

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 antivirals 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 antiviral agents per 1000 patient-days, and mean doses in mg/kg/day, in order to describe antiviral 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 antiviral treatment. Were excluded prescriptions for emergency room and outpatients clinics, antibiotics and antifungals.
- ◆ Exposure: The nine authorized antivirals on the institution's local formulary were analyzed : Oseltamivir, Acyclovir, Cidofovir, Famciclovir, Ganciclovir, Ribavirin, Valacyclovir, Valganciclovir, Foscarnet.
- ◆ Main outcome measures: Calculation of DDD and DOT per 1000 patient-days, per antiviral 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

Antivirals	2000-2001		2005-2006		2010-2011		Ratios	
	DDD ^a	DOT ^b	DDD ^a	DOT ^b	DDD ^a	DOT ^b	DDD ^a 2010-2011 / DDD ^a 2000-2001	DOT ^b 2010-2011 / DOT ^b 2000-2001
Acyclovir IV	3.7	16.0	4.4	21.3	2.7	17.0	0.73	1.06
Acyclovir PO	0.2	0.5	0.2	0.8	0.2	0.7	1	1.4
Cidofovir	NA	NA	1.0	0.2	2.1	0.4	-	-
Famciclovir	1.4	1.0	4.0	3.9	14.7	15.7	10.5	15.7
Foscarnet	NA	NA	1.4	3.0	0.2	0.1	-	-
Ganciclovir	2.3	4.0	1.7	4.0	0.9	1.9	0.4	0.5
Oseltamivir	NA	NA	0.1	0.1	0.7	1.2	-	-
Ribavirin	0.03	0.04	1.2	3.7	0.3	0.7	10	17.5
Valacyclovir	NA	NA	0.1	0.4	0.6	1.2	-	-
Valganciclovir	NA	NA	0.2	0.3	0.3	0.3	-	-
TOTAL	7.6	21.5	14.3	37.7	22.7	39.2	2.99	1.82

^aDDD per 1000 patient-days; ^bDOT per 1000 patient-days
DDD = defined daily dose; DOT = days of therapy; NA = Not Applicable (no antiviral use in this period)
IV = intravenous; PO = per os

- ◆ 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: $r = 0.902$, $p = 0.036$; $r = 0.789$, $p = 0.0073$; $r = 0.730$, $p = 0.017$.

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

Antivirals	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
Acyclovir IV	NA	40.4	46.7	54.9	38.9	38.4	39.3	29.7	27.0	20.8
Acyclovir PO	NA	NA	35.3	NA	74.5	59.1	51.8	42.4	32.9	59.5
Cidofovir	NA	NA	NA	NA	NA	NA	NA	NA	NA	3.0
Famciclovir	NA	NA	NA	NA	18.8	19.5	38.1	21.7	24.1	18.2
Foscarnet	NA	NA	NA	NA	NA	12.5	NA	NA	NA	177.2
Ganciclovir	NA	NA	9.7	9.9	10.4	NA	8.8	5.1	7.2	9.6
Oseltamivir	NA	NA	NA	6.8	NA	5.3	NA	4.4	NA	2.7
Ribavirin	NA	NA	NA	NA	NA	NA	NA	NA	14.8	41.7
Valacyclovir	NA	NA	NA	NA	NA	NA	NA	35.7	NA	30.1
Valganciclovir	NA	NA	NA	NA	NA	NA	NA	20.0	NA	23.6

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

Conclusion

- ◆ The increase in antivirals use may be related to numerous factors: tertiarization of clientele (e.g. more patients receiving immunosuppressive and/or immunomodulator treatments for chronic diseases), better diagnostic capacity to identify virus through PCR techniques and molecular virology.
- ◆ 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 antivirals, 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 antivirals use within a same institution. These data could be correlated among others with resistance patterns, in order to improve our daily practice concerning antiviral prescription.