ORIGINAL ARTICLE

Efficacy of Clarithromycin in Pityriasis Rosea

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ABSTRACT

Objective: To determine the efficacy of clarithromycin in the treatment of Pityriasis Rosea (PR).
Study Design: Double blind randomized controlled trial.
Place and Duration of Study: Dermatology OPD, Military Hospital, Rawalpindi, from July 2008 to July 2009.
Methodology: Patients aged above 10 years, diagnosed with PR, were randomly assigned to two groups of 30 each to receive either clarithromycin or similar-looking placebo for one week. Neither the patient nor the treating physician knew to which group the patient belonged. Patients were assessed at 1, 2, 4 and 6 weeks after presentation and compared for complete, partial or no response.
Results: Among the 60 patients, no significant difference was found between the two groups at 2 weeks after presentation ($p = 0.598$). In the placebo group, complete response was seen in 20 (66.7%), partial response in 3 (10.0%) while no response was seen in 7 (23.3%). In clarithromycin group, there was complete response in 23 (76.7%), partial response in 3 (10.0%) and no response in 4 (13.3%) patients.
Conclusion: Clarithromycin is not effective in treatment of pityriasis rosea.

Key Words: *Pityriasis rosea. Clarithromycin. Randomized controlled trial. Efficacy.*

INTRODUCTION

Pityriasis Rosea (PR) is characterized by a distinctive skin eruption and minimal constitutional symptoms. Most cases occur between ages of 10 - 35 years.[1] The incidence is 172.2/100,000 population/year and prevalence is 0.6% with a male to female ratio of 1:1.43.[2] The cause of the disease is uncertain but *Streptococci, Legionella, Spirochetes,* fungi and viruses especially Human Herpes Virus (HHV) 6 and 7 have been implicated.[1-4] History of preceding Upper Respiratory Tract Infection (URTI) is found in upto 69% of cases.[5] The disease usually starts with a herald patch (HP) followed 1 - 2 weeks later by crops of oval, dull pink scaly macules which tend to clear centrally and may cause itching.[6] Atypical patterns can occur.[1] Most people recover within 2 - 12 weeks.[7] Recurrence rate is around 2.5%.[1,7] The diagnosis is mainly clinical.[2] Dermoscopy may aid clinical diagnosis.[8] Differential diagnosis includes secondary syphilis, seborrhoeic dermatitis, guttate psoriasis, pityriasis lichenoides, tinea corporis and certain drug eruptions.[6,9] PR can lead to undesirable pregnancy outcomes specially when occurring in first 15 weeks.[10]

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Although PR is a self-limiting disease, the extensive rash, occurrence in crops, prolonged course and uncertain etiology are worrisome for the patients.[11] Studies on macrolides and acyclovir have shown conflicting results,[5,12-14] thus suggesting the need for more research.[15,16] There is no published data about PR in Pakistan. Clarithromycin, a macrolide, if found effective can be used on account of convenient dosage, greater activity and fewer adverse effects than erythromycin, leading to better patient compliance.

The objective of this study was to determine the efficacy of clarithromycin in the treatment of Pityriasis Rosea (PR).

METHODOLOGY

The study was a double blind Randomized Controlled Trial (RCT) carried out from July 2008 to July 2009 at the Dermatology Department, Military Hospital, Rawalpindi, a tertiary care center. Approval from Hospital Ethical Committee was obtained. After informed consent 60 patients were selected through consecutive (non-probability) sampling. Inclusion criteria were patients aged 10 years and above, presenting within 2 weeks of the onset of rash and two dermatologists agreed on the diagnosis of PR. The study excluded patients with renal disease (creatinine clearance less than 30 ml/minute), hypersensitivity to macrolides, pregnancy, prior use of antibiotics, topical or systemic steroids within 2 weeks, using bismuth, metronidazole, barbiturates, captopril and ketotifen and diabetes. History of a herald patch followed by a secondary eruption, itching and duration of disease at the time of initial eruption was recorded. Preceding history of URTI, sexual contact and similar disease in family members was recorded. Skin

examination was done to locate the herald patch and number and distribution of other lesions. Serum VDRL was done in all patients.

A doctor not involved in the treatment or follow-up of the patients was responsible for randomization and concealment. Randomization was done by lottery method keeping 30 patients in each group. The outcomes A or B were recorded separately on individual paper cards which were then placed in opaque sealed envelopes. Neither the patient nor the doctor who followed-up, knew to which group the patient belonged. Patients belonging to treatment group were given oral clarithromycin 500 mg twice daily for one week in adults and 250 mg twice daily in children 10 - 12 years of age. The rest were given similar looking placebo pills containing glucose. Subjects were followed-up in the OPD at 1, 2, 4 and 6 weeks. There were no dropouts. Efficacy was measured in terms of response categorized as complete when all lesions started healing in less than 2 weeks without the appearance of any fresh lesion, partial when lesions regressed partially or few new lesions appeared in 2 weeks, and no response when there was no regression or new lesions kept on appearing even after 2 weeks.

Statistical Package for Social Sciences (SPSS) version 14 was used to analyze the findings. Mean and standard deviation was calculated for numerical variables like age, number of lesions and duration of disease at the time of reporting. Frequencies and percentages were calculated for categorical variables like gender, socio-economic status (class of monthly income at Rs. < 10,000, 10,000 - 25,000 and > 25,000), preceding URTI, sexual exposure, similar disease in family members, herald patch, itching, response to treatment and serum VDRL. Chi-square test was used to compare the response. P-value of less than 0.05 was considered significant at 95% confidence interval.

RESULTS

The study included 60 patients, 30 each in group A and group B who were treated with placebo and oral clarithromycin respectively. Both the groups were comparable at presentation with respect to age, duration of disease and number of lesions (Table I).

In group A, monthly income was < Rs. 10,000 in 18 (60.0%) patients, Rs. 10,000 - 25,000 in 3 (10.0%), and > Rs. 25,000 in 9 (30.0%). In group B, it was < Rs. 10,000 in 15 (50.0%), Rs. 10,000 - 25,000 in 9 (30.0%) while > Rs. 25,000 in 6 (20.0%, p = 0.144).

PR rash was present on trunk and upper arms in all (100.0%) cases of group A and group B, on upper legs in 27 (90.0%) cases of both groups, on neck in 26 (86.7%) cases in group A and 25 (83.3%) cases in group B (p = 0.718) and on other sites in 4 (13.3%) cases in group A and 3 (10%) cases in group B (p = 0.688).

Table I: Comparison of age, duration of disease, and number of lesions.

	Group-A	Group-B	p-value (using t-test)
Age in years (mean ± SD)	21.67 ± 7.42	23.13 ± 10.34	0.530
Duration of disease in days (mean ± SD)	7.07 ± 2.728	6.23 ± 3.01	0.266
Number of lesions (mean ± SD)	137.90 ± 116.75	122.03 ± 105.49	0.583

Table II: Comparison of gender distribution, URTI, itching, family history, sexual contact, herald patch (HP) and VDRL.

	Group-A (n=30)	Group-B (n=30)	p-value (using chi-square test)
Gender			
Male	17(56.7%)	16 (53.3%)	0.795
Female	13 (43.3%)	14 (46.7%)	
URTI	13 (43.3%)	9 (30.0%)	0.284
Itching	12 (40%)	16 (53.3%)	0.301
Sexual contact	17 (56.7%)	13 (43.3%)	0.302
Family history	0 (0.0%)	0 (0.0%)	-
HP	22 (73.4%)	27 (90.6%)*	0.095
VDRL	0 (0.0%)	0 (0.0%)	-

** Two patients had 2 herald patches.*

Table III: Comparison of response to treatment.

	Response	Group-A (n=30)	Group-B (n=30)	p-value (using chi-square test)
1 week				
	Complete	5 (16.7%)	4 (13.3%)	0.866
	Partial	15 (50.0%)	17 (56.7%)	
	Nil	10 (33.3)	9 (30.0%)	
2 weeks				
	Complete	20 (66.7%)	23 (76.7%)	0.598
	Partial	3 (10.0%)	3 (10.0%)	
	Nil	7 (23.3%)	4 (13.3%)	
4 weeks				
	Complete	22 (73.3%)	24 (80.0%)	0.084
	Partial	2 (6.7%)	5 (16.7%)	
	Nil	6 (20.0%)	1(3.3%)	
6 weeks				
	Complete	24 (80.0%)	29 (96.7%)	0.126
	Partial	5 (16.7%)	1 (3.3%)	
	Nil	1 (3.3%)	0 (0.0%)	

Comparison of gender distribution, URTI, itching, family history, sexual contact, herald patch and VDRL is shown in Table II. No significant difference between the two groups was seen regarding response to therapy at 1, 2, 4 and 6 weeks after presentation (Table III).

DISCUSSION

There is no effective treatment to decrease the duration and severity of PR.[17] Multiple treatment regimens have been tried including reassurance, antibiotics, antivirals and phototherapy with varying results in different studies.[5,12-14,18,19] The incidental finding of improvement in 2 patients with PR while receiving erythromycin for URTI,[5] led to trials on erythromycin and other macrolides.

The hypothesis of this study was that clarithromycin was effective in treatment of PR. The results were contrary to the hypothesis. Response at 2 weeks was the main outcome measure. The difference between treatment and placebo group was insignificant. This finding was augmented by the observation that no significant difference in response between the two groups was seen at 1, 4 and 6 weeks follow-up. As it was the first study about PR in Pakistan, there was no local studies available to compare with those results but the results are comparable with the recent regional[12] and international studies.[13]

PR affects the younger age group mainly in second and third decade.[20] Similar results were noted in this study. There was slight male preponderance comparable with a recent epidemiological study[7] but opposed to Chuh's analysis[2] and Ayanlowo's seven years review.[20] It may be overestimated because of smaller sample size.

Similar to this study, Traore *et al*. also found PR to be more prevalent in unfavorable social and economic backgrounds.[21] Hence, it is important to avoid the drugs which are not found effective thus, reducing the unnecessary economic burden.

Most of the patients had one HP. Two patients had two herald patches. The incidence of HP was slightly higher in this study, 81.6% compared to 40 - 76% in various studies.[2]

The incidence of pruritus is variable from mild to severe itching.[1] It was higher in this study (46.5%), may be because of making patients conscious by direct questioning about itching.

Rash of PR typically involves trunk, with a Christmas tree pattern on back and upper third of arms and legs.[1] Most of the patients had similar distribution of rash. Face was involved in one patient. Whole of the limbs were affected in 6 patients who otherwise had extensive rash.

Sharma PK *et al*. and Shorma L *et al*. found that in at least one half of the patients, the first symptoms of PR were non-specific and consistent with URTI.[5,7] The results are comparable with this study.

All the patients who had a history of sexual relationship were married and their sexual contacts were with their spouses only. No case was seen in which both partners were affected with PR or had a positive family history. VDRL was negative in all cases of group A and B. This ruled out the possibility of secondary syphilis which is one of the closest mimickers of PR.

No patients were lost to follow-up mainly because the study was conducted in a military hospital where treatment is free and the patients can be easily called upon. Besides, personal contact numbers of all the patients were obtained.

Few controlled trials on the treatment of PR have been conducted. A placebo-controlled study of 90 patients by Sharma *et al*. showed complete clearance of the rash in 73% of patients who received 2 weeks of erythromycin, compared with persistence of the rash in the placebo group [Evidence level B, single controlled trial].[5] The results were in contrast to this study but this study was not randomized, and allocation to groups was not concealed; therefore, the benefit may have been overestimated. Since studies have failed to identify an increase in antibody titers against *Streptococci, Mycoplasma, Chlamydia* or *Legionella* species, the effect of macrolides may be related to their anti-inflammatory and immunomodulatory properties.

Chuh *et al*. reviewed different studies regarding treatment of PR[15] and came across a small good quality trial (40 people) that compared oral erythromycin and placebo and found erythromycin effective in decreasing the rash and itch. The results were not consistent with our study. However, these results should be treated with caution since they come from only one small RCT.[6] In general, the authors found inadequate evidence for efficacy of most treatments for PR.

Rasi *et al*. compared oral erythromycin with placebo (an emollient cream) in a study on 184 patients with PR and found no significant difference between the two groups.[12] The physicians were not blinded to the treatment group and the placebo was not similar looking. However, the results were consistent with this study.

The results of efficacy of azithromycin, another macrolide in a RCT by Amer *et al*.,[13] were comparable with that of clarithromycin in this study i.e. clarithromycin was ineffective in treatment of PR.

CONCLUSION

Clarithromycin is not effective in decreasing duration or severity of PR. Reassurance and symptomatic treatment is all that is required. However, there are only a few RCTs thus suggesting the need for more research in this field.

REFERENCES

1. Drago F, Broccolo F, Rebora A. Pityriasis rosea: an update with a critical appraisal of its possible herpes viral etiology. *J Am Acad Dermatol* 2009; **61**:303-18.
2. Chuh A, Lee A, Zawar V, Sciallis G, Kempf W. Pityriasis rosea-an update. *Indian J Dermatol Venereol Leprol* 2005; **71**:311-5.
3. Rebora A, Drago F, Broccolo F. Pityriasis rosea and herpes viruses: facts and controversies. *Clin Dermatol* 2010; **28**: 497-501.
4. CanpolatKirac B, Adisen E, Bozdayi G, Yucel A, Fidan I, Aksakal N, *et al*. The role of human herpes virus 6, human herpes virus 7, Epstein-Barr virus and cytomegalo virus in the aetiology of pityriasis rosea. *J Eur Acad Dermatol Venereol* 2009; **23**:16-21.
5. Sharma PK, Yadav TP, Gautam RK, Taneja N, Satyanarayana L. Erythromycin in pityriasis rosea: a double-blind, placebo-controlled clinical trial. *J Am Acad Dermatol* 2000; **42**:241-4.

6. Browning JC. An update on pityriasis rosea and other similar childhood exanthems. *Curr Opin Pediatr* 2009; **21**:481-5.

7. Sharma L, Srivastava K. Clinicoepidemiological study of pityriasis rosea. *Indian J Dermatol Venereol Leprol* 2008; **74**: 647-9.

8. Lallas A, Kyrgidis A, Tzellos TG, Apalla Z, Karakyriou E, Karatolias A, *et al*. Accuracy of dermoscopic criteria for the diagnosis of psoriasis, dermatitis, lichen planus and pityriasis rosea. *Br J Dermatol* 2012; **166**:1198-205.

9. Atzori L, Pinna AL, Ferreli C, Aste N. Pityriasis rosea-like adverse reaction: review of the literature and experience of an Italian drug-surveillance center. *Dermatol Online J* 2006; **12**:1.

10. Drago F, Broccolo F, Zaccaria E, Malnati M, Cocuzza C, Lusso P, *et al*. Pregnancy outcome in patients with pityriasis rosea. *J Am Acad Dermatol* 2008; **58**:S78-83.

11. Kaymak Y, Taner E. Anxiety and depression in patients with pityriasis rosea compared to patients with tineaversicolor. *Dermatol Nurs* 2008; **20**:367-70, 377.

12. Rasi A, Tajziehchi L, Savabi-Nasab S. Oral erythromycin is ineffective in the treatment of pityriasis rosea. *J Drugs Dermatol* 2008; **7**:35-8.

13. Amer A, Fischer H. Azithromycin does not cure pityriasis rosea. *Pediatrics* 2006; **117**:1702-5.

14. Rassai S, Feily A, Sina N, Abtahian S. Low dose of acyclovir may be an effective treatment against pityriasis rosea: a random investigator-blind clinical trial on 64 patients. *J Eur Acad Dermatol Venereol* 2011; **25**:24-6.

15. Chuh AA, Dofitas BL, Comisel GG, Reveiz L, Sharma V, Garner SE, *et al*. Interventions for pityriasis rosea. *Cochrane Database Syst Rev* 2007; **(2)**:CD005068.

16. Krishnamurthy K, Walker A, Gropper CA, Hoffman C. To treat or not to treat? Management of guttate psoriasis and pityriasis rosea in patients with evidence of group A, *Streptococcal* infection. *J Drugs Dermatol* 2010; **9**:241-50.

17. Drago F, Rebora A. Treatments for pityriasis rosea. *Skin Therapy Lett* 2009; **14**:6-7.

18. Chuh AA. Narrow band UVB phototherapy and oral acyclovir for pityriasis rosea. *Photodermatol Photoimmunol Photomed* 2004; **20**:64-5.

19. Laxman M. Pityriasis rosea occurring during acyclovir therapy. *Indian J Dermatol Venereol Leprol* 2007; **73**:200-1.

20. Ayanlowo O, Akinkuqbe A, Olumide Y. The pityriasis rosea calendar: a 7-year review of seasonal variation, age and sex distribution. *Niq Q J Hosp Med* 2010; **20**:29-31.

21. Traore A, Korsaga-Some N, Niamba P, Barro F, Sanou I, Drabo YJ. [Pityriasis rosea in secondary schools in Ouagadougou, Burkina Faso]. *Ann Dermatol Venereol* 2001; **128**:605-9. French.