating an Airway Mega-code exercise.

7. The participant will understand the mechanism by which the field paramedic will enter patient care data into the QA-Net for study evaluation, as demonstrated on the QA-Net to an instructor, and via written examination.

In the event that endotracheal intubation efforts remain unsuccessful for individual patients who have received NMB, field personnel (including some EMT-1 Defibrillation agency personnel) will be expected to attempt to position an esophageal-tracheal double lumen airway ("Combitube™") for improved airway control.

Attachments List

I. Research Protocol (prepared for presentation to Trauma Center Investigative Review Boards and Scope of Practice Committee).

Protocol Summary
Master Protocol
Treatment Protocol
Paramedic Data Worksheet
Standing Orders

II. Training Plan

III. Trauma Registry Complications List

IV. Letters of Support

V. Supporting Literature

Rapid Sequence Intubation - Protocol Summary

Protocol Title	Neuromuscular Blocking Agent Use by Field Paramedics in Endotracheal Intubation of Adult Trauma Patients with Glasgow Coma Scores of 8 or less
Study Objectives	Evaluate decrease in hypoxia-mediated secondary brain injury and improvement in success rates of intubation.
Primary Endpoints	pO_2 on arrival at Trauma Center pH on arrival at Trauma Center In-house complications during the first 30 days Glasgow Outcome Score at discharge, 3 months and 6 months Mortality
Subject Population	All adult trauma patients (≥ 18 years of age) with Glasgow Coma Score of 8 or less
Study Design	Prospective, matched cohort study
Study Medications	Midazolam (Versed), 5 mg/ml, 2 ml vials. Succinylcholine, 20 mg/ml, 10 ml vials. Rocuronium (Zemuron), 10 mg/ml, 5 ml vials. Morphine Sulfate, 10 mg/2ml
Dosage form	Sterile solution
Route of Administration	Intravenous
Dose and Regimen	Midazolam 3-5 mg IV for induction/amnesic effect if necessary, pre-intubation. Succinylcholine, 80 -160 mg IV (weight related dose) prior to intubation. Rocuronium, 40 mg - 80 mg IV (weight related dose) following successful intubation; repeated doses at 10-20 mg IV as needed for maintenance. Morphine sulfate, 2 mg IV, after intubation, for hypertensive stress response if heart rate is greater than 90/minute and BP is greater than 160 systolic. May be repeated every 3 minutes.
Duration of treatment	During field treatment and transport to trauma center.
Duration of Subject Participation in Study	Final Glasgow Outcome Score at 6 months.
Number of Evaluable Subjects Required to Meet Protocol Objectives	100 patients
Number of Study Centers	5 Trauma Centers (10-20 patients/Trauma Center/year)

Rapid Sequence Intubation - Master Protocol

Title

Neuromuscular Blocking Agent Use by Field Paramedics in Endotracheal Intubation of Adult Trauma Patients with Glasgow Coma Scores of 8 or less.

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Facilities

All patients treated in the field under the study protocol will be taken to Trauma Centers where outcome data will be collected. No treatment portion of the study will be carried out in the hospitals. The receiving facilities are:

UCSD Medical Center

Mercy Hospital Medical Center

Palomar Hospital Medical Center

Scripps Memorial Hospital, La Jolla

Sharp Memorial Hospital

Duration of the study

3 years (18 month study with anticipated 18 month continuation)

Specific Aims

1. Evaluate the effectiveness of neuromuscular blocking agents in improving prehospital intubation success rates in adults with severe head injury.

2. Evaluate the effectiveness of rapid sequence intubation by paramedics in the prehospital setting in preventing hypoxia related secondary brain injury based on clinical outcome measurements of:
   a. Hypoxia on admission
   b. Mortality
   c. Complications
   d. 3 and 6 month Glasgow outcome score

Background and Significance

Improvements in prehospital care over the past 25 years with rapid response and advanced airway management have resulted in increased survival rates and improved outcomes. While field treatment protocols aim at prevention of hypoxia in severely head injured patients by endotracheal intubation and controlled ventilation, analysis of intubation success rates in adult trauma patients with Glasgow coma scores of 8 or less show that intubation is successful in only 9% of patients with a GCS of 8, ranging up to 50% success in GCS of 3. (1)

Chesnut (2), et al, reviewed a large, prospectively collected data set from the Traumatic Coma Data Bank and demonstrated that hypoxia (apnea/cyanosis in the field or a PaO_2 < 60 mm Hg by arterial blood gas analysis) was among the 5 most powerful predictors of outcome, with hypoxia occuring in over 1/3 of the cases. A single instance of hypoxia was associated with a 42% mortality rate and of hypotension was associated with a 53% mortality. If neither was present, the mortality rate was 6%.

Winchell (3), et al, analyzed data from a 4 year period and showed that in 671 blunt trauma patients with severe head injury (GCS $\leq$ 8), those who were intubated in the field had a 37% improved survival (mortality 36% vs. 57%) compared to those who were not. In cases of isolated severe head injury, mortality fell from 50% to 23% with intubation.

Vilke (4), et al, has shown, in a review of 630 patients treated by aeromedical personnal that rapid sequence induction orotracheal intubation had a higher success rate, fewer complications, and a better patient outcome compared to noninduced orotracheal intubation and blind nasotracheal intubation.

It is postulated therefore, that by expanding the scope of practice of the paramedics to include use of neuromuscular blocking agents, we can improve intubation success, lessen the incidence of hypoxia and improve outcome by minimizing secondary brain injury.

References

1. Unpublished data. San Diego County QA net. Intubation success on trauma patients based on Glasgow Coma Score. 1/1/95 through 6/30/95.

2. Chesnut RM, Marshall LF, Klauber MR, et al: The role of secondary brain injury in determining outcome from severe head injury. J Trauma 34:216-222, 1993

3. Winchell RJ, Hoyt DB and Simons RK. Unpublished data. Abstract to be submitted to Western Surgical. 1996.

4. Vilke GM, Hoyt DB, Epperson M, et al. Intubation techniques in the helicopter. J Emerg Med 1994 Mar-Apr;12(2):217-24.