

Acyclovir induced nephropathy – A case report

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Abstract

Acyclovir is frequently used in the management of suspected or proven serious viral infections in children. Despite its good safety profile serious side effects are known to occur. We describe a case of suspected viral encephalitis treated with intravenous acyclovir and complicated by acute, reversible, renal failure. To our knowledge this is the first such report in a Maltese Paediatric patient.

Case report

An eleven year old, previously well boy, presented to casualty following a prolonged first seizure. The patient remained confused and agitated in the postictal phase with a Glasgow coma scale (GCS) of 6. He had a mild viral-like illness in the preceding days. He was afebrile on admission. There were no rashes and as the patient was unconscious neck stiffness could not be assessed. Due to persistent irregular breathing the patient was transferred for further monitoring to the intensive care unit. A computerised tomography (CT) scan of the brain was normal as were initial biochemical and haematological investigations. No contrast was administered during the CT examination. Serum creatinine level on admission was 40 μ mol/l. In view of the prolonged seizure a provisional diagnosis of suspected viral encephalitis was made and the patient was started on triple therapy with ceftriaxone, clarithromycin and acyclovir at a dose of 500mg/m²/8 hourly. A lumbar puncture was postponed in view of the prolonged loss of consciousness. Fluid replacement was restricted to sixty percent of requirements in view of the possible encephalitis. Twelve hours post admission the patient's level of consciousness improved. He was alert and no longer confused and was transferred to a general paediatric ward for further management. On day three post admission a routine renal profile revealed a serum creatinine level of 364 μ mol/l. Electrolytes were normal and urea rose to 11.8mmol/l. Urine output remained good and blood pressure was on the 97th. Percentile for age. At this stage the possibility of acyclovir induced acute renal damage was considered. Renal ultrasound examination was normal. Examination of the urine under polarized light could not be performed as the investigation was not available locally. Hyperhydration (3 liters/m²/day) and diuretics (frusemide 1mg/kg/eight hourly) were started and a urine output of 4-6ml/kg/hour was maintained. Creatinine levels increased to 450 μ mol/l and subsequently 552 μ mol/l on day two and three respectively. An elevated blood pressure was

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Key Words

Acyclovir, crystal deposition, acute renal failure

Introduction

Acyclovir is an effective antiviral drug. Its use is particularly important in proven or suspected Herpes or Varicella infections. Reports of adverse effects are uncommon and occur almost always in adults, with renal dysfunction and neurotoxicity being the most frequently reported.¹ Adverse effects have been reported with both oral and intravenous administration of acyclovir as well as with slow or rapid intravenous administration of the drug.² Adequate hydration is essential with acyclovir therapy to reduce the risk of drug induced renal damage. We report a case of non-oliguric acute renal failure with complete recovery in an eleven year old boy treated with acyclovir.

treated with nifedipine 5mg twelve hourly. Acid base balance and electrolytes remained within normal. Following a maintained high urine output the patient's creatinine level started to decrease from the end of day three. By day five his creatinine level had decreased to 99umol/l, blood pressure normalised and his intravenous fluids were stopped. Outpatient review at three, seven and ten days following discharge was normal. Long term follow-up at three and six months did not reveal any abnormalities and renal function remained normal.

Discussion

The pharmacokinetics of acyclovir in children and adolescents are similar to those of adults.³ Acyclovir is generally well tolerated. Adverse effects associated with acyclovir in children and adults include nausea and/or vomiting (2-8%), diarrhoea (0.3-4%), headache or malaise (0.6-12% of patients), asthenia or paraesthesia (0.8-2%), and skin rash (0.3-2%). Additional adverse effects associated with intravenous infusions of acyclovir include local inflammation or phlebitis (9%), transient neutropaenia (3%), elevations in serum creatinine or urea (5-10%), and elevation of hepatic transaminases (1-2%).^{4,5} Recommended dosing regimen for children is 500mg/m²/eight hourly given by intravenous infusion over a one hour period. The kidney accounts for 75-80% of the total clearance of Acyclovir. In addition, acyclovir is relatively insoluble in the urine, particularly in the distal tubular lumen, where urine flow is sluggish. These characteristics explain why intravenous infusion of acyclovir may cause intratubular precipitation of crystals in the kidney.⁽⁶⁾ Adequate hydration is essential with intravenous use of acyclovir. Our patient was suspected of having viral encephalitis and his fluid replacement was restricted to sixty percent of requirements. This undoubtedly would have contributed to the crystallization and deposition of the drug in the renal tubules.

Risk factors for acyclovir *Nephrotoxicity* include high blood concentration of acyclovir caused by doses greater than 1500mg/m²/day, rapid intravenous administration, pre-existing renal disease, dehydration and associated use of other nephrotoxic drugs.⁷ Nephrotoxicity usually is a self-limiting condition that resolves with discontinuation of the drug and hyperhydration (3 liters/m²/day). Severe cases of renal failure may need hemodialysis. The risk of nephrotoxicity can be minimized by ensuring adequate hydration and a high urine flow and by giving acyclovir as a slow infusion rate over one hour.⁸ In patient with pre-existing renal disease, acyclovir dosage should be modified according to creatinine levels.

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