Poster number:1278

Factors associated with low posaconazole plasma concentrations and impact of structured patient education: a cohort study

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Background: The objectives of the study were to analyze factors associated with low posaconazole plasma concentrations among patients with hematological malignancies receiving the suspension prophylactically and to evaluate the impact of a structured patient education on low levels.

Methods: The study was conducted from July 1st 2012 to June 1st 2013 at the Division of Hematology, Medical University of Graz, Austria. Steady sate PPCs measured on day 7 or later in patients with hematological malignancies and posaconazole prophylaxis were included. Concentrations above the target of 0.5 mg/L were defined as satisfactory and those below the target as low PPCs. In patients with low drug levels a structured personal on-site education concerning the intake of posaconazole was performed.

Risk Factors	Satisfactory PPCs (≥0.5 mg/L)					
	Univariate Analysis *			Multivariate Analysis		
	OR	95% CI	P Value	OR	95% CI	P Value
Age (per Year)	1.03	0.99 - 1.03	0.091			
Male Sex	0.09	0.03 - 0.31	<0.001			
BMI	1.10	1.04 - 1.17	0.002	1.09	1.04-1.15	0.001
Concomitant Systemic Corticosteroids	4.17	1.61 - 10.79	0.003	1.88	1.01-3.5	0.047
Concomitant T-cell Suppressants	54.25	6.58 – 447	<0.001	4.20	1.18-14.94	0.026
Diarrhoea	0.10	0.02 - 0.62	0.013	0.14	0.03-0.67	0.014
Mucositis	9.75	0.53 - 179	0.125			

Table 1: Univariate and Multivariate Analysis of Factors Associated with Satisfactory PPCs (≥0.5 mg/L). Odds ratios (OR), 95% Confidence Interval (CI) and P Value Displayed.

Results: 258 trough PPCs were measured in 65 patients (23 GVHD phase after haematopoietic stem cell transplantation, 42 neutropenia after induction therapy; median PPC 0.59 mg/L, IQR 0.25-0.92). 141/258 (55%) of PPCs were satisfactory, while 54 (21%) were below 0.2 mg/L. Diarrhea at the time the PPC was obtained remained an independent predictor of low PPCs in multivariable analysis (OR 0.14; 95% CI 0.03-0.67). Higher BMI, receipt of systemic corticosteroids and T-cell suppressant were predictors for satisfactory PPC´s. Initial steady state PPCs were sufficient in 29 (45%) and low in 36 (55%) patients. In 28/36 patients with low PPCs a personal on site education was performed. In 12/28 (42.9%) patients the personal on-site education led to sufficient levels, while in 16 (57.1%) the PPCs stayed below the target, although increasing from below 0.2 to above 0.3 in 6 of those patients.

Conclusion: Low PPCs were frequently observed and diarrhea remained the strongest predictor of low PPCs in multivariable analysis. A structured personal on site education led to sufficient levels in more than 40% of patients and may therefore be a promising tool to increase low PPCs.