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Acyclovir induced hypokalemia

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Intravenous (IV) acyclovir, a mainstay antiviral for herpesviruses, may cause crystalluria and lead to acute kidney injury.¹ Acyclovir has been associated with lower levels of potassium in canines but acyclovir induced hypokalemia has been reported only once in humans as part of a large adverse drug reaction monitoring program.^{2,3} A patient with a potassium of 2.8 mEq/L (2.8 mmol/L) following treatment with IV acyclovir prompted us to evaluate whether acyclovir poses an increased risk of hypokalemia.

We used the Cleveland VA Quality Improvement and Clinical Research Database to evaluate the rate of hypokalemia (potassium < 3.5 mEq/L) in the four days after receipt of IV acyclovir for all patients treated between January 1, 2002 and January 1, 2012. As a comparison, we evaluated the rate of hypokalemia in the 14 days after admission for all subjects not treated with acyclovir who were admitted to the same ward within 30 days of a patient who received IV acyclovir. The rates of hypokalemia were evaluated in subgroups after excluding those with prior hypokalemia or a low estimated glomerular filtration rate

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Competing interests

The authors report no relevant conflicts of interest.

Ethical approval

The Cleveland Veterans Affairs Medical Center Institutional Review Board determined that the study was exempt.

The study was presented as an oral presentation on Thursday, November 1 at Kidney Week 2012, the annual meeting of the American Society of Nephrology.

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and then subjects who received diuretics. Pearson's chi squared test was used to compare the rates of hypokalemia in subjects without prior hypokalemia, low estimated glomerular filtration rate, or diuretic use. The Institutional Review Board determined that the study was exempt.

Intravenous acyclovir was administered to 423 patients; 29,634 patients were admitted to the same ward within 30 days of a patient who received IV acyclovir. Hypokalemia developed in 46% of patients treated with IV acyclovir and in 21% of hospitalized patients not treated with acyclovir (see Table 1). The rate of moderate to severe hypokalemia was more than threefold greater among acyclovir recipients than in the non-exposed group. The increased risk associated with acyclovir was more pronounced in subjects without prior hypokalemia, low estimated glomerular filtration rate, or diuretic use. In this group, acyclovir treatment was associated with an increased rate of hypokalemia (P value < 0.001). None of the acyclovir treated subjects with hypokalemia in this latter group had a magnesium level < 1 mEq/L (0.5 mmol/L).

Our data demonstrates that administration of IV acyclovir is associated with an increased risk of hypokalemia in hospitalized patients. Strengths of our analysis include a large sample size, exclusion of subjects with other common causes of hypokalemia, and a contemporary comparison group. A weakness of the study is our inability to assess for urinary and gastrointestinal potassium losses.

Reduced renal plasma flow and crystal induced distal tubular damage may be two mechanisms by which acyclovir induces hypokalemia.^{1,4} Further research is necessary to determine whether hypokalemia may serve as an early marker of kidney injury in patients treated with IV acyclovir.

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Table 1

Rate of hypokalemia in patients treated with IV acyclovir and in untreated patients admitted to same ward within 30 days of a patient who received acyclovir (%).

Potassium levels within 4 days after IV acyclovir (or within 14 days after admission, if untreated) (mEq/L)	All patients		Excluding subjects who received diuretics			
	Acyclovir (N = 423)	No acyclovir (N = 29,634)	Excluding subjects with K < 3.6 mEq/L in week prior to first acyclovir dose (or week prior to admission if untreated) and subjects with eGFR < 60 within one week of acyclovir dose (or one week prior to two weeks after admission if untreated)		Excluding subjects who received diuretics	
			Acyclovir (N = 154)	No acyclovir (N = 16,157)	Acyclovir (N = 124)	No acyclovir (N = 11,147)
<3.5	45.6	21.3	29.2	8.6	26.6	6.9
<3.4	38.5	15.9	23.4	5.8	19.4	4.5
<3.3	30.0	11.5	16.2	3.7	12.9	2.8
<3.2	25.1	8.2	13.6	2.4	10.5	1.6
<3.1	19.4	5.7	9.1	1.5	6.5	1.0
<3.0	12.1	4.1	5.8	1.0	4.8	0.7
<2.9	8.9	2.7	3.2	0.6	2.4	0.4

Abbreviation: IV, intravenous.