Infection and gut colonization by KPC-producing Klebsiella pneumoniae as risk factors for mortality in patients with diabetic foot infections: a multicentre case-control study

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STATE OF THE KNOWLEDGE

Infections caused by carbapenem-resistant Enterobacteriaceae have emerged as the most challenging to treat. The most clinically important of these highly resistant Enterobacteriaceae is Klebsiella pneumoniae carbapenemase producer (KPC-Kp).

In endemic or epidemic settings, diabetic patients with a foot infection have show a particularly high-risk of becoming gut colonized in the gastrointestinal tract with KPC-Kp. This likely occurs in these patients for several reasons, including frequent need for acute-care hospitalizations; requirement for either re-vascularization procedures or lower-extremity amputations; and, prolonged, repeated courses of antibiotic therapy (often with fluoroquinolones).

After a patient acquires gastrointestinal colonization with KPC-Kp, infection of any diabetic foot wound might be likely.

AIM OF THE STUDY

The aim of our study was to evaluate the role of KPC-Kp foot infection and gut colonization in influencing the mortality of patients with diabetic foot infection (DFI).

PATIENTS AND METHODS

From December 2010 to July 2015 we collected data about 62 DFI patients and divided them into three different group:

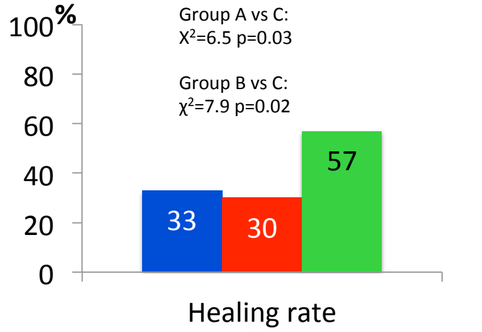
- ✓Group A: patients with diabetic foot infection due to KPC-Kp;
- ✓Group B: patients with gut KPC-Kp colonization and DFI associated to micro-orgamisms different from KPC-Kp;
- ✓Group C: patients without KPC-Kp gut colonization and in which DFI is related to micro-orgamisms different from KPC-Kp.

We analyzed healing rate and mortality at the end of follow up (22.37 ± 17.43 months).

RESULTS

Characteristics	Group A	Group B	Group C	p
Patients (n - %)	42 – 37.8	20 – 18.0	49 – 44.2	---
Male/Female (n)	31 - 11	13 – 7	33 – 16	n.s.
Age (yr)	64.6 ± 11.3	65.8 ± 10.8	65.7 ± 9.5	n.s.
Length of admission (days)	64.3 ± 51.7	24.6 ± 13.6	19.6 ± 13.2	p<0.02
Previous admission (n)	1.2 ± 1.0	1.4 ± 1.0	1.2 ± 0.9	---
Total Haemoglobin (mg/dl)	10.0 ± 1.7	10.3 ± 1.8	10.6 ± 1.4	---
Procalcitonin (ng/ml)	1.96 ± 1.06	1.15 ± 0.80	0.64 ± 0.10	p<0.05
C-Reactive Protein (mg/dl)	13.5 ± 7.8	8.3 ± 3.5	4.4 ± 3.5	p<0.05
Charlson's Index	13.5 ± 2.3	6.3 ± 2.8	3.2 ± 2.6	p=0.002

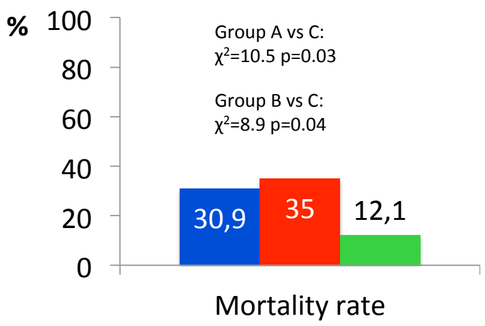
HEALING RATE

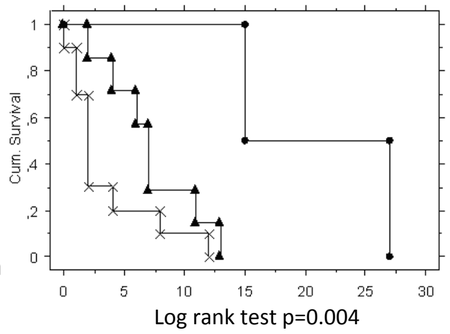


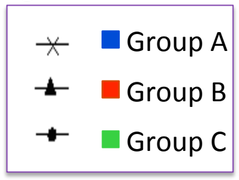
COX REGRESSION ANALYSIS

	Cox regression for healing rate				Cox regression for mortality rate			
	Univariate (HR and 95% CI)	p	Multivariate (HR and 95% CI)	p	Univariate (HR and 95% CI)	p	Multivariate (HR and 95% CI)	p
KPC-Kp infection	3.66 (1.58-8.45)	0.002	2.48 (1.46-4.23)	0.04	2.92 (1.21-7.05)	0.01	2.35 (1.29-5.71)	0.04
Kpc-Kp Gut colonization	3.15 (1.44-6.87)	0.003	2.26 (0.86-6.03)	0.11	5.02 (1.84-13.07)	0.001	6.32 (2.40-15.37)	0.01
Age	0.96 (0.93-1.05)	0.09			1.03 (0.98-1.07)	0.16		
Lenght of in-hospital stay	1.01 (1.00-1.03)	0.49			1.00 (0.99-1.01)	0.13		
Number of admission	1.37 (0.73-2.56)	0.65			1.58 (1.02-2.45)	0.04	1.21 (0.40-3.67)	0.71
Total haemoglobin	0.78 (0.61-0.99)	0.04	0.82 (0.62-1.06)	0.13	0.79 (0.59-1.04)	0.09		
Procalcitonin	0.99 (0.63-1.56)	0.99			1.99 (1.14-3.42)	0.01	2.38 (1.11-5.12)	0.02
C-reactive protein	1.01 (0.96-1.08)	0.63			1.06 (0.99-1.14)	0.07		
Charlson's index	1.83 (1.71-1.98)	0.02	0.85 (0.71-1.02)	0.81	1.04 (0.88-1.23)	0.60		
3D Ulcers (accoring TUSS)	1.36 (0.62-2.98)	0.43			1.98 (0.75-5.18)	0.16		
Multiple antibiotic therapy	1.41 (0.63-3.13)	0.39			2.01 (0.83-4.84)	0.11		
Polymicrobial infection	0.74 (0.29-1.90)	0.53			1.35 (0.45-4.08)	0.59		

MORTALITY







As reported in the first table, the groups were similar regarding the main clinical and demographic characteristics, except that length of in-hospital stay, Charlson index and level of inflammatory markers, both procalcitonin and C-reactive protein, which were all significantly higher in Group A and Group B than in Group C. The overall healing rate for patients in all three groups was 54.9% during the follow-up period. The healing rate was lower in both those who were infected (in the foot) and colonized (in the gut) with KPC-Kp, compared to control Group. The overall mortality rate during the follow-up period was 23.4%, but it was significantly higher in patients in Group A and Group B than for those in Group C. The Kaplan-Meier survival curves showed a significantly higher survival rate for patients in the Group C, as compared to those in Group A or B. In the table above is reported Cox proportional regression analysis for both healing and mortality.

CONCLUSIONS

KPC-Kp foot infection and gut colonization are associated with a reduction in healing rate and a significant increase in mortality rate.

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