Experiences with Regional Anesthesia for Analgesia During Prolonged Aeromedical Evacuation

Jeffrey M. Carness; Melissa A. Wilson; Mark J. Lenart; Danny E. Smith; Susan F. Dukes

INTRODUCTION: There is much debate regarding the appropriate analgesic management of patients undergoing medical evacuation following combat trauma. Our primary objective was to review the utility of regional anesthetic techniques in patients undergoing aeromedical evacuation following surgical limb amputation as treatment for combat trauma.

METHODS: This study was conducted as an observational retrospective cohort whereby acutely injured amputee patients were identified via the U.S. Transportation Command's patient movement database. The Theater Medical Data Store was cross-referenced for additional patient care data including opioid consumption, duration of regional technique, pain scores, and rates of intubation.

RESULTS: Eighty-four records were retrieved from the Theater Medical Data Store. All 84 patients were victims of improvised explosive device detonation requiring limb amputation and subsequent transport from Kandahar Airfield or Camp Bastion, Afghanistan, to the United States. The majority of interventions remained in place throughout the evacuation process. A significant decrease in opioid consumption in patients receiving regional anesthesia was identified at each leg of the medical evacuation process. Pain scores were sporadically reported and not statistically different. Higher rates of intubation were identified in the nonregional anesthetic group.

DISCUSSION: Our analysis demonstrates the feasibility and effectiveness of applying regional anesthetic techniques for pain management to our combat wounded trauma patients throughout multiple stages of aeromedical evacuation. Benefits include the potential for less sedation and less opioid consumption while potentially foregoing the requirement for intubation during transport.

KEYWORDS: amputation, acute pain, pain management, trauma, ketamine, intubation.

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Regional anesthesia is an effective modality for perioperative analgesia with applications now expanding well beyond the operating theater. Both intensive care and emergency medical providers have recognized the benefit of regional anesthesia for early pain control in both critically ill and acute trauma patients, respectively.[10,12] Military service members often experience polytrauma with the development of a critically ill state when suffering wounds which result from high-energy blast injuries (improvised explosive device, rocket propelled grenade, suicide bomber) and penetrating trauma.[1] Previous studies have identified the limitations of opioid monotherapy in this setting, demonstrated the necessity for multimodal analgesic techniques in treating patients suffering from polytrauma, and have suggested an association between higher pain scores 48 h after injury and an increased incidence of PTSD.[2,3,6] Adequate pain control, in this setting of polytrauma and potentially predominant opioid monotherapy, may also provide the means to forego patient intubation and its accompanying medical and logistic complexities during intubated aeromedical transport. Combined, this generates a necessity for tenacious, appropriate, and continuous pain control beginning as close to the point of injury as possible.

The Joint Theater Trauma System (JTTS) Clinical Practice Guideline (CPG) for the Management of Pain, Anxiety and

From the U.S. Air Force School of Aerospace Medicine, Wright-Patterson AFB, OH, and the U.S. Naval Medical Center Portsmouth, Portsmouth, VA.

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Address correspondence to: Jeffrey M. Carness, M.D., Department of Anesthesiology, U.S. Naval Hospital Yokosuka, Japan, PSC 474 Box 9805, FPO AP 96351; jeffrey.m.carness.mil@mail.mil.

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Delirium in Injured Warfighters[4] correspondingly encourages the use of epidural catheters, peripheral nerve catheters, and ketamine infusions as part of a multimodal strategy for en route pain management. This multimodal approach remains a cornerstone to the provision of continuous effective analgesia. Additional benefits may also include improved recovery time, shortened hospital length of stay, improved cardiopulmonary function, and promotion of early return of bowel function.[12] Despite these seemingly supportive data for the use of regional techniques for en route pain management, overall rates of opioid consumption and total pain scores (as recorded from multiple combat operational hospitals and tracked throughout the medical evacuation process) are still lacking.

Our primary objective was to review the utility of regional anesthetic techniques in amputee patients undergoing aeromedical evacuation following combat trauma. As an initial observational study, it was our primary objective to generate grounds for an a priori hypothesis from the collection of this retrospective data. Secondary and supporting objectives included the measurement of oral morphine equivalents, analysis of reported pain scores, analysis of the duration of pain catheters throughout the medical evacuation process, analysis of the rates of intubation, and observation of associated analgesic usage.

METHODS

Subjects

The research protocol was reviewed and approved by the Institutional Review Board of the Air Force Research Laboratory at Wright-Patterson Air Force Base in Dayton, OH. The protocol was approved for and executed via a Department of Defense Institutional Agreement in collaboration with Naval Medical Center Portsmouth. The study was subsequently conducted as an observational retrospective cohort. Amputee patients were identified through the use of the U.S. Transportation Command's (TRANSCOM's) patient movement database, TRANSCOM Regulating and Command and Control Evacuation System (TRAC^{2}ES). This system is used to regulate and validate patient movement during aeromedical evacuation. The Theater Medical Data Store (TMDS), which contains medical record information for all patients injured in combat and treated in military treatment facilities along the en route care system, was cross referenced for additional patient care data. A treatment group of amputee patients receiving regional anesthesia was then created based on amputee data from patients departing Kandahar Airfield or Camp Bastion between the years of 2009 and 2013. A control group, in which patients suffered similar amputation injuries and received opioid therapy in the absence of a regional anesthetic technique, was also created using this data. The two hospitals were chosen because they are the large military medical treatment facilities in the southern region of Afghanistan. Patients departing Kandahar Airfield or Camp Bastion typically undergo a sequential three segment aeromedical transfer to the United States. This transfer, lasting an average of 5 d and consisting of transit via C-17 and C-130 aircraft, proceeds to the United States via Bagram Airfield (North Afghanistan) and Landstuhl Regional Medical Center (LRMC – Germany).

Statistical Analysis

Demographic data was analyzed with descriptive statistics and are depicted in **Table I**. Nonparametric tests for continuous and categorical variables were used to determine whether the treatment and control groups were demographically similar. The data in **Table II**, **Table III**, and **Table IV** were extracted from each patient's medical record after being identified and cross referenced as described above. Total morphine equivalents were calculated for each subject. Morphine consumption during each leg of the evacuation journey was assessed based on the usage of regional anesthesia at any point during that leg. In order to detect a difference in the amount of morphine equivalents between the two groups, a sample size of seven subjects per group was determined to achieve 80% power to detect a difference of −33.3 between the null hypothesis (that both group means are 20.8) and the alternative hypothesis (that the mean of group 2 is 54.1). This would provide an estimated group standard deviation of 15.0 and 22.0 and a significance level (alpha) of 0.05 using a two-sided Mann-Whitney test (assuming that the actual distribution is uniform, based on Richman et al., 2006).[8] Two-sample *t*-tests were used to determine a difference in pain score minimums, maximums, and means reported between the two groups for each leg of the process. Descriptive statistics were used to address the length of time that a peripheral nerve catheter remained in place during the en route care of an amputee patient. Chi-squared testing and Fisher's exact tests were performed using the rates of ketamine administration to determine the presence or absence of association between the use of regional anesthesia or nonuse of regional anesthesia and the administration of ketamine. Statistical analysis using Chi-squared testing was performed to identify the presence or absence of an association between the incidence of tracheal intubation and the administration of regional anesthetic techniques.

RESULTS

Patient Characteristics

A total of 84 records were retrieved from the Theater Medical Data Store. Of the 84 records, 42 records detailed the receipt of regional anesthetic techniques while 42 records were matched for controls. All 84 subjects were men with traumatic amputations ranging in age from 19–40 with a mean of 24 yr of age. Double limb amputations were suffered by 21 patients in the regional group and 26 patients in the nonregional group ($P = 0.47$). All 84 patients were victims of improvised explosive device detonation. Of the 42 regional techniques, 33 patients received isolated epidurals, 4 patients received an upper extremity peripheral nerve catheter in addition to an epidural, and 5 patients received sole peripheral nerve catheters (3 femoral/

Table I. Demographic Characteristics of Study Patients.

CHARACTERISTIC	CASES (RA) MEAN ± SD OR *N* (%)	CONTROLS (NO RA) MEAN ± SD OR *N* (%)	SIGNIFICANCE *P*-VALUES
Age	23.7 ± 3.4 yr	24.7 ± 5.2 yr	χ^2 $P = 0.04$*
Range	19–32 yr	19–40 yr	
Sample size	$N = 42$	$N = 42$	
Service			χ^2 $P = 0.007$*
Army	19 (45.2%)	33 (78.6%)	0.052
Marine Corps	21 (50%)	8 (19.0%)	0.016*
Navy	2 (4.8%)	1 (2.4%)	0.564
Air Force	0	0	-
Year of injury			χ^2 $P = 0.080$
2009	2 (4.8%)	0	0.157
2010	2 (4.8%)	4 (9.5%)	0.414
2011	14 (33.3%)	19 (45.2%)	0.384
2012	15 (35.7%)	17 (40.5%)	0.723
2013	9 (21.4%)	2 (4.8%)	0.035*
Number of limbs amputated			χ^2 $P = 0.382$
Single	20 (47.6%)	14 (33.3%)	0.189
Double	21 (50.0%)	26 (61.9%)	0.466
Triple	1 (2.4%)	2 (4.8%)	0.564
Days from injury to BAF†	0.95 ± 0.50 d	1.26 ± 1.13 d	χ^2 $P = 0.260$
Days from injury to LRMC‡	2.43 ± 1.02 d	2.41 ± 0.74 d	χ^2 $P = 0.634$
Days from injury to CONUS§	5.26 ± 1.81 d	5.98 ± 3.22 d	χ^2 $P = 0.393$

* Indicates significance at $\alpha = 0.05$ (95% confidence interval).
† BAF = Bagram Airfield; ‡LRMC = Landstuhl Regional Medical Center; §CONUS = continental United States.
Definition of amputation: amputation site at or proximal to wrist and/or ankle.

sciatic combinations and 2 sole sciatic peripheral nerve catheters). Patient demographic data is further depicted in Table I.

Secondary Endpoints

At some point along the medical evacuation route from Kandahar Airfield/Camp Bastion to the United States, 16 patients (or 38% of the 42 regional patients) had their regional intervention removed. The duration of the evacuation process from the operational theater to the United States averaged approximately 5.26 d and 5.98 d (for the regional and nonregional groups, respectively). Analysis of mean opioid consumption (as measured via conversion to oral morphine equivalents) indicated significant variation between regional and nonregional group patients during each segment of aeromedical evacuation (Tables II–IV). Pain scores, in theater and throughout the medical evacuation process, were inconsistently reported. Some of the missing data is a consequence of the austere wartime casualty environment and patients that were sedated and intubated. As a secondary endpoint, a significant difference in the frequency of intubation (with associated sedation) between patients in the regional anesthetic and nonregional anesthetic groups was noted ($\chi^2 = 6.4062$, $P = 0.041$; *P*-value significance set at 0.05). At certain stages as much as 30 times the frequency of sedation (using medications such as midazolam, lorazepam, or propofol) and intubation was noted (such as in comparing the number of intubated patients in the regional anesthesia group to the nonregional anesthesia group during transport from LRMC to the United States: 1:34).

Long acting analgesics were also used during en route care delivery. Two patients were identified in this cohort who received methadone for analgesia during transport (both in the regional anesthesia group). Ketamine, a similar N-methyl-d-aspartate receptor antagonist, was also used. The rate of ketamine administration progressively decreased (based on descriptive analysis) from a peak of 16 ketamine infusions in the nonregional anesthesia group at Kandahar Airfield to three ketamine infusions in the nonregional anesthesia group between LRMC and the United States. Differences in ketamine infusion administration rates between the two groups did not reach statistical significance.

DISCUSSION

Pain is routinely defined as a multidimensional sensation associated with actual or threatened tissue damage in the presence of an unpleasant emotional or noxious stimulus. Inadequate pain management is associated with a stress response, resulting in several detrimental physiological processes, including "fever, tachycardia, tachypnea, hypertension, gastrointestinal ileus, hypercoagulability, protein catabolism, and immunosuppression," all of which are known to delay rehabilitation and recovery.[4] By contrast, early and aggressive pain management is associated with better rehabilitation, better patient satisfaction, and likely slows central pain sensitization.[1,4,11] Aggressive pain management may be therefore seen as an imperative for the overall health and wellbeing of an injured service member. This can be challenging, however, as wound patterns shift.

Table II. Morphine Equivalents, Rate of Intubation, and Ketamine Usage During Intratheater Transport.

OUTCOMES	CASES (RA) MEAN ± SD mg/ FLIGHT	CONTROLS (NO RA) MEAN ± SD mg/ FLIGHT	STATISTICS TWO-SAMPLE *t*-TEST - SIGN. $\alpha = 0.05$, 1-TAILED
Oral morphine equivalents (mg)	5.19 ± 13.92	45.01 ± 100.45	$P = 0.008$*; Observed power: 0.507
Intubated	7 (16.7%)	39 (92.9%)	$\chi^2 = 6.4062$; $P = 0.041$*
Ketamine	9 (21.4%)	16 (38.1%)	$P = 0.162$

* Indicates significance at $\alpha = 0.05$.

Table III. Morphine Equivalents, Rate of Intubation, and Ketamine Utilization During Transport from Bagram Airfield, Afghanistan, to Landstuhl Regional Medical Center, Germany.

OUTCOMES	CASES (RA)	CONTROLS (NO RA)	STATISTICS
Oral morphine equivalents Mean ± SD mg/flight	4.16 ± 7.51	93.47 ± 54.64	Two-Sample *t*-test, Sign.; $\alpha = 0.05$, 1-Tailed; $P = 0.000$*; Observed power: 0.999
Intubated	1 (2.4%)	38 (90.5%)	$\chi^2 = 6.4062$; $P = 0.041$*
Ketamine	2 (5.9%)	6 (14.3%)	$P = 0.235$

* Indicates significance at $\alpha = 0.05$.

Shifting wound patterns, seen in recent conflict, now reflect an increased number of high energy penetrating wounds to the head, neck, and extremities.[7] Fortunately, these extremity injuries are amenable to regional anesthesia. Previously investigated for utility, military acute pain medicine services are currently active in delivering regional anesthetic techniques in combat environments. The new challenge, however, lies in the continuous provision of analgesic care throughout the aeromedical evacuation process in the tumultuous environment of combat care delivery. This is the focus of our investigation. Our data shows a statistically significant decrease in the amount of opioid administered to the patients in the regional anesthesia group during all stages of aeromedical evacuation. Because isolated opioid management is ineffective and inappropriate as an analgesic technique,[2,5,9] and when considering the known side effect profile of opioids and the complexity of long-duration intertheater aeromedical transport, this data would lend support to the continuing provision of regional anesthesia for combat wounded military members. Our data further identified a significant difference in the number of military members that required continued intubation and sedation in the nonregional anesthesia group in comparison with those that received regional anesthesia. It is known that Critical Care Air Transport Teams use "deep sedation for safety during prolonged transport" due to "increased risk of adverse events secondary to the constraints of monitoring."[4] Because of this, the ability to extubate the patient after surgery and forego continued intubation, deep sedation, and associated opioid administration in the setting of polytrauma and amputation should be considered significant and positive. Otherwise, a patient would remain intubated for days during the aeromedical evacuation due to concerns for adequate postoperative pain control during transport. Where possible, the risks of continued intubation (i.e., endotracheal tube dislodgement, arytenoid injury/fixation, hard and soft palate injury, tracheal stenosis, and tracheomalacia) and the risks associated with mechanical ventilation (i.e., pneumothorax, acute lung injury, hemodynamic fluctuation secondary to diminished cardiac output associated with preload reduction, and ventilator-associated pneumonia) can be avoided. One is also able to avoid the requirement for sedation holidays, the overall logistical requirement for patient ventilation during transport, the requirement for monitoring neuromuscular blockade, and, perhaps most significantly, the potential for patient confusion/discomfort/awareness under anesthesia while undergoing intubated transport.

Despite the recognized benefits of using regional techniques in theater, our data demonstrates the sporadic discontinuation of regional interventions prior to arrival in the United States. In our cohort, one epidural was replaced secondary to intrathecal migration during medical evacuation. Another patient received a neuraxial catheter to replace their lower extremity catheters. However, the underlying medical reasoning for the discontinuation of regional techniques in our cohort was not routinely reported.

It is also important to acknowledge the major limitations of regional techniques in our patient population. These limitations include anticoagulation (trauma-induced or administered prophylactically prior to a potential nerve block), concern for early diagnosis of compartment syndrome, and intubation/sedation (in which providers may be reticent to provide regional techniques without consent and in the potential presence of nerve injuries). Patient selection includes the consideration of coagulation labs obtained intraoperatively. Recognizing the potential for compartment syndrome in trauma patients, a close working relationship with orthopedic and trauma surgeons is necessary to identify patients at high risk for postoperative compartment syndrome based on the nature of their injuries.

Our study had several limitations such as limited access to military medical records, including comprehensive pain scores, interventions, and complications (neurological injury, spinal hematoma, infection, etc.). Pain scores were not always recorded in the same manner, requiring significant data mining efforts to perform pain score comparisons. The inconsistent reporting of pain scores invalidated attempts at significant statistical analysis. Ultimately, there were not enough recorded data to be useful and we were unable to show any association (positive or negative) with regional anesthetic techniques. Additionally, our retrospective study is only able to demonstrate a relationship between items such as opioid administration and regional anesthetic techniques. Though we recognize the benefits of regional anesthesia as described previously, we are unable to comment regarding any relationship associated with regional anesthesia and these items due to a lack of data. Furthermore, our study is

Table IV. Morphine Equivalents, Rates of Intubation, and Ketamine Utilization During Transport from Landstuhl Regional Medical Center, Germany, to the Continental United States.

OUTCOMES	CASES (RA)	CONTROLS (NO RA)	STATISTICS
Oral morphine equivalents Mean ± SD (mg/flight)	6.82 ± 15.72	102.73 ± 95.22	Two-Sample T-test: Sign.; $\alpha = 0.05$, 1-Tailed; $P = 0.000$*; observed power: 0.938
Intubated	1 (2.4%)	34 (80.9%)	$\chi^2 = 6.4062$; $P = 0.041$*
Ketamine	3 (11.5%)	3 (8.3%)	$P = 0.637$

* Indicates significance at $\alpha = 0.05$.

small, including only 84 patients due to the significant limitation in data availability and analysis. As a small study, aggregating the varying pain treatment methods into a single broad category of regional anesthesia may be considered a study limitation that will hopefully be addressed with a larger retrospective or prospective study. Finally, though intuitively and statistically our data would support a diminished rate of persistent intubation in the regional arm, a secondary analysis regarding injury severity (which may have impacted intubation criteria) was not performed due to the lack of consistently reported data. Thus, it was difficult to determine if the patients remained intubated solely due to injury severity or due to concern regarding adequate pain control. Future short- and long-term prospective studies should accurately depict injury severity in combination with the receipt of regional techniques as they pertain to the presence or absence of a requirement for persistent tracheal intubation. They should further be designed to acquire data regarding discontinuation, complications, and the additional beneficial postoperative effects of regional anesthesia. In doing such, they may more distinctively define the relationship between the delivery of regional anesthetic techniques to this patient population and improvements in both short-, and long-term postoperative outcomes.

In conclusion, this study broaches the utility of regional anesthesia as an analgesic option for amputee patients undergoing prolonged aeromedical evacuation. It identifies several areas for follow-on study, including the potential for different rates of intubation when regional anesthesia is employed. We have further identified the continuing need for improved medical data acquisition and recording throughout the aeromedical evacuation process.

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Authors and affiliations: Jeffrey M. Carness, M.D., Anesthesiology, U.S. Naval Hospital, Yokosuka, Japan; Melissa A. Wilson, Ph.D., MSN, and Danny E. Smith, M.Ed., B.A., U.S. Air Force School of Aerospace Medicine, Wright-Patterson AFB, OH; Mark J. Lenart, M.D., M.P.H., Naval Medical Center Portsmouth, Portsmouth, VA; and Susan F. Dukes, Ph.D., MSN, Daniel K. Inouye Graduate School of Nursing, Uniformed Services of the Health Sciences, Bethesda, MD.

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