Outcome and impact of empirical antimicrobial treatment in bacteremia with Bacteroides species

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Objectives

Anaerobic infections are an important cause of bacteremia and severe Infections. Due to an increasing part of extended spectrum β-lactamase (ESBL) producing bacteria, the treatment recommendations for abdominal infections in Sweden have changed during the past ten years (fig 1). The effects of anaerobic resistance and outcomes for patients with anaerobic infections are unclear.

Methods

A retrospective cohort study was conducted in patients with bacteraemia due to Bacteroides species in the Region of Skåne in Sweden between 2011 and 2015. Data on patients were reviewed from medical and microbiological records and the factors associated with 28-day mortality were determined using a multivariate regression model. We used the matrix-assisted laser desorption/ionizationer (MALDI-TOF) to enable the specific species identification.

Results

Data on 454 patients were reviewed from medical and microbiological records and 389 (median age, 76 years; male, 54%) met the inclusion criteria. The 28-days all-cause mortality rate was 19% (72/389). Independent risk factors associated with 28-days mortality included; age, female sex, lactate and CRP (table 1). Inadequate empirical antibiotic therapy occurred among 182 (47%) patients and we found a trend towards that inadequate antibiotic treatment increased the 28- days mortality (p = 0.063).

Independent risk factors of receiving wrong empirical antibiotic therapy was an elevated CRP and factors associated with receiving adequate antibiotic were immunosuppression and having source control (Table 2).

The frequency of bacteraemia with Bacteroides sp. increased during the period of time and Bacteroides fragilis was the most common bacteria, 55% (212/389). The resistance against piperacillin/tazobactam was higher in comparison to other studies. The most frequent isolate that was resistant to piperacillin/tazobactam was Bacteroides thetaiotamicron with 60% (50/83) being resistant (table 3). Piperacillin/tazobactam was the most used antimicrobial agent against bacteroides infections and the utilization was increasing over time. We did not find any resistance among the bacteroides isolates against metronidazole and only three isolates were resistant against carbapenems.

Conclusions

Anaerob resistance is an increasing problem and especially against a common antibiotic treatment such as piperacillin/tazobactam. Early recognition and appropriate treatment is important since there was a trend that inadequate treatment increased 28-days mortality.

	Total	Survived >28d	Died 28d	P	Adjusted OR (95% CI)	P adjusted
Number of patients	389	207	182			
Age years (median, IQR)	76 (63-83)	74 (62-82)	79 (73-88)	<0.001	1.016-1.085	0.004
Male	211	185	26 (12.3%)			
Female (%)	178	132	46 (25.8)	0.001	1.910-8.819	<0.001
Charlson index (median, IQR)	2 (1-5)	2 (0-4)	4 (2-6)	<0.001	0.999-1.341	0.051
Immune compromise n (%)	72 (19)	50 (69)	22 (31)	.004	0.816-4.659	0.133
Source control n (%)	170 (45)*	149(56)	21(30)	<0.001	0.235-1.147	0.105
Septic shock n (%)	20 (5)	10 (50)	10 (50)	0.001	0.725-9.044	0.144
CRP mg/L (median, IQR)	240 (140-320)	232 (126-310)	277 (210-390)	<0.001	1.003-1.010	<0.001
Lactate (median, IQR)	2.4 (1.7-3.9)	2.2 (1.6-3.5)	3.6 (2.2-6.2)	<0.001	1.147-1.510	<0.001
Indequate initial antibiotic therapy (%)	182	143	39 (21.4)	0.166	0.219-1.042	0.063
WBC (median, IQR)	16 (13-22)	16 (13-20)	18 (13-25)	0.023	0.992-1.038	0.196

Table 1
Comparison of clinical and laboratory characteristics and outcomes between 28-day survivors and non-survivors

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Figure 1
Empirical antibiotic used %

	Total	Adequate antibiotics	Inadequate antibiotics	P-value	Adjusted OR (95% CI)	Adjusted P-value
Number of patients	389	207	182			
Age years (median, IQR)	76 (63-83)	73 (61-81)	78 (69-84)	0.001	0.966-1.002	0.087
Sex (% male)	54	51	58	0.138	0.899-2.620	0.116
Charlson index (median, IQR)	2 (1-5)	2 (0-5)	2.5 (1-5)	0.037	0.887-1.114	
Immunosupression n (%)	72 (19)	41 (20)	31 (17)	0.482	1.097-4.715	0.027
Nosocomial infection n (%)	41 (11)	26 (13)	15 (8)	0.164	0.709-3.904	
Polymicrobial infection n (%)	172 (44)	84 (41)	88 (48)	0.438	0.579-1.682	
Source control n (%)	170 (44)	116 (56)	54 (30)	<0.001	1.411-4.247	0.001
Hospital stay, days (median, IQR)	10 (6-19)	11 (6-20)	10 (6-18)	0.217	0.966-1.008	
Severe sepsis n (%)	37 (10)	19 (9)	18 (10)	0.811	0.474-2.769	
Septic shock n (%)	20 (5)	14 (7)	6 (3)	0.130	0.461—5.939	
Mortality 28 days n (%)	72 (19)	33 (16)	39 (21)	0.166	0.217-1.050	0.066
Mortality 1 year n (%)	50 (13)	25 (12)	25 (14)	0.578	0.304-1.635	
CRP mg/L (median, IQR)	240 (140-320)	208 (122-295)	260 (168-339)	<0.001	1.001-1.006	0.008
WBC (median, IQR)	16 (13-22)	17 (13-23)	16 (12-22)	0.728	0.986-1.027	
Lactate (median, IQR)	2.4 (1.7-3.9)	2.4 (1.7-3.8)	2.4 (1.6-4)	0.388	0.928-1.174	

Table 2
Comparison of clinical and laboratory characteristics between receiving adequate vs inadequate antibiotics

Antibiotic	species	Sensitive (n)	Resistant /Intermediate (n)	Total (n)
Piperacillin/tazobactam	bacteroides species	8	4	12
	B. fragilis	216	0	216
	B. thetaiotaomicron	33	50	83
	B. ovatus	18	2	20
	B. uniformis	15	0	15
	other	19	2	21
	B. vulgatus	17	3	20
	Total	326 (84%)	61 (16%)	387
Carbapenem	bacteroides species	12	0	12
	B. fragilis	215	1	216
	B. thetaiotaomicron	81	2	83
	B. ovatus	20	0	20
	B. uniformis	15	0	15
	other	21	0	21
	B. vulgatus	21	0	21
	Total	385 (99%)	3 (1%)	388
Metronidazole	bacteroides species	12	0	12
	B. fragilis	217	0	217
	B. thetaiotaomicron	83	0	83
	B. ovatus	20	0	20
	B. uniformis	15	0	15
	other	21	0	21
	B. vulgatus	21	0	21
	Total	389	0	389
Clindamycin	bacteroides species	7	1	8
	B. fragilis	152	22	174
	B. thetaiotaomicron	61	5	66
	B. ovatus	11	5	16
	B. uniformis	11	2	13
	other	16	2	18
	B. vulgatus	9	2	11
	Total	267 (87%)	39 (13%)	306

Table 3
Susceptibilities to piperacillin/tazobactam, clindamycin, carbapenems and metronidazole of the isolates by species

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