Naylor et al., J Trauma Treat 2018, 7:1
DOI: 10.4172/2167-1222.1000424

Journal of Trauma & Treatment

Research Article Open Access

Effects of Prehospital Wound Prophylaxis in Iraq and Afghanistan on Mortality

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Abstract

Introduction: A significant proportion of traumatic injuries sustained during the recent conflicts in Afghanistan and Iraq developed subsequent wound infections. Previous studies demonstrate lower infectious rates with timely administration of antibiotics, but do not evaluate impact on mortality. We compare demographics, injury characteristics, and survival rates among adult combat casualties receiving prehospital wound prophylaxis versus casualties not receiving antibiotic prophylaxis.

Methods: We used a series of emergency department (ED) procedure codes to identify subjects within the Department of Defense Trauma Registry (DODTR) from January 2007 to August 2016. We included subjects that sustained a gunshot wound (GSW), traumatic amputation, or open-fracture proximal to the digits. We stratified our comparisons of characteristics between casualties receiving antibiotic prophylaxis to those not receiving antibiotic prophylaxis by specific injury pattern.

Results: During the study period, our predefined ED search codes captured 28222 of the total 38769 subjects encountered in the DODTR. We identified 6662 subjects with a GSW, 1899 subjects with an amputation, and 6553 subjects with an open fracture. Among subjects with these injuries, 9.8% (1483 of 15114) received prehospital wound prophylaxis. There was no difference in survival to discharge rates between casualties that received prehospital wound prophylaxis and those that did not among subjects who sustained amputations (93.9% vs. 90.7%, p=0.271) or open fractures (96.8% versus 95.9%, p=0.368). In the GSW group, subjects that received antibiotics had a significantly higher survival rate compared to subjects that did not receive prehospital wound prophylaxis (96.2% versus 92.8%, p<0.001). This association persisted on multivariable regression analysis (OR 1.61, 95% CI 1.09-2.38).

Conclusion: Military prehospital providers infrequently administered wound prophylaxis during the recent conflicts in Afghanistan and Iraq. There is an association between prehospital administration of antibiotics and increased survival among casualties suffering gunshot wounds.

Keywords: Combat; Wound; Prophylaxis; Antibiotic; Antimicrobial; Prehospital; Mortality

Introduction

Military service members in combat operations experience significant rates of traumatic injuries. The most recent conflicts Operation Iraqi Freedom (OIF)/Operation Enduring Freedom (OEF) had an increase in injuries from explosions compared to the previous conflicts, specifically World War II, Korea, and Vietnam [1]. In OIF/OEF, 19% of injuries stemmed from gunshot wounds (GSW) and 79% from explosions, including improvised explosive devices, landmines, mortars, shrapnel, bombs, and grenades [1]. The wounds incurred by these high-powered weapons are at high risk of infection due to contamination by soil, debris, and shrapnel [2-4] Wound infection prevention is critical to optimize outcomes in the austere combat setting [5,6].

Antibiotic prophylaxis is one potential intervention to prevent wound infections and their concomitant morbidity and mortality [7,8]. Pre-clinical studies exist which suggest that prophylactic antibiotics decrease infection rates when given within a short time period following injury [9,10]. Several randomized clinical trials have reported significant reductions in the incidence of wound infection and sepsis in groups treated with antibiotics prior to surgery versus those given placebo [11-13]. Early application of antibiotics appears to be especially effective in reducing infection rates in open fracture wounds [7,14-19]. However, past studies have not analyzed the association between prophylactic antibiotic administration and mortality. More research is necessary to demonstrate the impact of antibiotic prophylaxis on mortality rates.

Goal of this study

We compare demographics, injury characteristics, and survival rates among adult combat casualties that did versus did not receive prehospital wound prophylaxis, stratified by specific injury pattern.

Methods

Data acquisition

We identified subjects as part of a larger study seeking to describe emergency department (ED) interventions for trauma patients in Iraq and Afghanistan during January 2007 to August 2016. Within the database, we searched for all subjects with a documented GSW,

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Received May 22, 2018; **Accepted** May 31, 2018; **Published** June 01, 2018

Citation: Naylor JF, Burbank K, April MD, Wenke JC, Maddry JK, et al. (2018) Effects of Prehospital Wound Prophylaxis in Iraq and Afghanistan on Mortality. J Trauma Treat 6: 424. doi: 10.4172/2167-1222.1000424

amputation proximal to the digits, and open fracture proximal to the digits, including the pelvis. We placed eligible subjects into more than one category (e.g. a single subject sustained both an open-fracture and an amputation). We categorized subjects as having received no antibiotics if their data did not include listing of a specific type of antibiotic or if prehospital providers administered the antibiotic topically (e.g. ointment, ocular).

The US Army Institute of Surgical Research (USAISR) regulatory office reviewed protocol H-16-005 and determined it was exempt from Institutional Review Board review. We obtained only de-identified data.

Department of Defense Trauma Registry (DODTR) Description

The DODTR, formerly known as the Joint Theater Trauma Registry (JTTR), is the data repository for DoD trauma-related injuries [20,21]. The DODTR includes documentation regarding demographics, injury-producing incidents, diagnoses, treatments, and outcomes of injuries sustained by US/non-US military and US/non-US civilian personnel in wartime and peacetime (including humanitarian) from the point of injury to final disposition. Short-term outcome data are available for non-US casualties. The DODTR comprises all patients admitted to a Role 3 (fixed-facility) or forward surgical team (FST) with an injury diagnosis using the International Classification of Disease 9th Edition (ICD-9) between 800-959.9, near-drowning/drowning with associated injury (ICD-9 994.1) or inhalational injury (ICD-9 987.9) and trauma occurring within 72 hours from presentation. We defined the prehospital setting as any location prior to reaching a FST or a combat support hospital (CSH) to include the Role 1 (point of injury, casualty collection point, battalion aid station) and Role 2 (temporary limited-capability forward-positioned hospital inside combat zone without surgical support). We categorized interventions performed upon arrival at the FST or CSH as emergency department and not prehospital.

Analysis

We performed all statistical analysis using Microsoft Excel (version 10, Redmond, Washington) and JMP Statistical Discovery from SAS (version 13, Cary, NC). We compared study variables between the patients receiving prehospital antibiotics versus patients not receiving prehospital antibiotics using a student t-test for continuous variables, Wilcoxon Rank Sum test for ordinal variables, and chi-squared test for nominal variables. We reported categorical variables as numerators with percentages, ordinal variables as medians with interquartile ranges, and continuous variables as means with standard deviations. For groups demonstrating differences in our primary outcome of mortality between subjects receiving prehospital antibiotics versus no prehospital antibiotics, we constructed regression models to control for potential confounders. Statistical significance was set as $p=0.05$.

Results

From January 2007 to August 2016, there were a total of 38769 encounters in the DODTR. Our predefined ED search codes captured 28222 (72.8%) of those subjects. Within that 28222, we identified 6662 subjects with a GSW, 1899 subjects with an amputation, and 6553 subjects with an open fracture. Among subjects with those injuries, 9.8% (1483 of 15114) received prehospital wound prophylaxis (Table 1). Subjects that received antibiotics were more likely to be male and host nation military, paramilitary, or civilian personnel.

Composite injury severity scores (ISS) were greater among subjects that did not receive prehospital antibiotics within all three injury groups (GSW, $p<0.001$; amputation, $p=0.016$; open fracture, $p<0.001$). Subjects within the traumatic amputation group experienced higher composite ISS in comparison to casualties in the GSW and open fracture groups. Within the open fracture group, subjects that did not receive wound prophylaxis had higher scores for all abbreviated injury scale by body region (AISBR) categories. Within the amputation group, AISBR for face and extremities were significantly higher in those that did not receive antimicrobial therapy. Within the GSW group, subjects that did not receive prehospital wound prophylaxis had higher AISBR for head/ neck and face.

There was no difference in survival to discharge rates between casualties that received prehospital wound prophylaxis and those that did not among subjects who sustained amputations (93.9% vs. 90.7%, $p=0.271$) or open fractures (96.8% versus 95.9%, $p=0.368$). In the GSW group, subjects that received antibiotics had a significantly higher survival rate compared to subjects that did not receive prehospital wound prophylaxis (96.2% versus 92.8%, $p<0.001$). This association persisted on multivariable regression analysis (OR 1.61, 95% CI 1.09-2.38).

Discussion

This analysis described prehospital antibiotic administration to adult combat trauma casualties during the recent conflicts in Afghanistan and Iraq. Host nation personnel comprised the majority of subjects that received prehospital wound prophylaxis. Less than 10% of subjects with GSW, traumatic amputation, or open fracture received prehospital wound prophylaxis. For GSW victims only, we identified an association between prehospital wound prophylaxis and increased rate of survival that persisted upon regression analyses.

High-velocity ballistic injuries sustained during armed conflict may be at high risk for infectious complications. Recent studies of war wounds sustained in Afghanistan and Iraq reported infectious complications in 4-31% of penetrating abdominal injury, 2-25% of penetrating chest trauma, and 0-24% of injuries to the head and face [14,22,23] Published military data for previous armed conflicts reported infection rates from GSW, generally with underlying fractures, ranging from 10-50% [19,24-26] Although some studies attributed decreased infectious complications to early prehospital antibiotic administration, other studies reported no benefit [16,19,27-29] However, these reports evaluated infection rates only and not mortality among a total of 1137 combat casualties suffering GSW [19,24-28]. Our study analyzed 6662 GSW victims and demonstrated a significant survival benefit in those treated with prehospital antibiotics. Uncomplicated, through-and-through GSW may be managed non-operatively [30,31]. Prehospital wound prophylaxis may benefit this subgroup of GSW victims. Our finding of increased survival associated with prehospital wound prophylaxis should be considered preliminary and future prospective, controlled trials may be beneficial.

We did not find an association between survival and prehospital wound prophylaxis in subjects with traumatic amputations and open fractures. Blast injuries accounted for most traumatic amputations and open fractures in Iraq and Afghanistan [1,2,27,32-35]. Given the complexities of blast injuries, intra-theater operative strategies favored damage control surgery techniques [8,33,34,36-39]. Rapid evacuation to surgical capabilities and wound irrigation and debridement decreased wound infection rates [8,16,27,28,37]. Consequently, our findings may be partially explained by severely injured subjects rapidly undergoing surgical management. Subjects with more severe injuries received wound prophylaxis less often. This observation is likely multifactorial; however, prehospital providers may have subordinated antimicrobial

Variables		Gunshot Wound (6662)			Amputation (1899)			Open Fracture (6553)		
		+Abx (n=782)	-Abx (n=5880)	p-value	+Abx (n=133)	-Abx (n=1766)	p-value	+Abx (n=568)	-Abx (n=5985)	p-value
Demographics	Age	25 (21-30)	25 (21-30)	0.0789	24 (21-29.5)	24 (21-29)	0.739	25 (21-30)	25 (21-30)	0.189
	Male	97.1% (5708)	98.2% (768)	0.0819	97.6% (1723)	94.7% (126)	0.081	98.2% (558)	97.4% (5832)	0.321
Patient Category	US military	8.9% (161)	91.1% (1644)	NR	5.8% (47)	94.2% (756)	NR	6.4% (156)	93.6% (2269)	NR
	Coalition	7.1% (31)	92.9% (403)		2.1% (4)	97.9% (188)		5.0% (25)	95.0% (477)	
	Contractor	10.4% (16)	89.6% (138)		3.6% (2)	96.4% (53)		9.2% (24)	90.8% (236)	
	Humanitarian	13.1% (269)	86.9% (138)		10.7% (43)	20.4% (360)		10.7% (169)	89.3% (1411)	
	Host Nation Force	13.7% (301)	86.3% (1894)		8.4% (37)	91.6% (406)		10.9% (192)	89.1% (1563)	
	Other	15.4% (4)	84.6% (22)		0% (0)	100% (3)		6.5% (2)	93.5% (29)	
Injury Score Data	Composite	9 (4-14)	9 (4-17)	<0.001	18 (11-24.5)	19 (14-29)	0.016	10 (9-18)	13 (9-22)	<0.001
	AIS (head/neck)	0 (0-0)	0 (0-0)	<0.001	0 (0-1)	0 (0-1)	0.066	0 (0-0)	0 (0-1)	<0.001
	AIS (face)	0 (0-0)	0 (0-0)	0.004	0 (0-1)	0 (0-1)	0.002	0 (0-0)	0 (0-1)	0.001
	AIS (thorax)	0 (0-0)	0 (0-0)	0.204	0 (0-0)	0 (0-0)	0.676	0 (0-0)	0 (0-1)	0.001
	AIS (abdomen)	0 (0-0)	0 (0-0)	0.232	0 (0-2)	0 (0-2)	0.128	0 (0-0)	0 (0-2)	<0.001
	AIS (extremities)	0 (0-3)	0 (0-3)	0.110	3 (3-4)	4 (3-4)	0.026	3 (2-3)	3 (2-3)	<0.001
	AIS (skin/ superficial)	1 (0-1)	1 (0-1)	0.654	1 (1-2)	1 (1-2)	0.155	1 (0-1)	1 (0-1)	0.005
Outcomes	Survival	96.2% (752)	92.8% (5451)	<0.001	93.9% (125)	90.7% (1601)	0.271	96.8% (550)	95.9% (5738)	0.368

*Subjects could have been included in more than one group
Abx: Antibiotic; AIS: Abbreviated injury scale; NR: Not reported

Table 1: Comparison between included cohorts that received wound prophylaxis versus non-recipients.

therapies to interventions for life-threatening processes. In turn, this may have introduced selection bias.

Open fractures with significant soft tissue injury are at particularly high risk for infection. A stateside military treatment facility receiving war casualties evacuated out of theater reported 15% of all orthopedic admissions developed osteomyelitis, and 27% of Gustilo-Anderson Type III tibia fractures had deep wound infections with 22% progressing to surgical amputation [2,40]. Civilian studies demonstrated 25-50% of Gustilo-Anderson Type III tibia fractures developed infection, and early antibiotics decreased deep wound infection rates [15,18,41]. Consensus guidelines, including TCCC, recommend early wound prophylaxis to mitigate infectious complications when delayed evacuation is anticipated [5,7,16,42,43]. Yet we found prehospital providers administered antibiotics to only 7.0% (133 of 1899) of traumatic amputations and 8.7% (568 of 6553) of open fractures. These wound prophylaxis rates are substantially lower than a previous report limited to special operations soldiers that indicated 27.9% of its casualties received prehospital antibiotics [16]. The differences in prehospital wound prophylaxis rates may be due to special operations units outperforming conventional military forces with respect to combat pill pack issuance and prehospital documentation rates [44-46]. Pre-deployment training emphasizing TCCC guidelines for wound prophylaxis may improve administration rates.

Our study has several important limitations. First, we were unable to identify timing of antibiotic administration, surgical intervention, and casualty evacuation in relation to the time of injury. Additionally, we did not account for the class and dosage of antimicrobials administered prehospital and during inpatient management. Second, we were unable to determine the proportion of subjects by injury type that were surgically managed, and then describe the number and types of surgical procedures performed. This data may have enabled analysis between subjects that underwent conservative versus surgical management. Third, our study population was limited to intra-theater military hospital in patient populations managed in facilities without microbiology laboratory capabilities necessary for culture and antimicrobial resistance testing. Therefore, we were unable to identify pathogenic bacteria and medication resistance patterns. A previous report noted most war wound infections were detected in stateside military hospitals, with rates of diagnosis increasing from 1% in Landsthul, Germany to 18% stateside [37]. Fourth, the available data did not permit identification of infectious complications (e.g. sepsis) strictly from wounds and analysis of susceptibility factors, such as comorbid medical conditions and massive transfusion of blood products [27,47]. Fifth, as a retrospective analysis we were unable to control for unmeasurable confounders and biases [48]. We attempted to mitigate these factors by performing univariable and multivariable regression analyses, but we could not control for confounders for which we did not have data such as operative interventions, blood product administration, comorbidities, etc. Finally, the trauma registry data is subject to human errors in data entry, retrieval, and omission. Previous studies have demonstrated that US military prehospital documentation rates are poor which limits data quality in the registry [49,50].

Conclusion

Military prehospital providers infrequently administered wound prophylaxis during the recent conflicts in Afghanistan and Iraq. There is an association between prehospital administration of antibiotics and increased survival among casualties suffering gunshot wounds.

Acknowledgement

We would like to thank the Joint Trauma System Data Analysis Branch for their efforts with data acquisition.

Disclaimer

Opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Air Force, the Department of the Army, or the Department of Defense.

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