Evaluation of the impact of intervention on improving aciclovir intravenous usage effectiveness in a Vietnamese tertiary referral hospital

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Introduction

In 2013, a significant increase of the consumption of aciclovir IV in previous months was noticed in a tertiary referral hospital. An investigation started in April 2013 in this hospital confirmed that aciclovir intravenous (IV) was indicated mainly in treatment of Herpes simplex encephalitis (HSE), an acute sporadic encephalitis which may lead to many serious consequences, event death [2]. Evidence-based guidelines for treatment of suspected HSE patients with aciclovir IV have been published in regions with high HSE prevalence, which aimed to improve cost-effectiveness of the therapy. Take into consideration that marked elevation of consumption seemed to be associated with inappropriate drug utilization, the hospital Drugs and Therapeutic Committee (DTC) developed interventions focusing on principal recommendations. As a successor, Guidelines for HSE Management and appropriate usage of intravenous aciclovir in hospital were established and then applied to clinical practice.

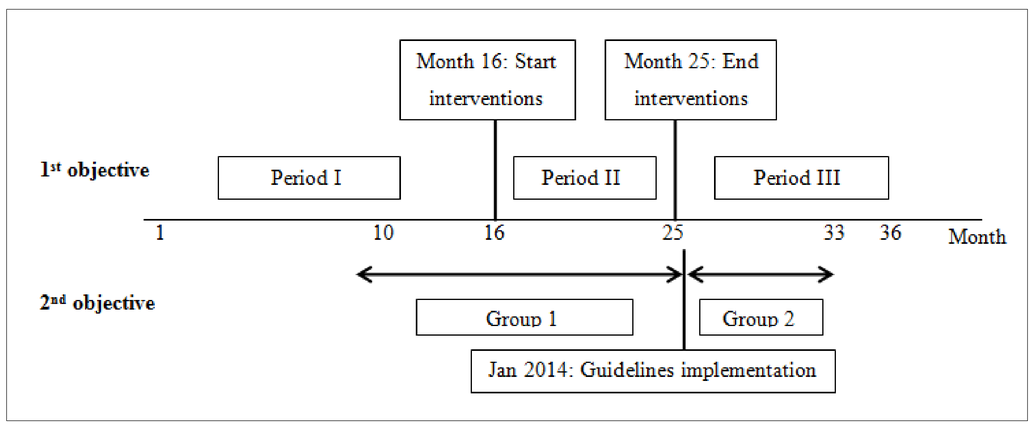
Objectives

This study was aimed at:

1. Evaluating the impact of DTC's intervention on aciclovir IV consumption
2. Evaluating the appropriateness in treatment of HSE by aciclovir IV in the hospital.

Methods

Drug usage and treatment information was collected retrospectively, using interrupted time series (ITS) analysis to detect change in consumption (change in level, change in slope, conservative and maximum prediction) [1, 3] between 3 periods of interventions and pre-post analysis to evaluate outcomes in the second objective.

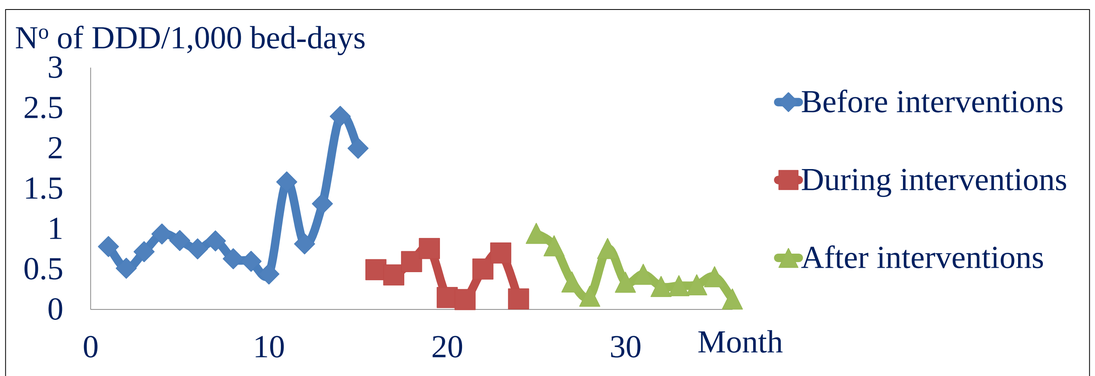


- In the 1st objective, ITS analysis was used to assess change in consumption through 3 periods:
Period I: Before interventions (January 2012 – March 2013)
Period II: During interventions (April 2012 – December 2013: investigation of drug use, scientific seminar, construction of the guidelines in the hospital)
Period III: After interventions (January 2014 – December 2014)
- In the 2nd objective, the official publication of the Guidelines in hospital (January 2014) divided the collected medical records into 2 groups to compare:
Group 1: Before guidelines implementation (aciclovir IV indication before January 2014)
Group 2: After guidelines implementation (aciclovir IV indication from January 2014).

Figure 1 – Study's design

Results

Impacts on aciclovir IV consumption



Parameters	Period I & II (i=1)*	p	Period II & III (i=2)*	p
Change of level immediately	-1.050	0.001	0.401	0.179
Change of slope (trend)	-0.109	0.003	-0.022	0.669
Conservative prediction	-1.234	0.000	-0.432	0.190
Maximum prediction	-1.909	0.000	-0.269	0.531

** Unit: number of Daily Defined Dose (DDD) per 1000 bed-days*

Figure 2 – Monthly consumption of aciclovir IV in each period of studied hospital

Use of aciclovir IV increased before interventions then decreased in level (change in level : -1.050 numbers of DDD/1000 bed-days, p=0.001), trend (change in slope: -0.109 numbers of DDD/1000 bed-days, p=0.003) and also in conservative and maximum prediction (p=0.000) during interventions. After interventions, no significant difference in changes comparing with intervention period was observed.

Results (cont.)

Impacts on HSE management and appropriate usage of aciclovir IV

Table 1 - Study population's characteristics

Characteristics	Group 1 (n=107), %/median	Group 2 (n=52), %/median	p	Characteristics	Group 1 (n=107), %	Group 2 (n=52), %	p
Demographic/biologic				**Initial symptoms suspected HSE**			
Female	60.7	48.1	0.130	**Fever**	58.9	82.7	0.003
Age (year)	46.0	37.0	0.085	**Headache**	77.6	61.5	0.034
Weigh (kg)	53.0	55.0	0.459	**Convulsion**	29.0	42.3	0.094
Renal insufficiency	11.5	3.8	0.144	**Confuse**	78.5	73.1	0.447
				Coma	21.5	42.3	0.006
Immuno-insufficiency	2.8	3.8	0.662	**Nausea/Vomit**	30.8	38.5	0.339
				Neck stiffness	40.2	38.5	0.835
PCR HSV-ADN (+)*	17.4	27.0	0.244	**Kernig's sign(+)**	9.3	5.8	0.549

** Patients with initial PCR implementation – Group 1: 69, group 2: 37.*

Of 159 selected medical records in hospital's database, 107 were in group 1 and 52 were in group 2. Patients characteristics of population such as age, sex, weigh, renal function, immunity, certain onset symptoms (convulsion, confuse…) and PCR test result positive with HSV DNA showed no significant difference between 2 groups. Despite minor differences in several aspects, such as fever (increase from 58.9% to 82.7%, p=0.003) or headache (decrease from 77.9% to 61.5%, p=0.034), there was no clear trend however.

Table 2 – Appropriateness of aciclovir IV treatment in each study group

Outcomes	Group 1 (n=107)		Group 2 (n=52)		p
	n	%/day	n	%/day	
Indication					
Aciclovir IV	46	43.0	28	53.8	0.198
Median of treatment delay (day)		13.0		7.0	0.000
Administration					
Dose*	54	94.7	19	86.4	0.340
Regimen**	89	85.6	42	80.8	0.440
Administration route	107	100.0	52	100.0	-
Solvent for dilution	107	100.0	52	100.0	-
Final aciclovir concentration	105	98.1	52	100.0	1.000
Infusion rate	105	98.1	49	94.2	0.331
Treatment monitoring					
Treatment monitoring by PCR test	63	58.9	35	67.3	0.305
Appropriate stop of aciclovir IV	28	26.2	25	48.1	0.006
Aciclovir treatment days (median)		10.0		5.5	0.000
Irrational treatment days (median)		5.5		1.0	0.000
Length of hospitalization days (median)		23.0		12.0	0.000

** Patients with available weight: Group 1: 57; Group 2: 22.*
*** Patients with available renal function test result: Group 1: 104; Group 2: 52.*

Appropriate aciclovir indication was observed on 43.0% and 53.8% of patients in group 1 and group 2 respectively (p=0.198). High compliance in aciclovir IV administration in both groups was observed (>80% in appropriate dose, regimen and infusion preparation and 100% in administration route and solvent for dilution). Indication of HSV-DNA PRC test for treatment monitoring was showed no difference (58.9% vs. 67.3%, p=0.305). However, appropriateness in stop of aciclovir was improved in which, hospitalized and delayed time decreased 7.0 days and 6.0 days respectively. Time of aciclovir IV treatment and time of irrational use dropped significantly by 4.5 days after the guidelines release (p=0.000).

Conclusion

The high aciclovir IV consumption before interventions decreased in both level and trend during interventions. Intervention of DTC had significant impact on the appropriate use of aciclovir IV in HSE treatment in hospitalized patients. Further effort needs put on these activities to maintain this achievement.

References

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