

# The Discussion of Peritoneal Dialysis Patients Taking Proper Portion of Valacyclovir

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**Abstract:** Dialysis patients have risk in Zoster virus because of low immune. Valacyclovir, used for *Zoster virus*, is digested in kidney and it has side effect of nerve virus on patients with malfunction kidneys. This article reviews 8 dialysis cases and discusses the proper Valacyclovir portion for peritoneal dialysis patients.

**Key words:** Herpes zoster, valacyclovir, peritoneal dialysis, health education.

## 1. Introduction

Taiwan has become an aged society, and so have the dialysis patients. Among dialysis populations, peritoneal dialysis exceeds 10%. These patients have low immune ability and are easy to get virus. Zosters are often seen on dialysis patients, it caused great discomfort to the patient. When we give them Valacyclovir to cure, as their digestion speed is slower, they have side effect due to high portion of medicine. Therefore, we need to think about the proper Valacyclovir portion for dialysis patients and reach balance of toxicity and efficacy.

## 2. Varicella Zoster and Its Medicine

People get Varicella zoster because they have reaction to *Varicella zoster virus*. The patients who get VZV for the first time might have varicella. When the Varicellas are gone, the virus may hide in the nerves. When the immune declines the virus will

revive and cause Varicella zoster throughout the body. The causes to revive the virus include aging, low immune and fatigue. It is not clear how virus hides in body and revive [1].

When it occurs, the patients have pain on nerves and get skin rash. Normally, new skin rash stop growing in 7 days. Healthy people recover in 2 weeks [1]. Valacyclovir (product name): Valtex 500 mg/tab, is anti-virus medicine (L-Valyl ester of acyclovir) and will turn into acyclovir and valine quickly. Acyclovir is specially used to control virus and it can fight against HSV (*Herpes simplex virus*) first type and second type and VZV. When Acyclovir becomes active triphosphate, it can control the DNA combination of *Zoster virus*. Valacyclovir can produce 54% bioavailability of acyclovir and the percentage is higher than the of 10%-20% of oral acyclovir [2]

The dosage: About the treatment of zoster virus, the portion for adults is 1,000 mg, 3 times a day for 7 days. For people with malfunction kidney and the elderly, the acyclovir will be exhausted through the kidney. For the final stage of kidney cancer, the

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average exhaust period for acyclovir, which the patients have, is 14 hours. It takes 3 hours for patients with normal kidney. For patients whose kidney has malfunction, if the creatinine rate is between 15 and 30 cc/min, the dosage will be 1,000 mg, twice a day. If the rate is over 15 mL/min, the dosage will be 1,000 mg, once a day [2].

These two kinds of chronicle kidney patients have risks in having side effect, including headache, nausea (commonly seen), dizziness, illusion, loss of consciousness, vomiting stomachache and kidney disorder (rarely seen). We should supervise these side effects closely. It is reversible when we stop giving medicine [2].

Treatment: When excessive symptoms appear, the blood dialysis can be used to remove the acyclovir in blood [2].

### 3. Related Reference Discussion

#### 3.1 Peritoneal Dialysis Patients Are High Risk in Herpes Zoster

Lin et al. [3] traced the patients over 18th who had herpes zoster through the database from Taiwanese Health Insurance. They divided patients into five categories: normal people, CKD (chronic kidney disease), End stage renal disease (which includes PD (peritoneal dialysis) and HD (hemodialysis)) and RT (renal transplantation). Each has its occurrence percentage. The data contain 79,581 normal patients, 15,802 CKD patients, 3,964 HD patients, 317 PD patients and 159 RT patients. They use cohort study to analyze the data. The data of community population indicated:

(1) PD and RT patients are younger than others.

(2) In terms of common symptoms, the DM (diabetes mellitus) rate of HD patients is highest (52.4%). Hypertention rates of RT and HD patients are highest. SLE (Systemic Lupus Erythematosus) rate of PD patients is highest (4.7%). The rate of taking immune control of RT patients is highest (82.4%). The research indicates:

(a) When we use Kaplan-Meier approach, the disease-free rate of PD and RT patients decreases with time more clearly than other teams.

(b) In terms of occurrence density (100 people per year), PD patients have highest density (3.82), close to RT patients (3.7), and higher than HD patients (1.7).

(c) Using multivariate regression analyses, we found that the risk of developing zoster is highest on RT patients (HR 8.46; 95% CI 5.85-12.2). The risk of PD patients (HR 3.61; 95% CI 2.69-4.83) is higher than that of HD patients (HR 1.35; 95% CI 1.18-1.55;  $p < 0.0001$ ).

The author also mentioned the errors of International Classification of Disease, and the use of traditional health care, which are causes of limitation. They made the results with difference.

#### 3.2 Literature Review: Small Samples

Izzedine et al. [4] suggested that the patient's half-life period (15 hours) was similar to the package insert. The average patients, CAPD (Continuous Ambulatory Peritoneal Dialysis = PD), were switched with 4 times a day. It could be found that the removal rate of the drug was 1%. Therefore, Valacyclovir 500 mg was used to avoid side effect in 48 hours and also the acyclovir was soluble in water but not easy to enter the peritoneum. As a result, the most effective side effect treatment is HD.

Pipili et al. [5] report states that although these two pharmacodynamics reports indicated CAPD patients mediation half-life period was 14 to 20 hours, Valacyclovir 500 mg was recommended to use for 24 hours.

Haudhari and Ginn [6] pointed out that VAN (Valacyclovir-associated neurotoxicity) appeared that after 48 to 72 hours taking the medicine, and then the patients could be eased within 4 to 14 days. In the article, it mentioned that to adjust the drug dose should be in accordance with the degree of renal failure and dialysis, but it did not recommend any suitable dose.

**Table 1 Literature review of small sample.**

Year	Number of cases	Age	Rest function of kidney	Dosage	Time to occur side effect	Medical half-life	Treatment	Revised dosage
2001	1	60	6 mL/min	500 mg/daily	3 days	15 hours	2 L liquid change, remain 4 times 2 L more at night	500 mg/QOD
2013	1	72	N	3 g/daily	1 day	N	2 L liquid change, remain 6 times instead of 4 times	Non medication
2014	1	66	6 mL/dL	1,000 mg/daily	2~3 days	N	Water supply liquid change remains	500 mg/daily for 7 days

N:no mention.

**Table 2 Date of 8 patients in our hospital.**

No.	Age	Gender	PD period	Residual renal function	Portion	Time to occur side effect	Side effects
1	63	M	10 y	N	500 mg QD	3 days	Nonsense, hand and foot waving
2	55	M	3 y	N	500 mg Q8H	2 days	Emotional excitement, restlessness
3	41	F	9 y	N	1,000 mg QD	3 days	Nonsense
4	46	M	3 y	N	unclear	unclear	General weakness, irritability, forced shaking, nonsense
5	61	F	12 y	N	500 mg QD	3 days	Lisp
6	60	M	4 y	N	500 mg BID	1.5 days	Speech is not clear, weak and involuntary trembling, appear illusion
7	54	F	2 y	Urine: 300 mL/day; CCr: 0.5 mL/min.	500 mg BID	1.5 days	Hands and feet weakness, fluttering, eyes open, chest tightness
8	64	M	4 y	Urine: 520 mL/day; CCr: 0.7 mL/min.	500 mg QD	2 days	Drowsiness, feeling unable to self-control, irritability, nonsense

N: Urine: 0 mL/day and CCr: 0 mL/min.

### 3.3. In the Aspect of Pharmacokinetics (PK)

Stathouloupoulou [7] added 12 peritoneal dialysis patients in the 2002 report. They monitored the patients for 24 hours after taking Valacyclovir. Half of the patients are male. The average age is 58.66 years old. Most of them have no urine. The effective treatment is taking HZV and VZV of 4~8  $\mu\text{mol/L}$ , 12 patients took 500 mg/24 hours with the mean of 8.1 and 95% CI 5.88~10.32. The above information is compiled in Table 1.

Therefore, we suggest the portion: 250-500 mg/24 hours. It maintains the effect and reduces the related nerve poison.

According to Table 2, Case 4 brain CT in ER in this hospital is normal, but they often take prescription outside the hospital, they already forgot the portion they took, and neither did their family. Case 8 has TCC history. In the reference, for dialysis patient whose CCR is less than 10 mL/min, we suggest that

they take 500 mg Valacyclovir. However, in Ref. [3] and the cases in our hospital, some patients' Kt/V match the standard of dialysis, and still go to the toilet, they still have side effect seriously with 500 mg portion. The solution to this includes stopping medicine, reduction of medicine, increase of liquid changes and timely blood dialysis and all of them speed up the recovery.

## 4. Conclusions

In terms of bothering herpes zoster, the safety of medication needs extra attention of medical care employee. They should remind patients and their family to go to the hospital when they find side effect. If they can tell the doctor if the patient has urine or not and his or her data of Kt/V, the doctor can prescribe the medicine accordingly. Drugs cause side effects that make the family think that the patient is mentally abnormal, even family want to transfer patients to

psychiatric clinics. About the limitation, due to the lack of cases, related PK numbers and other information, we can only assume from the aftermath upon taking medication. In the package insert, the PK traits are not proportional to the portion taken. Therefore, for peritoneal patients, we think 500 mg/48 hours is the saves. We also want to remind pharmaceuticals to revise the portion taken by patients, so that the doctor may judge the use. We hope that future researchers can collect more patients, as well as pharmaceutical companies can include peritoneal dialysis patients when conducting drug experiments. This will make it convenient to investigate whether the dose should be modified.

## References

- [1] Hamborsky, J. 2015. "Epidemiology and Prevention of Vaccine-Preventable Diseases 13." In *Washington D.C. Public Health Foundation*, pp. 353-74.
- [2] Mayo Foundation for Medical Education and Research (MFMER). 1988. "Drugs and Supplements: Valacyclovir (Oral Route)." Accessed: March 01, 2017. <https://www.mayoclinic.org/drugs-supplements/valacyclovir-oral-route/proper-use/drg-20066635..>
- [3] Lin, S. Y., Liu, J. H., Lin, C. L., Tsai, I. J., Chen, P. C., Chung, C. J., et al. 2012. "A Comparison of Herpes Zoster Incidence across the Spectrum of Chronic Kidney Disease, Dialysis and Transplantation." *American Journal of Nephrology* 36 (1): 27-33.
- [4] Izzedine, H., Mercadal, L., Aymard, G., Launay-Vacher, V., Martinez, V., Issad, B., and Deray, G. 2001. "Neurotoxicity of Valacyclovir in Peritoneal Dialysis: A Pharmacokinetic Study." *American Journal of Nephrology* 21 (2): 162-4.
- [5] Pipili, C., Pantelias, K., Deda, E., Tsiamalos, P., Kostis, E., and Grapsa, E. 2013. "Intensification of Peritoneal Dialysis Improves Valacyclovir Neurotoxicity." *Renal Failure* 35 (2): 289-90.
- [6] Haudhari, D., and Ginn, D. 2014. "Valacyclovir-Associated Neurotoxicity in Peritoneal Dialysis Patients." *American journal of therapeutics* 21(6):215-17.
- [7] Stathouloupoulou, F., Dhillon, S., Thodis, H., Stathakis, C., and Vargemezis, V. 2002. "Evaluation of Valaciclovir Dosage Reduction in Continuous Ambulatory Peritoneal Dialysis Patients." *Nephron* 91 (1): 164-6.