

Cost-of-Illness Analysis of Candidemia in Patients on the Intensive Care Unit

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Abstract (Updated Version)

Objectives Direct and indirect costs caused by candidemia in ICU patients are currently unknown. We performed an analysis comparing costs depending on the type of antifungal treatment.

Methods Comprehensive data of patients from the University Hospital of Cologne with at least one blood culture positive for *Candida* spp. while staying on the ICU between 2005 and 2010 were documented into a database provided by the Cologne Cohort of Neutropenic Patients (CoCoNut). Indirect costs caused by illness-conditioned disability and death before retirement age were calculated using the friction cost method. Analysis was split for patients treated with new antifungals (i.e. echinocandins, liposomal amphotericin B, or voriconazole) or conventional antifungals (i.e. amphotericin B deoxycholate or fluconazole).

Results Out of 147 identified patients, 45 received new and 66 conventional antifungals, and 36 patients were excluded from analysis (21 died within 96 hours after positive blood culture, seven were rated as contamination, eight patient files were missing). Both groups were well matched by age and baseline intubation status. Twenty-one (47%) and 11 (17%) patients had infections with *Candida non-albicans*. Mean APACHE IV score was 113 (105.7-121.2) vs. 96 (90.3-100.8, $P < 0.001$). Mean direct costs per patient in the new and the conventional antifungal groups were as follows: ICU treatment 24,922 € (95% CI: 17,054-31,789 €) vs. 17,971 € (95% CI: 13,203-22,740 €, $P = n.s.$), antifungal treatment 4,271 € (95% CI: 2,983-5,560 €) vs. 2,079 € (95% CI: 1,246-2,912 €, $P = 0.005$), total direct costs 41,060 € (95% CI: 30,184-51,935 €) vs. 28,885 € (95% CI: 22,116-35,654 €, $n.s.$), indirect costs per patient due to productivity loss of illness-related disability 1,202 € (95% CI: 474-1,930 €) vs. 1,087 € (95% CI: 570-1,604 €, $n.s.$), due to death before retirement age 1,047 € (95% CI: 236-1,858 €) vs. 1,309 € (95% CI: 584-2,034 €, $n.s.$), and combined overall costs 43,309 € (95% CI: 32,180-54,439 €) vs. 31,281 € (95% CI: 24,104-38,459 €, $n.s.$). Of the new and conventional antifungal group, 25 (56%) and 33 (50%) patients survived hospitalization, 20 (44%) and 22 (33%) patients survived one year after diagnosis.

Conclusion Our cost-of-illness analysis shows the high treatment costs of patients with candidemia. In our analysis, treatment with new antifungals was associated with higher costs. Although sicker patients were significantly more likely to receive new antifungals, outcomes were comparable to less sick patients treated with conventional antifungals.

Methods

Trial design

The objective of this retrospective chart review was to describe the direct & indirect costs of patients with candidemia on the ICU. Patient data were documented in our cohort database (CoCoNut) by a team of investigators. This trial was initiated and designed by the academic documents. The evaluation was performed by health economists.

Setting

Only cases contracting candidemia from 2005 until 2010 were included. We split the cases into group I and group II and compared new (i.e. echinocandins, liposomal amphotericin B, or voriconazole) with conventional (i.e. amphotericin B deoxycholate or fluconazole) antifungals. Furthermore we analysed severity of illness by using the APACHE IV, APS and PRISM score [figure 5], the species of *Candida* spp. [figure 4, 7 & 8] and the survival of hospitalization and the survival after one year [figure 6].

Inclusion criteria

- All cases of candidemia, defined as isolation of *Candida* spp. in one or more blood cultures
- Inpatient on the intensive care unit for at least 48 hours after diagnosis of candidemia

Exclusion criteria

- Patients with hematological malignancy
- Solid organ or stem cell transplantation recipients
- Patient did not receive antifungal treatment for at least 72 hours
- Absence of patient file or missing documentation

Cost definitions

The following direct cost factors were part of the evaluation using accounting factors derived from the German Diagnosis Related Group (G-DRG) Report Browser, Lauer-Taxe and the Gebührenordnung für Ärzte (GoÄ) [figure 9, 11 & 12]:

- Duration on ICU
- Mechanical ventilation
- Central venous catheters
- Duration on general ward
- Drug administration and preparation
- All anti-infective drugs (antifungals, antibacterials, antivirals)
- Renal replacement therapy
- Numbers of all diagnostic procedures

Following indirect costs factors were calculated using the friction cost method [figure 10 & 13]:

- Productivity loss due to illness-conditioned disability
- Productivity loss due to death before retirement age

Introduction Candidemia is an important factor of morbidity and mortality for patients on the Intensive Care Unit (ICU) (01). Patients contracting candidemia need prolonged antifungal treatment and are often treated as inpatients for more than 14 days (02). New treatment options allow improved treatment outcomes with low toxicity compared to traditional antifungals like fluconazole. The actual direct and indirect treatment costs caused by candidemia in German hospital with regards to modern and conventional antifungal agents were unknown. Primary aims of this study were:

- To describe the mean candidemia-related treatment cost parameters
- To analyze how the choice of initial antifungal agent and severity of illness influence the costs
- To determine the amount of indirect costs of overall costs.

We developed a retrospective chart review using our cohort database the Cologne Cohort of Neutropenic Patients (CoCoNut) and performed a health economic evaluation to answer the questions above.

References: (01) Bohme A., et al. 2009. Treatment of invasive fungal infections in cancer patients-recommendations of the Infectious Disease Working Party (AGIHO) of the German Society of Hematology and Oncology (DGHO). *Ann Hematol* 88: 97-110

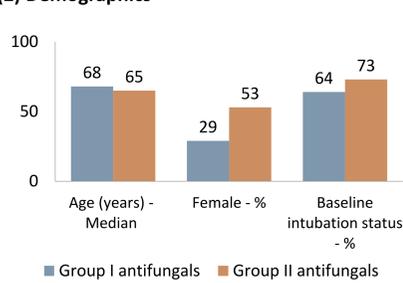
(02) Menzlin J., et al. 2009. Mortality, length of hospitalization, and costs associated with invasive fungal infections in high-risk patients. *Am J Health Syst Pharm* 66: 1711-7

Results I (group I antifungals n=45, group II antifungals n=66)

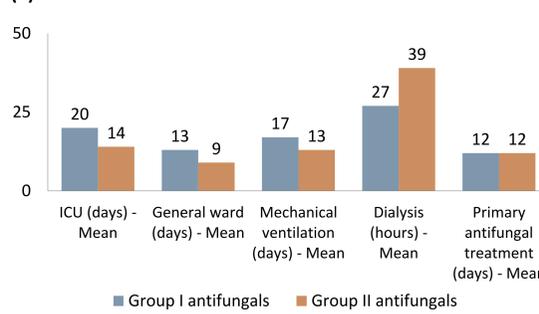
(1) Definition group I & II

Antifungal	Group I	Group II
Anidulafungin	14	-
Caspofungin	22	-
Voriconazol	4	-
Micafungin	4	-
Isavuconazol/ Caspofungin (study)	1	-
Fluconazol	-	64
Liposomal amphotericin B	-	2

(2) Demographics

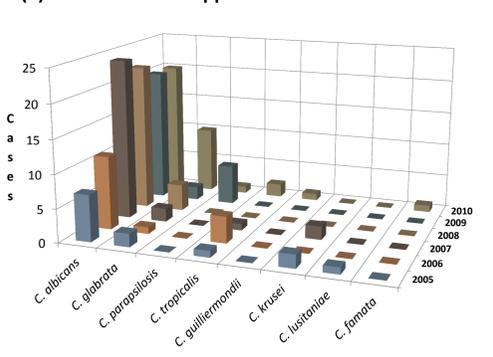


(3) Treatment times

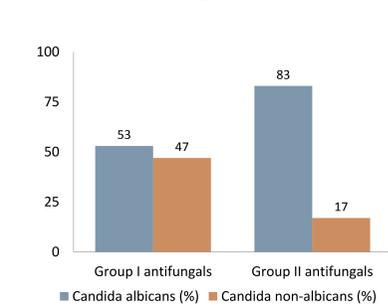


Results II (Candida spp.)

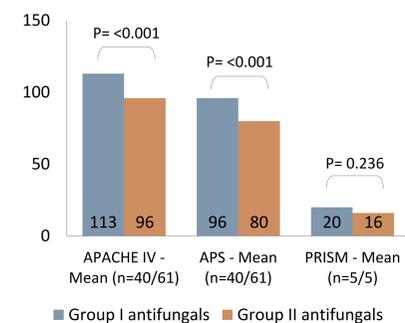
(7) Overall Candida spp.



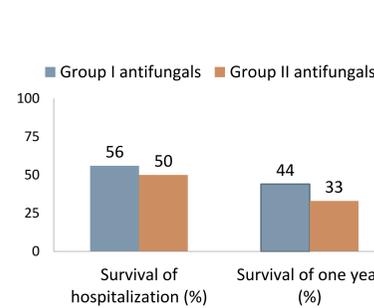
(4) Candida spp. per group



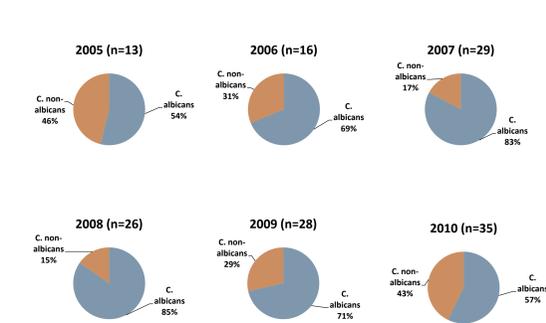
(5) Scores



(6) Survival

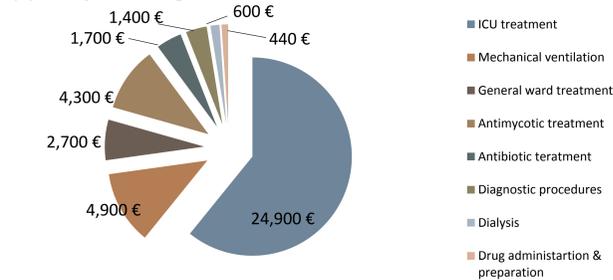


(8) Candida spp. per year (2005 - 2010)



Results III (direct & indirect costs group I antifungals)

(9) Group I antifungals, direct cost factors - Mean



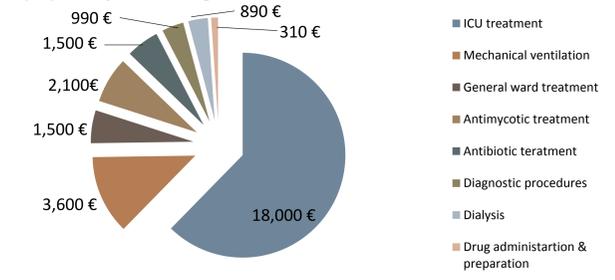
(10) Group I antifungals - indirect costs: productivity loss due to - Mean



(11) Overview direct & indirect cost factors

Cost parameter (€)	Group I (95% CI)	Group II (95% CI)	P
ICU treatment	24,920 (17,050-31,780)	17,970 (13,200-22,740)	n.s.
Mechanical ventilation	4,920 (3,220 - 6,610)	3,610 (2,550 - 4,680)	n.s.
General ward treatment	2,690 (1,520 - 3,860)	1,500 (870 - 2,130)	n.s.
Antifungal treatment	4,270 (2,980 - 5,560)	2,080 (1,250 - 2,910)	0.005
Antibiotic treatment	1,720 (1,240 - 2,200)	1,480 (1,120 - 1,840)	n.s.
CRP/PCT	700 (500 - 900)	520 (370 - 670)	n.s.
Radiology	580 (350 - 800)	350 (230 - 480)	n.s.
Microbiology	120 (70 - 170)	110 (80 - 140)	n.s.
Dialysis	600 (160 - 1,050)	890 (440 - 1,340)	n.s.
Central venous catheters	43 (30 - 56)	34 (27 - 42)	n.s.
Other drug application	390 (290 - 480)	270 (210 - 330)	0.043
Death before retirement age	1,050 (240 - 1860)	1,310 (580 - 2,030)	n.s.
Illness-related disability	1,200 (470 - 1,930)	1,090 (570 - 1,600)	n.s.
Overall direct costs	41,060 (30,180-51,940)	28,880 (22,120-35,650)	n.s.
Overall indirect costs	6,330 (4,590 - 8,060)	5,860 (4,170 - 7,550)	n.s.

(12) Group II antifungals, direct cost factors - Mean

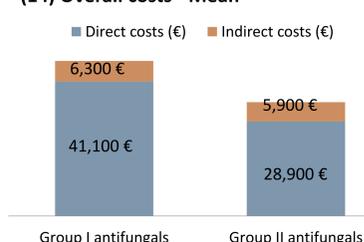


(13) Group II antifungals - indirect costs: productivity loss due to - Mean

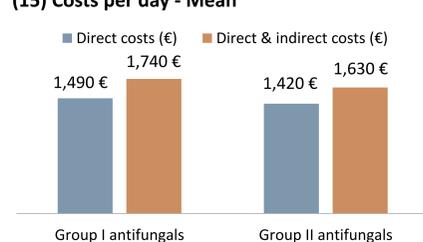


Results V (Overall costs/costs per day)

(14) Overall costs - Mean



(15) Costs per day - Mean



Conclusion

Our cost-of-illness analysis shows the high treatment costs of patients with candidemia. The main direct cost factors are:

- ICU treatment
- Mechanical ventilation
- Antifungal treatment

The treatment with new antifungals (group I) was associated with:

- Sicker patients
- Candida non-albicans* infections
- A trend towards higher direct & indirect costs
- A trend towards a higher rate of survival of hospitalization & survival after one year

Conflicts of interest

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