Sürekli Ayaktan Periton Diyalizi Hastasında Tek Doz Asiklovir Kullanımına Bağlı Delirium: Olgu Sunumu

Delirium With a Single Dosage of Acyclovir in a Continuous Ambulatory Peritoneal Dialysis Patient: Case Report

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ÖZET

Asiklovirin farmakokinetiği kronik böbrek hastalığında değişir ve azalmış renal atılımdan dolayı ciddi yan etkiler görülebilir. Baş ağrısından komaya kadar geniş bir yelpazede nörolojik yan etkiler görülebilir. Tek doz 400 mg asiklovir alan bir sürekli ayaktan periton diyalizi (SAPD) hastasında gelişen deliryum olgusu sunuldu.

Anahtar sözcükler: asiklovir, toksisite, deliryum, SAPD

ABSTRACT

The pharmacokinetics of acyclovir changes in chronic renal failure (CRF). Because of decreased renal clearance, serious adverse effects may be seen. Neurological adverse effects may be seen in a wide spectrum, from headache to coma. Delirium in a continuous ambulatory peritoneal dialysis (CAPD) patient who received a single dose of 400 mg acyclovir was presented.

Keywords: acyclovir, toxicity, delirium, CAPD

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Introduction

Acyclovir, an antiviral agent, is an effective choice particularly for the treatment of herpes virus and varicella zoster virus infections. However, the pharmacokinetics of the drug changes in chronic renal failure (CRF) (1), and severe adverse reactions may be seen. A clinical situation of these adverse reactions is neurotoxicity. The clearance of acyclovir from the body is directly related to the decrease in body-surface-area corrected creatinine clearance. However, the clearance of acyclovir is usually greater than predicted because of its renal tubular secretion and the dosage must be modified in response to the degree of impairment in renal failure (2).

Although acyclovir is removed by hemodialysis, and the manufacturer recommends receiving a supplemental oral dosage of the drug after each period of hemodialysis for patients undergoing hemodialysis, the serious neurological adverse effects such as agitation, delirium, and coma may be seen like in our patient. The treatment of this adverse effect is cessation of the drug immediately and removal of acyclovir by hemodialysis if it is necessary. In this article, we aimed to present a case of delirium in a patient undergoing continuos peritoneal dialysis who received a single dose of 400 mg acyclovir.

Case Report

Twenty-seven-year-old male patient who had had renal failure for 6 years and been undergoing CAPD for 18 months was hospitalized with delirium.

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Delirium began after administration of a single dosage of 400 mg acyclovir peroral, which was given for Zona-Zoster infection. In the neurological examination there was delirium and in physical examination there was no important finding. In the laboratory findings; Hbg: 10.3 g/dL, Hct: 30%, platelet: 379 K/uL, WBC: 7800 K/UL, urea: 150 mg/dL, creatinine: 11.9 mg/dL, glucose: 87 mg/dL, Na: 137 mmol/L, K: 5.09 mmol/L, Cl: 105 mmol/L, P: 6.1 mg/dL, TP: 7 g/dL, albumin: 3.5 g/dL, ALT: 17 U/L, AST: 17 U/L, total bilirubin: 0.5 mg/dL, LDH: 206 U/L, CK: 40 U/L, cholesterol: 293 mg/dL, uric acid: 7.8 mg/dL, ferritin: 179 ng/mL, HbsAg (-), anti-HBs: >1000, antiHCV (-). In the PET test: CR: 0.65 (low-mid), glucose: 0.38 (mid high), Kt/V: 1.9. Cerebrospinal fluid (CSF) was detected to search a central nervous system infection but the results were negative. There was no pathological finding in cranial magnetic resonance imaging (MRI). The patient had no fever and leukocytosis, so acyclovir toxicity was thought and the drug was discontinued. During the follow-up period delirium situation of the patient resolved rapidly. Hemodialysis was not necessary and the patient was discharged from the hospital with normal cerebral and physical functions.

Discussion

Acyclovir is a synthetic purine nucleoside analog derived from guanine, which has in vitro and in vivo inhibitory activity against herpes simplex virus types 1 (HSV-1), 2 (HSV-2), and varicella-zoster virus (VZV) (1). This inhibitory activity is highly selective because of its affinity for the viral thymidine kinase (TK) enzyme that is encoded by HSV and VZV, and converts acyclovir into acyclovir monophosphate. Then the monophosphate is converted into diphosphate by cellular guanylate kinase and into triphosphate by cellular enzymes. This active form of acyclovir (acyclovir triphosphate) shows its effect by stopping replication of viral DNA in vitro (1). In clinical practice acyclovir is used for the treatment of HSV (HSV-1, HSV-2) infections in immunocompromised patients, initial episodes of herpes genitalis, HSV encephalitis, neonatal HSV infections and VZV infections in immunocompromised patients. Transient elevation of serum creatinine and/or BUN, nausea, vomiting, itching, rash, hives, and elevation of transaminases are frequent adverse effects of acyclovir. (1).

Headache is the most common neurological adverse reaction of oral acyclovir and occurs in approximately 2% of patients, particularly in patients who receive acyclovir for chronic suppressive therapy. Agitation, ataxia, coma, confusion, behavior changes, decreased consciousness, delirium, dizziness, encephalopathy, hallucinations, obtundation, paresthesia, psychosis, seizures, somnolence, and tremors have been reported during oral or IV acyclovir therapy, and these effects may be life treathening, especially in patients with renal failure. This kind of neurological adverse reactions have occured in about 1% of patients receiving IV acyclovir (2).

Although neurotoxicity associated with acyclovir is infrequently reported (3), when a patient with renal failure taking acyclovir is referred to hospital by neurological symptoms, acyclovir neurotoxicity should be thought and the treatment should not be delayed. For our patient, cranial MRI, and CSF analysis were normal, and also there were no symptoms of encephalitis such as meningeal irritation, focal neurological findings, and no findings of infection like fever, and leukocytosis, so, first of all, we thought acyclovir toxicity. The rapid recovery after cessation of drug supported diagnosis.

The half-life of acyclovir is greatly prolonged in patients with end-stage renal disease due to its elimination by kidneys and the dosage must be modified in response to the degree of renal failure [adjusted

Table I. Dosage adjustments for patients with renal impairment

Creatinine Clearance (mL/min/1.73 m^2)	Percent of Recommended Dose	Dosing Interval (hours)
>50	100%	8
25-50	100%	12
10-25	100%	24
0-10	50%	24

according to the creatinine clearance (CrCl)] (1-4). The dosage adjustments for patients with renal impairment are shown in Table 1 (1). Although acyclovir and its analogues are usually safe drugs they may be cause of serious neurologic effects in patients with renal failure. Almond et al calculated the half-life of acyclovir as 20.2 +/- 1.76 hours and 51 +/- 11.5% of the drug is eliminated by a dialysis period of 4-5 hours in a study made in 7 patients who are undergoing hemodialysis, and suggest that the recommended dose of 800 mg twice/day is too high (4).

Although in this study and other studies high dosage and prolonged half life of acyclovir had been accused, for our patient, a serious adverse effect was seen with a first single dosage of acyclovir (400 mg peroral). So it is important to be more careful during administration of the drug in patients with ESRD.

Severe central nervous system adverse effects like agitation, delirium, coma may be seen due to acyclovir in patients with chronic renal failure, especially who are undergoing hemodialysis or peritoneal dialysis just like our patient and most of them resolve after cessation of drug and removing the drug with hemodialysis (5). But during the follow-up period our patient did not need hemodialysis. Although acyclovir is removed by hemodialysis and the manifacturer recommends a supplemental oral dose just after each period of hemodialysis, especially because of the neurologic adverse effects, it should be used with caution in patients with end-stage renal disease. In patients with renal failure, these side effects are generally reversible with cessation of drug and hemodialysis but sometimes may be dangerous, life treathening, and also it may cause death (6). Adjusting of the dosage is very important but it does not guaranty sparing from adverse effects.

Neurotoxicity should be considered in patients with renal failure who have been treated with acyclovir for viral infections such as HSV1-2 or VZV. Other causes of neurologic symptoms must be evaluated rapidly and the drug should be discontinued immediately and if it is necessary hemodialysis should be thought. Hemodialysis is the preferred treatment for rapid removal of drug.

Acyclovir is an effective choice for treatment of HSV and VZV infections in patients with end-stage renal disease especially who are undergoing hemodialysis or peritoneal dialysis but the practitioners should be allert against its neurotoxicity and use it with caution.

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