Risk Factors Associated with Multidrug-resistant Gram-negative Bacilli Colonization in Wounded Military Personnel Deployed to Iraq and Afghanistan

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Abstract

Background: Previous studies have shown high rates of colonization and infection with multidrug-resistant gram-negative bacilli (MDR GNB) in patients injured during deployment to Iraq and Afghanistan. Using data from a longitudinal military trauma registry, we evaluated the risk factors associated with MDR GNB colonization.

Methods: Injury circumstances and post-injury management were collected from the Department of Defense Trauma Registry. Antibiotic use, microbiology results, and infection data were collected from the Trauma Infectious Diseases Outcomes Study (TIDOS). MDR GNB colonization was defined as growth of MDR (ESBL production or resistance to 3 or more of: carbapenems, aminoglycosides, fluoroquinolones, or beta-lactams) GNB from active surveillance cultures (groin/axilla) performed within 48 hrs of U.S. admission. Multivariate logistic regression was used to evaluate risk factors associated with colonization. Odds ratios (OR) are presented with 95% confidence intervals.

Results: From June 2009 to May 2012, 2079 deployment-injured patients were admitted to TIDOS-participating U.S. hospitals. Of these patients, 289 (14%) were colonized with a MDR GNB including *E. coli* (74%), *A. baumannii* (15%), *K. pneumoniae* (10%), *E. cloacae* (1%), and *Citrobacter* spp. (< 1%). There was no difference in duration between injury and admission between those with and without colonization (median 5 d in both). In the multivariate model, factors significantly associated with MDR GNB colonization include injury during fighting season (April – September, OR 1.8 [1.4-2.4]), massive blood transfusion (OR 2.7 [1.7-4.2]), fluoroquinolone use post injury (OR 1.8 [1.4-2.5]), and infection prior to U.S. arrival (OR 1.7 [1.1-2.6]). Factors not associated include branch of service, country of injury, mechanism of injury, ICU admission, injury severity score, indwelling orthopedic hardware, cefazolin, or carbapenem use.

Conclusion: Although several factors are associated with higher rates of MDR GNB colonization post deployment-related injury, fluoroquinolone use is the only modifiable one. This finding provides further support for current guidelines which do not recommend routine fluoroquinolone use for post-injury prophylaxis.

Background

- Increased rates of infections with multidrug resistant organisms (MDROs) seen in wounded military personnel returning from Iraq and Afghanistan in recent years
- Previous studies show high rate of MDR GNB colonization (over 12%) in those admitted to US Military Treatment Facility (US MTF) (Weintrob et al. *MSMR* 2013)
- Infection Control measures instituted at Landstuhl Regional Medical Center (LRMC, Landstuhl, Germany), Walter Reed National Military Medical Center (WRNMMC, Bethesda, MD), and San Antonio Military Medical Center (SAMMC, San Antonio, TX) in attempt to limit nosocomial transmission of MDROs
  - Active surveillance cultures (ASC) performed on wounded military personnel admitted to LRMC, WRAMC, NNMC, or SAMMC
  - Patients colonized with MDROs placed on contact precautions
- Department of Defense (DoD) - Veterans Administration (VA) Trauma Infectious Disease Outcomes Study (TIDOS) began in June 2009 and follows injured service members admitted to LRMC and then transferred to WRNMMC or SAMMC
  - Information collected includes: active surveillance cultures, infections, mechanism of injury, all antimicrobials administered, branch of service, location and severity of injury
  - Serves as the Infectious Disease (ID) module of the Joint Theater Trauma Registry (JTTR)
- Purpose of this study was to determine risk factors for colonization with MDR GNB to better determine if any are modifiable

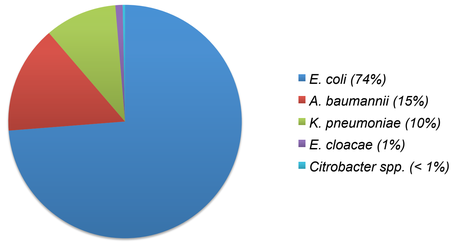
Methods

- Injured service members evacuated from Iraq or Afghanistan through Landstuhl, Germany and admitted to WRNMMC or SAMMC from June 2009 – May 2012 were included
- Data on patient characteristics, injury circumstances, ASC, infections, and antimicrobials administered was captured from the DoD JTTR including the ID module (TIDOS)
- Active surveillance cultures were defined as a cultured swab from either the groin or axilla performed within two days of admission to the US MTF
- MDR GNB defined as Gram negative organisms resistant to ≥ 3 of the 4 following classes of antibiotics: beta-lactams, carbapenems, aminoglycosides, or fluoroquinolones **OR** organisms producing extended-spectrum beta-lactamases (ESBLs) or carbapenemases
- Antimicrobial susceptibility determined in clinical laboratories at participating US MTF using automated microbiology technology
- Baseline characteristics, injury circumstances, and medical management were compared between those with and without MDR GNB colonization
- Univariate and multivariate logistic regression were performed to evaluate potential risk factors associated with MDR GNB colonization
- Analyses were repeated limiting the MDR GNB to the most common colonizing organism

Results

- 2079 patients admitted to either WRNMMC or SAMMC from June 2009 – May 2012
- 289 (14%) colonized with MDR GNB

Figure 1. Organism distribution for injured personnel colonized with MDR GNB



- *E. coli* found to be the most common organism isolated in those colonized with MDR GNB on active surveillance cultures

Results (cont.)

Table 1. Comparison of Patient Characteristics between those with and without MDR GNB Colonization

Patient Characteristics	Not MDR GNB colonized	MDR GNB colonized	P-value
Number of patients	1790	289	
Age (years) – median (IQR)	24.5 (22-29)	23.4 (21-28)	0.005
Male	1749 (98%)	289 (100%)	0.004
Combat related	1580 (88%)	276 (96%)	< 0.001
Branch of service			
Air Force	70 (4%)	6 (2%)	
Army	1107 (62%)	161 (56%)	
Navy	66 (4%)	9 (3%)	
Marine	507 (28%)	103 (36%)	
Non-US Military	17 (1%)	4 (1%)	
Mechanism of injury			< 0.001
Any IED blast	955 (53%)	193 (67%)	
Non-IED blast	245 (14%)	31 (11%)	
Non-blast + Gun Shot Wound	294 (16%)	44 (15%)	
Other	295 (16%)	21 (7%)	
Any amputation (excluding digits)	337 (19%)	91 (32%)	< 0.001
Injury calendar season			< 0.001
Apr-Sep (fighting season)	1040 (58%)	200 (69%)	
Oct-Mar	750 (42%)	89 (31%)	
Military Theater of Operation			0.041
Afghanistan	1571 (88%)	267 (92%)	
Iraq	178 (10%)	18 (6%)	
Injury place			0.016
Bagram	301 (17%)	39 (14%)	
Bastion	395 (20%)	70 (24%)	
Kandahar	362 (22%)	79 (27%)	
Other	732 (41%)	101 (35%)	
LRMC Injury Severity Score			< 0.001
0 – 9 (Mild)	731 (41%)	73 (25%)	
10 – 15 (Moderate)	394 (22%)	74 (26%)	
16 – 24 (Severe)	419 (23%)	92 (32%)	
>/= 25 (Life threatening)	245 (14%)	50 (17%)	
ICU admission at LRMC	871 (49%)	178 (62%)	< 0.001
First 24 hour blood transfusion			< 0.001
< 10 units	403 (22%)	88 (30%)	
10-20 units	184 (10%)	55 (19%)	
> 20 units	147 (8%)	46 (16%)	
Any infection	155 (9%)	45 (16%)	< 0.001
Any antibiotic use prior to ASC	1659 (85%)	284 (15%)	< 0.001
Antibiotic use prior to US MTF			
Carbapenem +/- other antibiotic	178 (10%)	42 (14%)	
Cefazolin only	9 (5%)	15 (5%)	
Floruoquinolone +/- other antibiotic	644 (36%)	148 (51%)	
No antibiotic prior to first US MTF ASC	131 (7%)	5 (2%)	
Other	742 (42%)	80 (28%)	
Mechanical ventilation at LRMC	571 (32%)	130 (45%)	< 0.001
Central line prior to US MTF	270 (15%)	65 (22%)	0.002
Indwelling hardware	545 (30%)	102 (35%)	0.099
No. of OR visits prior to US MTF (median, IQR)	1 (1-1)	1 (1-2)	0.454
Days between injury and US MTF admission (median, IQR)	5 (4-6)	5 (4-6)	0.231

Results (cont.)

Table 2. Multivariate logistic regression model for factors associated with MDR GNB colonization

Risk Factors	Odds Ratio (95% CI)
Injury season (Apr – Sep)	1.81 (1.36, 2.41)*
First 24 hour blood transfusion < 10 units 10-20 units > 20 units	 2.13 (1.5, 3) * 2.65 (1.67, 4.2)* 2.72 (1.64, 4.53)*
Fluoroquinolone plus other antibiotic prior to transfer to US MTF	1.84 (1.37, 2.45)*
Infection at LRMC prior to transfer to US MTF	1.72 (1.12, 2.64)*

*p<0.05

- Other factors included in the model but not statistically significant: branch of service, mechanism of injury, admission to ICU, cefazolin only use, indwelling hardware, age, theater of operation, injury place
- Analysis was repeated limiting it to MDR *E.coli* and results were the same

Conclusions

- Patients deployed to Iraq and Afghanistan are often colonized with MDR *E. coli*
- Being injured during fighting season (Apr – Sept) is associated with higher rates of MDR GNB colonization
  - May be secondary to increased number of persons transiting through combat support hospitals or military treatment facilities during this time or may have to do with warmer weather
- Fluoroquinolone use prior to US arrival, but not Cefazolin use, was associated with higher rates of MDR GNB colonization
  - Current guidelines do not recommend the use of prophylactic fluoroquinolones for closed or open soft tissue injuries or open fractures; however, previous studies have shown a significant amount of fluoroquinolone use for this purpose
  - More education regarding post-injury antibiotic prophylaxis and increased adherence to current guidelines may decrease MDR GNB colonization rates
- Higher numbers of blood transfusions are also associated with MDR GNB colonization
  - May be a marker of injury severity although other measures of severity were not associated with colonization
  - May also be associated with immunomodulatory effects of blood transfusions

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