Impact of Testing Posaconazole Plasma Concentrations on Epidemiology of Antifungal Prophylaxis and Therapy in Patients with Hematologic Malignancies: Case-control Study

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Objectives: Therapeutic drug monitoring (TDM) has shown useful for oral antifungal agents in patients with hematologic malignancies. The effect of introduction of TDM on prescribing praxis is unknown. Posaconazole is a new triazole antifungal agent that has broad activity against pathogenic fungi and increasingly used for prophylaxis and treatment of invasive mould infections (IMI). Posaconazole is available as oral formulation only with varying absorption from the gastro-intestinal tract. We evaluated the impact of posaconazole TDM on antifungal prophylaxis and therapy.

Methods: Applied antifungal prophylaxis and therapy were assessed in patients with underlying hematologic diseases by conducting a prospective observational single-centre study at the Division of Hematology, Medical University of Graz, Austria, for seven months in 2010. To analyze the impact of PPC testing on antifungal prophylaxis and therapy results obtained were compared to a representative collective of patients assessed by the same investigators at the same institution over seven months in 2007 before testing of posaconazole plasma concentrations (PPCs) has been introduced.

Results: In 2010, 129/729 (18%) of cases with hematologic malignancies received systemic antifungal prophylaxis and therapy. Of those, fifty-seven percent received prophylactic, 44% empiric, 30% preemptive and 6% directed antifungal therapy. Main reasons for prophylaxis were neutropenia in AML patients (40/74; 54%), followed by GVHD (18/74; 24%) and allogeneic HSCT (16/74; 22%). Eleven out of 39 (28%) cases receiving preemptive therapy had clinical/radiological and microbiological evidence of IFI, 26/39 (67%) had clinical/radiological and 2/39 (5%) only microbiological evidence of IFI. In 2010 posaconazole was the most commonly administered antifungal agent followed by caspofungin which had been the leading antifungal agent at the study site in 2007. Posaconazole usage increased significantly after introduction of posaconazole TDM when compared to 2007 ($P < 0.05$). Concerning prescription rates of antifungal agents other than posaconazole no significant difference was found. In both study collectives (2007 and 2010) posaconazole was the primary antifungal agent used for prophylaxis, while itraconazole was used mainly in allogeneic HSCT. Demographic data, chemotherapeutic approach and antifungal modalities for cases receiving antifungal therapy in 2007 and 2010, respectively, are depicted in table 1.

	Antifungal therapy 2007 [b]	Antifungal therapy 2010
Number	**117**/690 (17%)	**129**/729 (18%)
Sex		
male	70/117 (60%)	85/129 (66%)
female	47/117 (40%)	44/129 (34%)
Age		
median age	51,2	53,5
Chemotherapy		
high dose [a]	55/117 (47%)	81/129 (63%)
palliative [a]	39/117 (33%)	17/129 (13%)
Rational for antifungal therapy		
directed	4/117 (4%)	8/129 (6%)
preemptive [a]	50/117 (43%)	39/129 (30%)
empiric [a]	31/117 (36%)	57/129 (44%)
prophylactic	52/117 (44%)	74/129 (57%)
Antifungal agents		
posaconazole [a]	38/117 (32%)	81/129 (63%)
caspofungin	72/117 (62%)	65/129 (50%)
lip amph B	7/117 (6%)	10/129 (8%)
voriconazole	14/117 (12%)	18/129 (14%)
itraconazole	15/117 (13%)	19/129 (15%)
fluconazole	7/117 (6%)	7/129 (5%)
anidulafungin	0	1/129 (1%)

Conclusion: We found a significant increase of posaconazole usage after introduction of posaconazole therapeutic drug monitoring (TDM). As TDM was available for posaconazole only, the feasibility of monitoring plasma concentrations may have influenced the selection of this antifungal agent in clinical routine.

Prescribing regimens did not change significantly and study collectives were comparable concerning prescription rates of antifungal agents other than posaconazole. We did, however, observe a significant increase in the empiric and decrease in the preemptive treatment approach in 2010 compared to 2007.

Table 1. Demographic data, and antifungal therapy among patients with hematologic malignancies.

Note: a Significant difference between 2007 and 2010 in patient collective with antifungal therapy $P < 0.05$
b Data from 2007 previously published (11)

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