

RAPID SPECIES IDENTIFICATION OF CANDIDA BY SEPSITYPER[®] MALDI-TOF-MS: IMPACT ON ANTIFUNGAL THERAPY

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INTRODUCTION

- Candidaemia is the most common invasive fungal infection
- Early effective treatment reduces mortality
- Fluconazole and the echinocandins are widely used for treatment
- Fluconazole is cheap, fungistatic, active against *C. albicans*, unreliable against *C. glabrata*, inactive against *C. krusei*
- Echinocandins are expensive, fungicidal, broad-spectrum against *Candida* but *C. parapsilosis* isolates may have higher minimum inhibitory concentration
- Widespread use of echinocandins may lead to emergence of resistance

PREVALENCE OF CANDIDA SPECIES – EUROPE VS SCOTLAND

EUROPEAN DATA- 2004

EUROPEAN STUDY



SCOTTISH DATA 2016

SCOTTISH CANDIDAEMIA AUDIT

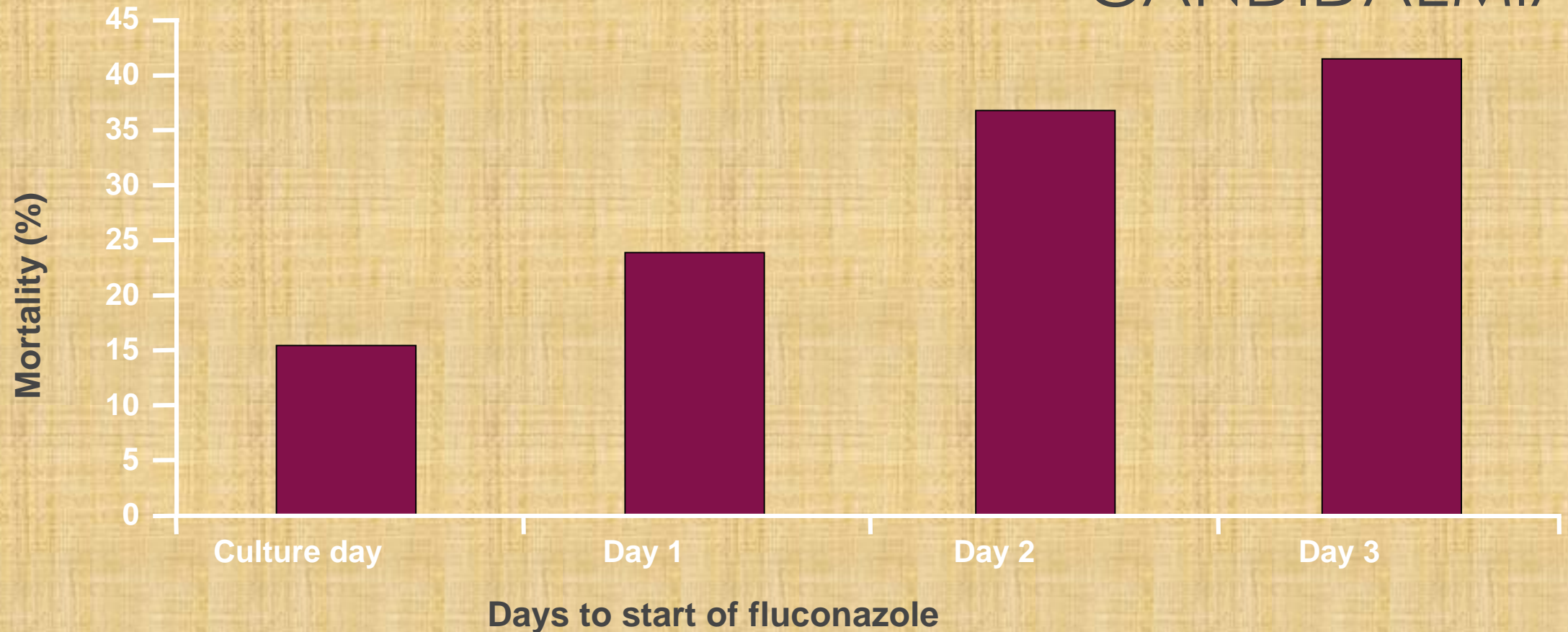


SPECIES SPECIFIC MORTALITY

Parameter	No. of episodes	Mortality (%)	p value*
Aetiological agent			
<i>C. albicans</i>	1,090	38.5	0.65
<i>C. glabrata</i>	269	45.0	0.02
<i>C. parapsilosis</i>	263	25.9	< 0.001
<i>C. tropicalis</i>	140	41.4	0.42
Underlying condition			
Surgery	892	35.3	0.26
Intensive care	791	42.4	0.02
Solid tumour	442	49.2	< 0.001
Haematological malignancy	247	44.9	0.03
HIV infection	61	23.4	0.03
Premature birth	123	26.8	0.02
Age group			
< 1 year	142	26.0	0.006
1–19 years	148	22.3	< 0.001
20–69 years	1,096	36.6	0.46
≥ 70 years	556	47.7	< 0.001
Total population	1,942	37.9	

*Calculated against overall crude mortality

IMPACT OF DELAYED TREATMENT ON MORTALITY IN 230 PATIENTS WITH CANDIDAEMIA



WHAT IS THE TREATMENT PRIOR TO SPECIES IDENTIFICATION

FLUCONAZOLE

OR

ECHINOCANDINS

Can we predict *C. glabrata* ?

Increasing incidence

Higher mortality

Non-susceptibility to fluconazole

THERAPEUTIC DECISIONS GUIDED BY IDSA AND ESCMID

- IDSA favours echinocandins in patients at risk of *C. glabrata*
 - Diabetes mellitus
 - Malignancy
 - Elderly
 - Recent azole use
- In addition, haemodynamically unstable patients should also be considered for echinocandins
- Therapy should be guided by species identification and antifungal susceptibility when available in patients who are clinically stable and whose follow up blood cultures are negative
- ESCMID favours echinocandins (A1) rather than fluconazole (C) for all patients

PATIENTS AND METHODS

- The objective of our study to find out whether rapid species identification had an impact on therapy. Period- January 2014 to May 2017
- Sepsityper[®]-MALDI-TOF-MS (Bruker Daltoniks, Germany) was carried out on blood culture broth within routine hours (Monday-Friday 9 AM to 4 PM)
- Antifungal susceptibility was carried out with the YeastOne Sensititer[®]
- Fluconazole and micafungin defined daily dosage- 200 mg and 100 mg respectively
- Cost of fluconazole and micafungin is £ 29.28 and £ 341 per DDD respectively

DEFINING APPROPRIATE TREATMENT

- Data were retrospectively analysed to determine appropriateness of therapy by matching prescribed treatment with identified species
- Fluconazole was considered appropriate/recommended for all species except *C. glabrata* and *C. krusei*
- Echinocandin was considered appropriate/recommended only for *C. glabrata* and *C. krusei*

RESULTS

- 66 candidaemic episodes (32 females, 34 males) yielded 67 *Candida* species
 - *C. albicans* 34
 - *C. glabrata* 17
 - *C. parapsilosis* 9
 - *C. krusei* 4
 - Others 3
- Age range – 27 to 93 years
- Risk factors: Age > 65 (n= 38), DM (n= 29), malignancy (n= 27), azole use (n= 3). Many patients had multiple risk factors.

RESULTS- SEPSITYPER[®]

- Total number of blood culture 66
- Out of hours/weekends 31/66
- Sepsityper[®] carried out 35/66
- Sepsityper[®] successful 22/35

- Overall, 22 episodes had rapid identification to species level, remaining 44 did not

RESULTS- NO SEPSITYPER[®]

- Total episodes 44
- Patients treated 40
 - Fluconazole 21
 - Echinocandin 19
- Risk factors present 37
- Only minority with risk factors had *C. glabrata* (n=12)

RESULTS- SEPSITYPER[®]

- Total episodes 22
- Patients treated 19
 - Fluconazole 15
 - Echinocandin 4
- Risk factors present 15
- Only minority with risk factors had *C. glabrata* (5)

RESULTS- TABLE 1

Parameters	Sepsityper [®] result available	Sepsityper [®] result not available	P value (Chi square test)
Total episodes	22	44	-
<i>C. albicans</i>	11	23	-
<i>C. glabrata</i>	5	12	-
<i>C. parapsilosis</i>	5	4	-
<i>C. krusei</i> and others	1 + 0	3 + 3	-
Risk factors for <i>C. glabrata</i>	15	37	0.13
Patients treated	19	40	-
Fluconazole	15	21	0.05
Echinocandin	4	19	0.05
Appropriateness of therapy	18 (94.7%)	23 (57.5%)	0.003

RESULTS- TABLE 1

Patient numbers	IDSA suggested risk factors (E, M, DM)	IDSA suggested treatment	Candida species by SEPSITYPER®	SEPSITYPER® guided treatment	Actual treatment (DDDs)	DDDs MCF (FLC) saved
3, 21	None	Fluconazole	<i>C. albicans</i>	Fluconazole	Fluconazole	0
31, 40, 43, 46, 50, 62, 66	≥ 1	Micafungin	<i>C. albicans</i>	Fluconazole	Fluconazole (46)	21
53	None	Fluconazole	<i>C. glabrata</i>	Micafungin	Micafungin (3)	-3 (8)
30, 34	≥ 1	Micafungin	<i>C. glabrata</i>	Micafungin	Micafungin (6)	0
20	≥ 1	Micafungin	<i>C. glabrata</i>	Micafungin	Fluconazole	0
57	None	Fluconazole	<i>C. parapsilosis</i>	Fluconazole	Fluconazole	0
8, 12, 35, 51	≥ 1	Micafungin	<i>C. parapsilosis</i>	Fluconazole	Fluconazole (22)	11
45	≥ 1	Micafungin	<i>C. krusei</i>	Micafungin	Micafungin (3)	0

RESULTS- COST SAVING COMPARED TO RISK FACTOR BASED THERAPEUTIC DECISION

- Cost estimated by presuming that echinocandin once commenced is given for 3 days
- DDDs of micafungin saved 29
 - Cost saving £ 9889
- DDS of fluconazole used 60
 - Expenditure £ 1756.80
- Net saving £ 8132.20
- Cost saving per treated patient £ 428.01
- (Staffing costs and cost of running the test not included)

DISCUSSION

- Overall numbers are small
- There is no clear favourite between fluconazole and echinocandin
 - IDSA favours risk-stratification for *C. glabrata* and favours echinocandins in critically ill patients
 - ESCMID favours echinocandin
 - European expert panel advises that therapy be tailored to individual circumstances
 - Anidulafungin may have a better response rate in patients with *C. albicans*
 - PATH registry showed that critically ill patients do better on fluconazole !
- Variables: Overall incidence of candidaemia, local guidelines, acquisition cost of antifungal agents, success rate of Sepsityper[®]
- Modest success rate of Sepsityper[®] in line with some published studies

CONCLUSIONS

- Sepsityper[®] contributes towards antifungal stewardship
- When Sepsityper[®] results were available, therapy was appropriate in an overwhelming majority of patients
- Where Sepsityper[®] was not available, therapeutic choice was random
- There is significant cost saving when compared against IDSA guided therapy (and even more when compared against ESCMID !)
- The success rate for rapid species identification is modest but may improve as technology becomes familiar
- Future updates of guidelines should include species identification as a determinant of therapy
- Clinical risk factor based prediction for *C. glabrata* is guesswork !



THANK YOU !