

AN EXPERIENCE OF ORAL ACYCLOVIR IN TREATING CHILDREN WITH VARICELLA INFECTION

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ABSTRACT

Objectives: To study the morbidity and complications of varicella infection in patients treated with acyclovir.

Methodology: It is a descriptive observational study conducted at Paediatric out patient department of Civil Hospital Karachi during September 1997 to March 1998. All children between the ages of 2-15 years presenting with clinical features of varicella but healthy otherwise and of average weight, and presenting within 72 hours of the onset of rash were treated with oral acyclovir in a dose of 80mg/ kg/ day for five days. At the end of five days the patients were evaluated for the duration of illness, severity of rash & itch and development of complications. The patients were also assessed for the side effects of the drug. Cost of the treatment was also calculated.

Results: A total of 31 children, 15 male and 16 females were studied. After the treatment the fever remained for 1- 8 days (mean 3.12 days). Eighteen (58%) patients had a moderate rash. Six(19.3%) had a severe rash while in seven(22%) the rash was of mild nature. Twenty (64.5%) of the patients had a moderate itch while five patients each (16.1%) had mild and severe itch. New rash continued to appear for three to nine days (mean 3.3 days). Complications were noted in three(6.9%) patients' only and included otitis media, pneumonia and secondary bacterial infection of vesicular lesions in one patient each. None of the patients developed any side effects to the drug. The average cost of treatment was Rs.3269/=.

Conclusion: Use of oral acyclovir in varicella infection (chicken pox) seems to limit new rash formation and total duration of illness to an average of <five days. A double blind case control study is needed to correctly assess its benefit cost ratio.

KEY WORDS: Varicella, Chicken pox, Acyclovir, Vesicular rash.

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INTRODUCTION

Chickenpox has affected more than three million children a year in the United States in early 90s.¹ It is prevalent in the US despite the availability of an effective vaccine.² Varicella is most commonly a mild, benign disease of preschool and school children.³ Between 75% and 90% of chickenpox cases occur in children under 10 years of age. According to a 2001 study, about 10% of children between ages five and nine and about 2% of 10 to 14 year olds get chicken pox each year. In immunocompetent

patients, symptoms are usually mild to moderate, but an uncomplicated severe case can have more than 1000 lesions and severe constitutional symptoms.⁴ Although usually self limited, chicken pox can cause prolonged discomfort and is associated with infrequent but serious complications including encephalitis, pneumonia, secondary bacterial infections, bleeding disorders, congenital infection and life threatening perinatal infections.^{1,5} About 60% of the 14,000 people who are hospitalized for chicken pox each year are children. Five out of every 1000 children who have the infection require hospitalization and in rare cases, chicken pox can be fatal.^{4,6} In all about 40 of the 100 patients who die each year of the disease are children.⁶ Mortality figures from the United States suggest an overall death rate from chickenpox of about one in 40000.⁷ Varicella can be atypical with distal involvement.⁸ The treatment of chickenpox is basically symptomatic and supportive.⁹ Acyclovir has been used to treat chickenpox in children. Most recommend its use to modify the severity of infection in high risk patients.¹⁰ Since chicken pox is a commonly acquired infection in our child population, we decided to assess the effect of Acyclovir in children with varicella infection who were healthy otherwise.

The main objectives were to study the course and complications of Varicella infection in patients treated with acyclovir and to assess the cost of drug therapy.

METHODOLOGY

This is a descriptive observational study carried out at the pediatric out patient department (OPD) of the Dow Medical College and Civil Hospital Karachi All children between the ages of 2–15 years presenting with clinical features suggestive of Varicella infection/ chickenpox including the characteristic

vesiculobullous rash from September 1997 to March 1998 were included in the study. The children were otherwise healthy and presented within 72 hours of the appearance of the rash. Patients who were immunosuppressed including severely malnourished children, children on steroids and cytotoxic drugs or who had used antiviral therapy during the preceding week or immunoglobulin in the preceding four weeks were excluded from the study. Patients less than two years old, with symptoms of fever greater than five days prior to presentation, presence of rash for more than 72 hours, prior immunization with varicella vaccine, history of acyclovir intolerance and history of preexisting renal disease were also excluded. After detailed history, examination and written consent of the parents / guardians the patients were put on oral acyclovir in a dose of 80mg/ kg/day for five days. At the end of five days they were recalled to the OPD and evaluated for the duration of the illness, severity of the rash and itch and development of complications such as scar formation, pneumonia and otitis media, encephalitis, eye complications etc. varicella was categorized as mild (<50 lesions), moderate (250-500 lesions) and severe (>500 lesions). The palatability of the drug and its side effects were also assessed. The cost of the drug was calculated at the end of the treatment.

Symptomatic treatment was also given including calamine lotion for local application as a soothing agent. The data was compiled and the results analyzed.

RESULTS

A total of 31 patients including 15 males and 16 females were enrolled in the study. Nineteen (61%) patients had a history of contact with a diagnosed case of Varicella. Most of the patients had moderate symptoms (Table-I)

Table-I: Severity of symptoms (n=31)

<i>Symptoms</i>	<i>Mild</i>	<i>Moderate</i>	<i>Severe</i>	<i>Nil</i>	<i>Total</i>
Rash	7(22%)	18 (58%)	6(93%)	-	31
Itch	5(16.1%)	20(64%)	5(16.12%)	1	31

while complications occurred only in minimal number of patients (Table- II) and consisted of ear infection in one, chest infection in one, pustule formation in one and scar in 17 (54.8%). Duration of illness and new rash is mentioned in Table-II. None of the patients developed any side effects of the drug. Cost of the treatment varied from Rs.2343/to Rs.6223/ with the average of Rs.3269/.

DISCUSSION

Chickenpox, is a self limited disease. The period from the appearance of the spots, to the end of the blister stage lasts about five to seven days. Most schools allow children with chickenpox back after ten days of onset. The numbers of blisters vary widely. It takes about four days for each blister to dry out and form a scab. The rash itches, sometimes severely. Usually separate crops of blisters occur over four to seven days, and the entire disease process lasts between seven and 10 days. Itching, a common symptom of the varicella infection can be very distressing; particularly for small children.⁶ The fever is usually the highest on the third or fourth day. Treatment so far has been mostly symptomatic and supportive. More recently specific treatment with antiviral drugs has been tried widely. In Germany acyclovir, valacyclovir, famciclovir and brivudin are approved for the systemic antiviral treatment of herpes zoster. These compounds are all well tolerated by the patients and do not differ with regard to efficacy and safety.⁹ Acyclovir is the drug of choice for varicella and herpes zoster. The clinical impact of acyclovir therapy is related directly to its use early in the clinical course and to the likely susceptibility of the patient to severe or life-threatening Varicella Zoster Virus (VZV) infection.¹¹ Immunocompetent children, ado-

lescents and adults with chickenpox displayed a gradation in their clinical responses to acyclovir that correlated with the time from onset of rash to initiation of therapy.² Most experts feel that the use of oral acyclovir helps only if started early in the course of the disease within 24 hours after sores appear.¹¹ Early intravenous administration of acyclovir is essential treatment for chickenpox pneumonia.¹² A multicenteric, double blind placebo controlled study involving 815 healthy children with chickenpox concluded that acyclovir is a safe treatment that reduces the duration and severity of chickenpox in normal children when therapy is initiated during the first 24 hours of the rash.¹ Such children had fewer varicella lesions and in over 95% of the recipients of acyclovir, no new lesions formed after day three.¹ Similar results were witnessed in our patients also where the duration of new rash formation was reduced to an average of three days as compared to new sores continuing to crop up daily for four to five days in untreated patients as mentioned in the literature. Severity of symptoms was also decreased with only 19% having severe rash and only 16% having severe itch. They had accelerated progression to the crusted and healing stages, itching and fewer residual lesions after 28 days. The results are further supported from world literature which reports sooner defervescence and earlier onset of cutaneous healing, as reflected by a decrease in number of lesions among the recipients of acyclovir.^{13,14} Analysis of the Cochrane Database Syst Rev. 2005¹⁵ and Cochrane Database Systemic Review 2002¹⁶ supported above findings. Results were less supportive with respect to the number of days to no new lesions and the number of days to the relief of itching.^{15,17} Similar results were reported by Biswas J, Nagpal A, et al but no

Table-II: Outcome of the varicella infection (n= 31)

Average Duration of New Rash After Treatment	3.3 days (3-9 days)
Mean Duration of Illness After Treatment	3.12 days (1-8 days)
Complication (no. of patients)	3 (9.6%)
Scar formation	17(54.8%)

significant difference was found in systemic complications such as bacterial sepsis.^{14,18} In our study also 7% developed complications in the form of acute otitis media, pneumonia while another 54% developed scars secondary to bacterial infection of the vesicles. Dunkle LM, et al¹ and Sadovsky¹⁰ reports limitation in the duration of fever and constitutional symptoms to four days which is consistent with our results where the mean duration of fever was limited to 3.12 days. Cost of the treatment in our study varied from Rs.2343/ to Rs.6223/ with the average of Rs. 3269/.

A five day course of acyclovir at a dose of 400 mg four times daily is recommended for patients aged two to five years. Over the age of six years the recommended dose is 800 mg four times daily for five days and over the age of 12 it is 800mg five times daily for seven days.⁷ The potential economic benefits of earlier return to work of parents seem unlikely to offset the cost of the drug and medical time.⁷ Oral acyclovir therapy is safe and effective for treatment of varicella in otherwise healthy adolescents¹⁴ and it is tolerated well.^{7,10} In our patients also adverse drug effects were not observed. Although acyclovir was well tolerated and no significant difference was observed between the groups in the titers of antibodies against Varicella zoster¹ concerns about viral resistance have also influenced the decision about acyclovir risk – benefit. So far short term treatment (5 day) with acyclovir does not seem to cause viral resistance.¹⁰

The use of acyclovir is unlikely to prevent spread in schools as the greatest contagiousness seems to be during the prodrome.⁷ Widespread use of an antiviral drug has theoretical disadvantages. The immune response may be impaired in some and this could alter the natural pattern of the infection and result in earlier reactivation in the form of zoster.⁷

The effect of acyclovir treatment on susceptibility to recurrent or reactivated varicella-zoster virus infection is controversial.¹⁷ These observations suggest that acyclovir, though lessening the severity of chickenpox, may interfere with the development of full immunity to the

varicella-zoster virus. The possibility that acyclovir may alter subsequent immunity is a concern.¹⁷ The clinical importance of acyclovir treatment in otherwise healthy children remains uncertain.^{15,16} In the USA, a routine childhood immunization programme has reduced disease incidence, complications, hospital admissions and deaths in children and in the general population.⁴ Most experts are of the opinion that indications for, acyclovir (and other antiviral agents) treatment are individuals who have suffered from severe forms of varicella and those, belonging to the high-risk group of patients (adults, viral, complications, immunocompromised host)³ such as neuroretinitis following chicken pox¹⁸ and acute retinitis after chicken pox in a patient with T-Cell acute lymphoblastic leukaemia¹⁹ where therapy with acyclovir resulted in complete recovery. Systemic antiviral therapy is able to shorten the healing process of acute herpes zoster, to prevent or to alleviate pain and other acute and chronic complications, particularly, when given within 48 hour to a maximum of 72 hour after onset of the rash.⁹

CONCLUSIONS

Acyclovir seemed safe and limited new rash formation and duration of illness to less than five days after start of treatment. However, due to concerns about interference with development of full immunity and cost, it should only be used in high risk immunocompromised and severe cases.

REFERENCES

1. Dunkle LM, Arvin AM, Whitley RJ. A controlled trial of acyclovir for chickenpox in normal children. *N Engl J Med* 1991;325:1539-44.
2. Balfour HH Jr, Edelman CK, Anderson RS, Reed NV, Slivken RM, Marmor LH, et al. Controlled trial of acyclovir for chickenpox evaluating time of initiation and duration of therapy and viral resistance. *Pediatr Infect Dis J* 2001;20(10):919-26.
3. Cvjetkovic D, Jovanovic J, Hrnjakovic-Cvjetkovic I. Primary varicella-zoster virus infection—current knowledge, diagnostic and therapeutic approaches. *Med Pregl* 2000;53(5-6):272-6.
4. Heininger U, Seward JF. Varicella. *Lancet* 2006;368(9544):1365-76 Erratum in: *Lancet*. 2007;17,369(9561):558.

5. Myers MG, Stanberry LR, Seward JF. Varicella Zoster Virus. In: Beherman RE, Kleighman RM, Jenson HB. eds Nelson Textbook of Pediatrics. 17th ed. W.B.Saunders, Philadelphia 2004;1058.
6. Simon H, Cannistra SA, Etkin MJ, Godine JE, Huang E, Heller D, et al. Stern: Shingles and Chickenpox (Varicella-Zoster Virus) December 2001 Nidus Information Services. Cynthia Chevins, Publisher, Carol Peckham, Editorial Director at <http://www.well-connected.com/>.
7. McKendrick MW. Controversies in Management: Acyclovir for childhood chickenpox. *BMJ* 1995;310:108-9.
8. Bhattarai S, Agrawal S, Rijal A, Dhali TK. Atypical varicella zoster as SJS-TEN overlap syndrome with involvement of palm and sole. *Nepal Med Coll J* 2006;8(1):69-71.
9. Gross G, Schofer H, Wassilew S, Friese K, Timm A, Guthoff R, et al. Herpes zoster guideline of the German Dermatology Society (DDG). *J Clin Virol* 2003;26(3):277-89; discussion 291-3.
10. Sadosky R. Acyclovir is useful in treating chicken pox in children. *American family physicians*. March 1, 2002. American Academy of Family Physicians. Accessed on 12/08/2003 (01/05/2007).
11. Arvin AM. Antiviral therapy for varicella and herpes zoster. *Semin Pediatr Infect Dis* 2002;13(1):12-21.
12. Simon H. How is chicken pox treated. University of Maryland Medicine. Reviewed on 12/03/2003.
13. Balfour HH Jr, Kelly JM, Suarez CS, Heussner RC, Englund JA, Crane DD, et al. Acyclovir treatment of varicella in otherwise healthy children. *J Pediatr* 1990;116(4):633-9.
14. Balfour HH Jr, Rotbart HA, Feldman S, Dunkle LM, Feder HM Jr, Prober CG, et al. Acyclovir treatment of varicella in otherwise healthy adolescents. The Collaborative Acyclovir Varicella Study Group. *J Pediatr* 1992;120(4 Pt 1):627-33.
15. Klassen TP, Hartling L, Wiebe N, Belseck EM. Acyclovir for treating varicella in otherwise healthy children and adolescents. *Cochrane Database Syst Rev* 2005;(4):CD002980.
16. Klassen TP, Belseck EM, Wiebe N, Hartling L. Acyclovir for treating varicella in otherwise healthy children and adolescents. *Cochrane Database Syst Rev* 2002;(4):CD002980.
17. Duvic M, Grossman D. More on Acyclovir for Chickenpox. *N Engl J Med* 1994;331(1):59.
18. Biswas J, Nagpal A, Chopra S, Karna S. Resolution of chicken pox neuroretinitis with oral acyclovir: a case report. *Ocul Immunol Inflamm* 2003;11(4):315-8.
19. Ross A, McLean TW, Farber R, Weaver RG Jr, Chauvenet A, Givner LB, et al. Retinitis following varicella in a vaccinated child with acute lymphoblastic leukemia. *Pediatr Blood Cancer* 2005;45(2):191-4.