Swine Influenza
Nephrologist's Perspective

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Swine influenza is caused by influenza A virus (H1N1) and is normally found in pigs. It is believed that antigenic shift has taken place in the virus, creating a new strain that has enabled the virus to infect humans and spread from person to person, leading to a pandemic.[1] Since immunocompromised patients are more prone to develop severe manifestations of this virus, nephrologists around the world need to be more cautious. Kidney transplant recipients and patients with chronic kidney disease could be a highly susceptible group. Preventive measures for community such as frequent hand washing are also applicable to this group. Social distancing is another tactic. Also, the two neuraminidase inhibitors, oseltamivir and zanamivir, are active against H1N1 strains, which would be prescribed to patients with a kidney allograft and those with chronic kidney disease in the pandemic situation. Thus, nephrologists and healthcare personnel need to know their dosage adjustments.

Oseltamivir is recommended by the Center for Disease Control and Prevention for both treatment and prophylaxis of H1N1 infection. The recommended dose in adults with normal kidney function is 75 mg, twice a day for 5 days, for curative treatment and 75 mg, once a day, for prevention. It is converted by hepatic esterases to its active metabolite, oseltamivir carboxylate. Neither oseltamivir nor oseltamivir carboxylate are substrates for, or inhibitors of, cytochrome P450 isoforms. Renal elimination of oseltamivir carboxylate accounts for more than 99% of the administered dose. Renal clearance occurs through both glomerular filtration and tubular secretion.[2] Therefore, it is necessary to adjust dosage in patients with kidney dysfunction (Table).

An open-label multiple-dose study was done to assess the pharmacokinetics and tolerability of oseltamivir in patients with end-stage renal failure undergoing maintenance hemodialysis and continuous ambulatory peritoneal dialysis (CAPD).[3] The patients received 30 mg of oral oseltamivir suspension over 6.5 weeks. The patients on hemodialysis received 9 doses given 1 hour after the completion of alternate hemodialysis sessions (3 times a week). The patients on CAPD received 6 doses given once weekly after a dialysis solution exchange. In the patients on hemodialysis, the peak plasma concentrations for oseltamivir carboxylate after single and repeated dosing were 943 ng/mL and 1120 ng/mL, respectively. The mean area under curve was 31 600 ng.h/mL for days 1 to 5. Similarly, in patients on CAPD, the mean peak plasma concentrations after the first and sixth doses were 885 ng/mL and 849 ng/mL, respectively. The mean area under curve values for days 1 to 6

Therapeutic Dosage Schedule of Oseltamivir and Zanamivir in Patients With Kidney Failure and in Kidney Transplant Recipients

Patient Status	Oseltamivir	Zanamivir
Glomerular filtration rate, mL/min		
> 30	75 mg twice daily	10 mg twice daily
15 to 30	75 mg once a day	10 mg twice daily
Hemodialysis	30 mg after alternate dialysis sessions	10 mg twice daily
Peritoneal dialysis	30 mg once a week after dialysis solution exchange	10 mg twice daily
Kidney transplant	According to glomerular filtration rate	10 mg twice daily

was 33 400 ng.h/mL, which persisted for 48 days. Oseltamivir was well tolerated in both of the patient groups. The researchers concluded that the 30-mg dose of oseltamivir given once weekly in patients on CAPD or after alternate sessions in patients on hemodialysis provides sufficient exposure to oseltamivir carboxylate to allow safe and effective anti-influenza treatment and prophylaxis.[3] In kidney transplant patients, oseltamivir has no interactions with cyclosporine, tacrolimus, mycophenolate mofetil, and steroids, and it can be safely used. The drug is usually well tolerated; however, side effects like dizziness and gastrointestinal disorder may be seen at higher doses.

Zanamivir is another neuraminidase inhibitor. The recommended dosage of zanamivir by oral inhalation is 10 mg, twice a day, for 5 days. Less than 20% of the dose is absorbed systemically, and 90% of the absorbed drug is excreted unchanged in urine. There are no data on the pharmacokinetics of zanamivir after oral inhalation in patients with kidney failure. However, given the good tolerance after daily intravenous dosages as high as 1200 mg and the limited systemic absorption after oral inhalation, the increased drug exposure for patients with kidney failure is not considered clinically significant. Therefore, for orally inhaled zanamivir, no dosage adjustment is required in patients with kidney impairment. Because the drug is almost not absorbed, it is unlikely to be removed by hemodialysis to a significant extent. It may thus be administered before or after the session on hemodialysis without significant influence on its pharmacokinetics. Side effects include headache, cough and nasal and throat discomfort.[4]

To conclude, with the pandemic of H1N1, nephrologists are bound to encounter this infection in their set of patients. Adequate preventive measures should be instituted before the infection sets in. A thorough knowledge of dosing schedule of oseltamivir and zanamivir is a must to avoid undesirable side effects.

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