Effects of Prehospital Wound Prophylaxis in Iraq and Afghanistan on Mortality

Jason F Naylor1, Kimberly Burbank2, Michael D April3, Joseph C Wenke3, Joseph K Maddry4, and Steven G Schauer2,4

1 Madigan Army Medical Center, Joint Base Lewis McChord, Washington D.C., USA
2 US Army Institute of Surgical Research, JBSA Fort Sam Houston, Texas, USA
3 Brooke Army Medical Center, JBSA Fort Sam Houston, Texas, USA
4 59th Medical Wing, Air Education and Training Command, JBSA Lackland, Texas, USA

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.

*pCorresponding author: Jason F Naylor, Madigan Army Medical Center, Joint Base Lewis McChord, Washington D.C., USA, Tel: 25396680599; E-mail: jason.f.naylor.mil@mail.mil

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

Copyright: © 2018 Naylor JF, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
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 peace-time (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 trauma 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
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 state-side military 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 developed infection, and 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 prophylaxis rates are substantially lower than 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.
References
1. Owens BD, Kragh JF, Wenke JC, Macaitis J, Wade CE, et al. (2008) Combat wounds in operation iraqi freedom and operation enduring freedom. J Trauma 2: 295-299.
2. Burns TC, Stinner DJ, Mack AW, Potter BK, Beer T, et al. (2012) Microbiology and injury characteristics in severe open tibia fractures from combat. J Trauma Acute Care Surg 72: 1062-1067.
3. Ficke JR, Pollak AN (2007) Extremity war injuries: development of clinical treatment principles. J Am Acad Orthop Surg 15: 590-595.
4. Penn-Barwell JG, Bennett PM, Fries A, Kendrew MJ, Midwinter MJ, et al. (2013) Severe open tibial fractures in combat trauma: management and preliminary outcomes. Bone Joint J 95: 101-105.
5. Putley EJ, Green AD (2009) Infection in wounds of conflict—old lessons and new challenges. J R Army Med Corps 155: 315-319.
6. Murray CK (2008) Infectious disease complications of combat-related injuries. Crit Care Med 36: S358-364.
7. Hospenthal DR, Murray CK, Anderson RC, Bell RB, Calhoun JH, et al. (2011) Guidelines for the prevention of infections associated with combat-related injuries: 2011 update, endorsed by the infectious diseases society of america and the surgical infection society. J Trauma 71: S210-234.
8. Murray CK, Hsu JR, Solomon JS, Keeling JJ, Andersen RC, et al. (2008) Prevention and management of infections associated with combat-related extremity injuries. J Trauma 64a: S239-251.
9. Brown KV, Walker JA, Corez DS, Murray CK, Wenke JC, et al. (2010) Earlier debridement and antibiotic administration decrease infection. J Surg Orthop Adv 19: 18-22.
10. Tennent DJ, Shielis SM, Sanchez CJ, Niece KL, Akers KS, et al. (2016) Time-dependent effectiveness of locally applied vancomycin powder in a contaminated traumatic orthopaedic wound model. J Orthop Trauma 30: 531-537.
11. Polk HC, Lopez-Mayor JF (1969) Postoperative wound infection: a prospective study of determinant factors and prevention. Surgery 66: 97-103.
12. Stone HH, Hooper CA, Kolb LD, Geheber CE, Dawkins EJ, et al. (1976) Antibiotic prophylaxis in gastric, biliary and colonic surgery. Ann Surg 184: 443-452.
13. Krueger WA, Lenhart FP, Neeser G, Ruckdeschel G, Schreckhase H, et al. (2007) Influence of combined intravenous and topical antibiotic prophylaxis on the incidence of infections, organ dysfunctions, and mortality in critically ill surgical patients: a prospective, stratified, randomized, double-blind, placebo-controlled clinical trial. Am J Respir Crit Care Med 166: 1029-1037.
14. Murray CK (2017) Field wound care: Prophylactic antibiotics. Wilderness Environ Med 28: S90-S102.
15. Lack WD, Karanukar MA, Angerame MR, Seymour RB, Sims S, et al. (2015) Type III open tibia fractures: immediate antibiotic prophylaxis minimizes infection. J Orthop Trauma 29: 1-6.
16. Murray CK, Hospenthal DR, Kotwal RS, Butler FK (2011) Efficacy of point-of-injury combat antimicrobials. J Trauma 71a: S307-313.
17. Penn-Barwell JG, Murray CK, Wenke JC (2012) Early antibiotics and debridement independently reduce infection in an open fracture model. J Bone Joint Surg Br 94: 107-112.
18. Patzakis MJ, Harvey JP, Iver D (1974) The role of antibiotics in the management of open fractures. J Bone Joint Surg Am 56: 532-541.
19. Jackson DS (2007) Soldiers injured during the fallakkans campaign 1982, sepsis in soft tissue limb wounds. J R Army Med Corps 153: 55-56.
20. Glenn MA, Martin KD, Monzon D, Nettles W, Rodriguez VM, et al. (2008) Implementation of a combat casualty trauma registry. J Trauma Nurs 15: 181-184.
21. O’Connell KM, Littleton-Kearney MT, Bridges E, Bibb SC (2012) Evaluating the joint theater trauma registry as a data source to benchmark casualty care. Mil Med 177: 546-552.
22. Martin GJ, Dunne JR, Cho JM, Solomon JS (2011) Prevention of infections associated with combat-related thoracic and abdominal cavity injuries. J Trauma 71: S270-281.
23. Petersen KM, Colyer MH, Hayes DK, Hale RG, Bell RB, et al. (2011) Prevention of infections associated with combat-related eye, maxillofacial, and neck injuries. J Trauma 71a: S264-269.
24. Hinsley DE, Phillips SL, Clasper JS (2008) Ballistic fractures during the 2003 gulf conflict—early prognosis and high complication rate. J R Army Med Corps 152: 96-101.
25. Jacob E, Epeplinger JM, Murphy KP (1992) A retrospective analysis of open fractures sustained by U.S. military personnel during operation just cause. Mil Med 157: 552-556.
26. Hamouda HM, Wtso E, Moghani NK, Shakwan A, Nyaar GP, et al. (2007) Soft tissue infection after missile injuries to the extremities-A non-randomized, prospective study in gaza city. Prehosp Disaster Med 22: 106-108.
27. Tribble DR, Li P, Warkentien TE, Lloyd BA, Schnaubelt ER, et al. (2016) Impact of operational theater on combat and noncombat trauma-related infections. Mil Med 10: 1259-1268.
28. Gerhardt RT, Matthews JM, Sullivan SG (2009) The effect of systemic antibiotic prophylaxis and wound irrigation on penetrating combat wounds in a return-to-duty population. Prehosp Emerg Care 13: 500-504.
29. Klein RS, Berger SA, Yekuel P (1975) Wound infection during the yom kippur war: observations concerning antibiotic prophylaxis and therapy. Ann Surg 182: 15-21.
30. Penn-Barwell JG, Brown KV, Fries CA (2015) High velocity gunshot injuries to the extremities: management on and off the battlefield. Curr Rev Musculoskeletal Med 6: 312-317.
31. Mannion SJ, Chabner E (2005) Principles of war surgery. BMJ 330: 1498-1500.
32. Huh J, Stinner DJ, Burns TC, Hsu JR (2011) Infectious complications and soft tissue injury contribute to late amputation after severe lower extremity trauma. J Trauma 71a: S47-51.
33. Manning MM, Hawk A, Calhoun JH, Andersen RC (2009) Treatment of war wounds: A historical review. Clin Orthop Relat Res 467: 2168-2191.
34. Sohn VY, Arthurs ZM, Herbert GS, Beekley AC, Sebesta JA, et al. (2008) Demographics, treatment, and early outcomes in penetrating vascular combat trauma. Arch Surg 143: 783-787.
35. Owens BD, Kragh JF, Macaitis J, Svoboda SJ, Wenke JC, et al. (2007) Characterization of extremity wounds in operation iraqi freedom and operation enduring freedom. J Orthop Trauma 21: 254-257.
36. Doukas WC, Hayda RA, Frisch HM, Anderson RC, Mazurek MT, et al. (2013) The military extremity trauma amputation/limb salvage (metals) study: outcomes of amputation versus limb salvage following major lower-extremity trauma. J Bone Joint Surg Am 95: 138-145.
37. Blyth DM, Yen HC, Tribble DR, Murray CK (2015) Lessons of war: combat-related injury infections during the vietnam war and operation iraqi and enduring freedom. J Trauma Acute Care Surg 79: S27-235.
38. Mazurek MT, Ficke JR (2008) The scope of wounds encountered in casualties from the global war on terrorism: from the battlefield to the tertiary treatment facility. J Am Acad Orthop Surg 14: 18-23.
39. Jansen JO, Thomas R, Loudon MA, Brooks A (2009) Damage control resuscitation for patients with major trauma. BMJ 338: b1778.
40. Yun HC, Bradstetter JG, Murray CK (2008) Osteomyelitis in military personnel wounded in iraq and afghanistan. J Trauma 64: S163-168.
41. Gustillo RB, Anderson JT (1976) Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg Am 58: 453-458.
42. Butler FK, Holcomb JB, Giebner SD, McSwain NE, Bagian J, et al. (2007) Tactical combat casualty care 2007: evolving concepts and battlefield experience. Mil Med 172: 1-19.
43. Pidcock H, Spinella P, Strandenes G, Tien HC, Beckett A, et al. Joint Trauma System Clinical Practice Guidelines.
44. Kotwal RS, Butler FK, Edgar EP, Schackelford SA, Bennett DR, et al. (2013) Saving Lives on the Battlefield: A Joint Trauma System Review of Pre-Hospital Trauma Care in Combined Joint Operating Area: Afghanistan (CJQOA-A) Executive Summary. J Spec Oper Med 13: 77-85.
45. Sauer SW, Robinson JB, Smith MP, Gross KR, Kotwal RS, et al. (2015) Saving lives on the battlefield (part ii): one year later a joint theater trauma system and joint trauma system review of prehospital trauma care in combined joint operations area, Afghanistan (CJQOA-A) Final Report. J Spec Oper Med 15: 25-41.
46. Kotwal RS, Montgomery HR, Kotwal BM, Champion HR, Butler FK, et al. (2011) Eliminating preventable death on the battlefield. Arch Surg 146: 1350-1358.
47. Lewandowski LR, Weintrob AC, Tribble DR, Rodriguez CJ, Petfield J, et al. (2016) Early complications and outcomes in combat injury-related invasive fungal wound infections: A case-control analysis. J Orthop Trauma 30: e53-99.

48. Kaji AH, Schriger D, Green S (2014) Looking through the retrospectoscope: Reducing bias in emergency medicine chart review studies. Ann Emerg Med 64: 292-298.

49. Schauer SG, April MD, Naylor JF, Oliver JJ, Cunningham CW, et al. (2017) A descriptive analysis of data from the department of defense joint trauma system prehospital trauma registry. US Army Med Dep J 3-17: 92-97.

50. Robinson JB, Smith MP, Gross KR, Suaer SW, Geracci JJ, et al. (2016) Battlefield documentation of tactical combat casualty care in Afghanistan. US Army Med Dep J 2: 87-94.