

### Background

- ◆ The World Health Organization (WHO) provides tools for monitoring the use of anti-infective agents, including the use of defined daily dose (DDD) to monitor the consumption patterns of anti-infective agents
- ◆ In pediatrics, the use of DDD is controversial given the dose adjustments depending on the patient weight, and several authors recommend the use of the days of therapy (DOT)
- ◆ In Quebec, an antimicrobial stewardship program has been set up, due to the increased use of antifungals and the increased resistance to some of them, and in response to a governmental circular in the province.

### Objectives

- ◆ Calculate and discuss ratios of defined daily doses (DDD) and days of therapy (DOT) for antifungal agents per 1000 patient-days, and mean doses in mg/kg/day, in order to describe antifungal drugs use.

### Methods

- ◆ Design: Retrospective, cross-sectional, descriptive study realized for the financial years 2000-2001, 2005-2006, and 2010-2011.
- ◆ Setting: A mother-child University Hospital Center, with 400 pediatrics beds and 100 obstetrics-gynecology beds. Were included all inpatients who received an antifungal treatment. Were excluded prescriptions for emergency room and outpatients clinics, antibiotics and antivirals.
- ◆ Exposure: The seven authorized antifungals on the institution's local formulary were analyzed : Fluconazole, Posaconazole, Voriconazole, Caspofungin, Amphotericin B (Fungizone®, Abelcet®, Ambisome®).
- ◆ Main outcome measures: Calculation of DDD and DOT per 1000 patient-days, per antifungal and overall, and mean doses in mg/kg/day within five weight ranges.
- ◆ Statistical analysis: Pearson's correlation tests were conducted to measure the degree of correlation between DDD/1000 patient-days and DOT/1000 patient-days

### Results

**Table 1 - Defined daily doses per 1000 patient-days and days of therapy per 1000 patient-days profile**

Antifungals	2000-2001		2005-2006		2010-2011		Ratios	
	DDD <sup>a</sup>	DOT <sup>b</sup>	DDD <sup>a</sup>	DOT <sup>b</sup>	DDD <sup>a</sup>	DOT <sup>b</sup>	DDD <sup>a</sup> 2010-2011 / DDD <sup>a</sup> 2000-2001	DOT <sup>b</sup> 2010-2011 / DOT <sup>b</sup> 2000-2001
Abelcet®	1.9	3.6	0.9	1.9	NA	NA	-	-
Ambisome®	1.5	1.8	6.1	8.4	3.9	8.0	2.6	4.4
Fungizone®	2.2	3.8	0.1	0.7	0.3	1.5	0.14	0.39
Caspofungin	NA	NA	3.6	3.8	2.6	3.6	-	-
Fluconazole	9.2	13.6	22.4	30.5	31.0	48.5	3.37	3.57
Posaconazole	NA	NA	NA	NA	0.6	1.1	-	-
Voriconazole	NA	NA	4.4	5.0	5.5	5.1	-	-
<b>TOTAL</b>	<b>14.8</b>	<b>22.8</b>	<b>37.5</b>	<b>50.3</b>	<b>43.9</b>	<b>67.8</b>	<b>2.97</b>	<b>2.97</b>

<sup>a</sup>DDD per 1000 patient-days; <sup>b</sup>DOT per 1000 patient-days

DDD = defined daily dose; DOT = days of therapy; NA = Not Applicable (no antifungal use in this period)

- ◆ The correlation coefficients between the DDD/1000 patient-days and the DOT/1000 patient-days for the 2000-2001, 2005-2006 and 2010-2011 fiscal years were, respectively:  $r = 0.995$ ,  $p = 0.005$  ;  $r = 0.998$ ,  $p = 0.000$  ;  $r = 0.995$ ,  $p = 0.000$ .

**Table 2 - Profile of the mean dose in mg/kg/day per antifungal for the 2000-2001 and 2010-2011 fiscal years for five weight ranges**

Antifungals	Mean dose in mg/kg/day, for each range of weight									
	≤ 1.5 kg		> 1.5-5 kg		> 5-15 kg		> 15-30 kg		> 30 kg	
	2000-2001	2010-2011	2000-2001	2010-2011	2000-2001	2010-2011	2000-2001	2010-2011	2000-2001	2010-2011
Abelcet®	NA	NA	4.8	NA	4.8	NA	5.0	NA	5.0	NA
Ambisome®	NA	4.8	NA	5.6	4.9	4.7	5.0	4.8	4.6	5.2
Fungizone®	1.0	0.9	0.6	0.8	0.7	0.8	0.9	NA	1.0	1.0
Caspofungin	NA	NA	NA	2.0	NA	2.6	NA	NA	NA	1.1
Fluconazole	6.8	2.9	6.9	4.5	6.0	5.5	5.3	5.3	5.2	4.9
Posaconazole	NA	NA	NA	NA	NA	19.8	NA	12.1	NA	14.0
Voriconazole	NA	NA	NA	NA	NA	8.1	NA	15.5	NA	9.9

NA = Not Applicable (no antifungal use in this period)

### Conclusion

- ◆ The increase in antifungals use may be related to numerous factors: tertiarization of clientele (e.g. more hematology-oncology patients and bone marrow transplants, more neonatology patients with suspected or proven infections), changes in protocols (e.g. increase use of fluconazole for prophylaxis for high risk patients).
- ◆ Using DDD/1000 patient-days in pediatrics has some limitations. In fact, the defined daily dose does not take into account the range of doses per patient weight because it determines a dose in mg irrespective of the weight. A number of authors believe that using DOT/1000 patient-days is more appropriate, since it does not under/overestimate the use of antifungals, but describes actual use per unit of time. While our local study highlights a high correlation between the DDD/1000 patient-days and DOT/1000 patient-days ratios, we believe that DOT/1000 patient-days represent the relevant ratio to be used in pediatrics.
- ◆ With respect to the data in mg/kg per weight range, they can help identify changes in practice that are specific to a given weight group for a given drug. In this case, the limited number of molecules and their recent introduction, in some cases, do not allow such trending.
- ◆ It can be difficult to compare the use of anti-infective drugs among institutions, due to numerous factors, but it gives an idea about the consumption outside the studied center. Moreover, these ratios help to evaluate the antifungals use within a same institution. These data could be correlated among others with resistance patterns, in order to improve our daily practice concerning antifungal prescription.