APPROPRIATE USE OF ANTIFUNGALS: IMPACT OF AN ANTIFUNGAL STEWARDSHIP PROGRAMME ON THE CLINICAL OUTCOME OF CANDIDAEMIA IN A UNIVERSITY HOSPITAL

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Candidaemia/invasive candidiasis are becoming an emerging problem in hospital practice due to an increased prevalence of susceptible hosts, i.e. patients with central venous catheters and/or immunosuppressive therapies added to a broad-spectrum antibiotic therapy. It is essential to identify risk factors for attributable mortality and to set up a stewardship program to improve infection management.

Objectives

The objective of this study is to compare clinical outcomes of patients with candidaemia before and after implementation of an antifungal stewardship program (AFSP).

Methods

All consecutive cases of candidaemia were included from January 2012 to December 2015 in a University Hospital. Data were collected retrospectively for a period of 2 years before implementation of the AFSP, and prospectively 2 years after. All cases were reviewed by a multidisciplinary panel of experts including 2 infectious disease physicians, a microbiologist and 2 pharmacists in order to have a complete follow-up of patients.

Results

Table 1. Demographic characteristics, predisposing factors, and site of entry of candidemia before and after AFSP.

Variable	Pre-intervention period (N=33)	Intervention period (N=37)	p-value
Demographic characteristics			
Sex, male, n (%)	24 (72.7)	26 (70.3)	0.82
Age, years, median (IQR)	63 (47-78)	66 (54-77)	0.47
Chronic comorbidity, n (%)			
Malignancy	15 (45.5)	21 (56.8)	0.34
Renal failure	10 (30.3)	11 (29.7)	0.96
Diabetes	5 (15.2)	6 (16.2)	0.90
Heart failure	7 (21.2)	3 (8.1)	0.17
Liver failure	3 (9.1)	0	0.10
Respiratory failure	0	2 (5.4)	0.49
Organ or stem cell transplantation	3 (9.1)	2 (5.4)	0.66
Charlson comorbidity index, median (IQR)	2 (1-5)	2 (1-4)	0.99
Acute comorbidity, n (%)			
Neutropenia	0	3 (8.1)	0.24
Severe undernutrition	6 (18.2)	6 (16.2)	0.83
Concomitant bacterial infection	16 (55.2)	19 (51.4)	0.76
ICU admission before diagnosis	18 (54.6)	10 (27.0)	0.02
Predisposing therapeutic factors, n (%)			
Antibacterial exposure the previous 30 days	28 (84.9)	25 (67.6)	0.09
Antibiotic at the time of candidemia,	25 (75.8)	23 (62.2)	0.22
Steroid or immunosuppressive therapy	5 (15.2)	9 (24.3)	0.34
Parenteral nutrition	4 (12.1)	10 (27.0)	0.12
Chemo/radiotherapy the previous 30 days	3 (9.1)	7 (18.9)	0.32
Central venous catheter	29 (87.9)	32 (86.5)	1
Abdominal surgery	8 (24.2)	10 (27.0)	0.79
Site of entry of candidemia, n (%)			0.07
Intra-abdominal	9 (27.3)	20 (54.1)	
Central venous catheter	13 (39.4)	8 (21.6)	
Other or unknown	11 (33.3)	9 (24.3)	

Table 2. Therapeutic management and clinical outcomes before and after implementation of AFSP

Variable	Pre-intervention period (N=33)	Intervention period (N=37)	p-value
Management of cases			
Infectiologist consultation, n (%)	12 (36.4)	32 (86.5)	$<10^{-3}$
CVC removal, n (%)	28/29 (96.6)	31/32 (96.9)	1
CVC removal ≤24h, n (%)	24/29 (82.8%)	22/32 (68.8)	0.20
Daily blood culture (until negative), n (%) (MD: 2)	27 (87.1)	37 (100)	*0.04*
Transesophageal/Transthoracic echocardiography, n (%) (MD: 1)	26 (81.3)	32 (86.5)	0.55
Eye funduscopic examination, n (%) (MD: 1)	12 (37.5)	22 (59.5)	0.07
Abdominal CT, n (%) (MD: 4)	14 (46.7)	21 (58.3)	0.34
Upper limb doppler (if CVC), n (%)	12/29 (41.4)	10/32 (31.2)	0.41
Antifungal treatment			
Delay between microbiological results and treatment			
≤48h, n (%)	31 (93.9)	36 (97.3)	0.60
0 day, n (%)	29 (87.9)	32 (86.5)	1
Drug used, n (%)*			$<10^{-3}$
Caspofungin	26 (78.8)	11 (32.4)	
Micafungin	0 (0)	22 (64.7)	
Fluconazole	7 (21.2)	1 (2.9)	
Loading dose (if applicable), n (%)	30/32 (93.8)	14/14 (100)	1
Adapted duration of treatment, n (%)	32 (97.0)	37 (100)	0.47
Antifungal de-escalation, n (%) (MD: 4)	12 (40.0)	19 (52.8)	0.30
Outcomes			
Relapse (positive blood culture after discontinuation of treatment), n (%) (MD: 3)	2 (6.5)	1 (2.8)	0.59
Delay between treatment and patient discharge**, days, median (IQR)	22 (15-29)	21 (13-40)	0.75
Secondary location infection, n (%) (MD: 1)	8 (25.0)	6 (16.2)	0.37
Mortality, n (%)			
≤day 7	1 (3.0)	1 (2.7)	1
≤day 30	7 (21.2)	7 (18.9)	0.81
≤day 90	12 (36.4)	10 (27.0)	0.40

MD: missing data * Initiation of treatment, 3 dual antifungal therapies excluded
**22 deceased patients excluded

70 patients were included

Table 1:

- The sites of entry for candidaemia were: **intraabdominal** in 29 cases (41.4%), **central venous catheter** in 21 (30.0%), other or unknown in 20 (28.6%).
- Sixty-one patients **had a central venous catheter (87.1%)** and 18 **had abdominal surgery (25.7%)** .

Table 2:

- Infectiologist consultations increased from 36.4% to 86.5% between the 2 periods with a **significative impact on daily blood cultures** which were more frequently performed in the second period (p=0.04).
- **Echinocandin use was also more frequent** in the second period (97.1% vs 78.8%, p=0.03).
- **The 3-month mortality rate declined from 36.4% in the first period to 27.0% in the second period**.

Conclusions

The strengths of this AFSP is its duration and the number of patients. Unfortunately, our study has lacked statistical power to show a significant impact on mortality. A decline tendency was observed in term of mortality but efforts on candidaemia management must be maintained.

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