Comparative study of narrow band UVB versus oral acyclovir in the treatment of pityriasis rosea

Thesis

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by

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List of Abbreviations

Abbreviation	*Meaning*
>	More than
<	Less than
≥	More than or equal
≤	Less than or equal
%	Percent
AIDS	Acquired immunodeficiency syndrome
ANOVA	Analysis of variance
BB-UVB	Broad band ultraviolet B
cm	Centimeter
CMV	Cytomegalovirus
DNA	Deoxyribonucleic acid
e	One side of the upper and lower extremities
E	Erythema
g	Gram
GMP	Guanosine monophosphate
GTP	Guanosine triphosphate
HHV	Human herpes virus
HIV	Human immunodeficiency virus
HSV	Herpes simplex virus
I	Infiltration
IFN	Interferon
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IL	Interleukin
J/cm²	Joule per square centimeter
KOH	Potassium hydroxide
MED	Minimal erythema dose
mg	Milligram
mRNA	messenger Ribonucleic acid
mW/ cm^2	milliWatt per square centimeter
N	Number of lesions
NB-UVB	Narrow band ultraviolet B
nm	Nanometer
No.	Number of patients
NS	Non-significant

PBMCs	Peripheral blood mononuclear cells
PCR	Polymerase chain reaction
PLEVA	Pityriasis lichenoides et varioliformis acuta
PR	Pityriasis rosea
PRSS	Pityriasis Rosea Severity Score
PUVA	Psoralen and ultraviolet A radiation
S (in Results)	Significant
S (in patients and methods)	Scale
SD	Standard deviation
t	One side of the trunk and the head
TK	Thymidine kinase
UV	ultraviolet
UVB	Ultraviolet B
UVA	Ultraviolet A
VZV	Varicella zoster virus

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Introduction

Pityriasis Rosea (PR) is a common acute self limited skin eruption with a distinctive and constant course. The initial lesion is a primary plaque that is followed after 1 or 2 weeks by a generalized secondary rash with a typical distribution lasting for about 6 weeks (***Bjornberg and Hellgren, 1962).***

The exact etiology of the disease is uncertain, but various hypotheses have been postulated; incriminating infective agents such as viruses, fungi, streptococci and spirochetes and non infective etiologies such as atopy and autoimmune causes have also been investigated ***(Bjornberg and Hellgren, 1962; sharma et al., 2000).***

It has been shown that PR may be associated with the reactivation of human herpes virus 7 (HHV-7) and sometimes human herpes virus 6 (HHV-6) ***(Watanabe et al., 2002;Broccolo et al., 2005).***The detection of HHV-7 and HHV-6 DNA or both in peripheral mononuclear cells, tissues and in cell-free plasma of PR patients corresponding to active viral replication supports a causal relationship ***(Drago et al., 1997a),***so it is possible that an effective treatment against these viruses may help in reduction of severity of this disease ***(Drago et al., 2006).***

Although many patients need no treatment except education about the disease course and reassurance, some patients need treatment because of their extensive lesions or

their annoying pruritus **(Drago *et al., 2006)*.** No specific therapy is available **(*Cheong and Wong, 1989*).**

Drago et al., 2006 demonstrated that high-dose acyclovir (800 mg five times daily for 1 week) may be effective in the treatment of PR and reduces the time of lesion clearing.

On the other hand, there have been reports that lesions do not occur in the body areas where UV radiation is utilized. Therefore, UV radiation through an artificial source or by intentional exposure to natural sunlight has been recommended to decrease the duration of rash and the intensity of itching in patients with PR. ***(Merchant and Hammond, 1974; Arndt et al., 1983; Leenut-aphong and Jiamton, 1995).***

AIM OF THE WORK

The aim of this thesis is to evaluate the clinical efficacy of narrow band ultraviolet B (UVB) versus oral acyclovir in the treatment of pityriasis rosea.

Chapter 1
1. Pityriasis Rosea

Pityriasis rosea (PR) is an acute, self limiting papulosquamous skin eruption. The initial lesion is a primary plaque that is followed after 1 or 2 weeks by a generalized secondary rash with a typical distribution and lasting for about 6 weeks ***(Bjornberg and Tegner, 2003)***.

1.1 Historical hint

Pityriasis rosea was probably first described by the Edinburgh dermatologist Robert Willan under another terminology (roseola annulata) in 1798 ***(Weiss, 1903).*** The disease has been given many names, such as erythema annulatum, herpes tonsurans maculosus et squamosus, lichen annulatus serpiginosus, pityriasis circiné, pityriasis disseminé, pityriasis margineé et circineé, pityriasis rubra aigu disseminé, pseudoexthanthème erythématodesquamatif, roseola annulata, roseola squamosa, and roseola furfuracea herpetiformis ***(Percival, 1932; Bjornberg and Tegner, 2003)***.

The macular variety of PR was first named as such by the French dermatologist Camille Melchoir Gibert in 1860 ***(Percival, 1932).***The more usual annular variety was first described by another French dermatologist Pierre-Antoine-Ernest Bazin in 1862 ***(Klauder, 1924).***Jean Baptiste Emile Vidal, another French dermatologist,described pityriasis circiné et marginé in 1882 ***(Klauder, 1924).***It has fewer and larger lesions, often localized at the axillae or groins, and runs a longer course ***(Sarkany and Hare, 1964).***The herald patch

was first described by a French dermatologist Louis-Anne-Jean Brocq in 1887 ***(Weiss, 1903).***

1.2 Epidemiology

1.2.1 Prevalence and Incidence

Pityriasis rosea is relatively common throughout the world. The prevalence of PR in total population has been calculated as 0.13 percent in males and 0.14 percent in females, most patients being in the age group of 10 to 43 years. The incidence at different dermatologic centers has varied between 0.3 and 3 percent ***(Bjornberg and Tegner, 2003)***.

1.2.2 Sex Incidence

The disease has been reported to be equally common in both sexes, or slightly more common in females by margin of 1.2: 1 ***(Olumide, 1987; Harman et al., 1998)***.

On the other hand, ***Cheong and Wong, 1989*** and ***Tay and Goh, 1999*** found that sex incidence slightly more common in males 1.2: 1.

1.2.3 Age Incidence

Pityriasis rosea is rare in both the very young and the very old ***(Bjornberg and Tegner, 2003)***. However, it has been described in infants as young as 3 months of age ***(Hendricks and Lohr, 1979)***. A feature common to several studies is a steeply rising incidence during childhood to a plateau-like

maximum between 10 and 35 years of age, followed by a slow decline ***(Bjornberg and Tegner, 2003)***.

1.2.4 Race Incidence

No apparent racial predisposition exists ***(Jacyk, 1980; Tay and Goh, 1999)***. However, ***Olumide, 1987*** reported that PR was more severe and extensive in Africans rather than Caucasians. In Africans, lesions on the face, neck, forearms, legs, hands, feet and also involve oral cavity with generalized lymphadenopathy were common features.

1.2.5 Seasonal Incidence

Pityriasis rosea seems to be prevalent all over the world, irrespective of climate. In temperature zones, it is usually considered to be most common during spring and autumn or during the cool part of the year, but it also has been reported to be most common during summer ***(Chuang et al., 1982; Chuh et al., 2003)***.

The incidence in the tropics peaked during the months of April to October rainy season ***(Pettit, 1983; Olumide, 1987)***. However, the seasonal incidence in the Sudan was highest in cold, dry months ***(Ahmed, 1986)***. Furthermore, no seasonal variation at all was observed in several studies ***(Vigh, 1983; Tay and Goh, 1999; Chuh et al., 2003)***.

Finally, ***(Chuang et al., 1982; Tay and Goh, 1999)*** believed that changes in incidence of PR from year to year, though not great, may be statistically significant.

1.3 Aetiology

The cause of PR is uncertain but many epidemiological and clinical features relatively suggest that an infective agent may be implicated.The suggested causes of PR are relatively numerous ***(Parsons, 1986)***. PR is probably viral in origin, although no specific organism has ever been isolated or shown to be directly linked ***(González et al., 2005).***It has been shown that PR may be associated with the reactivation of human herpes virus 7 (HHV-7) and sometimes human herpes virus 6 (HHV-6) ***(Broccolo et al., 2005).***

1.3.1 Infection

Infection has been implicated in the aetiology of PR on the basis of the following observations and reports:

The monomorphic clinical picture of PR with its characteristic primary plaque, dissiminated secondary eruption after an interval, a self limiting course and infrequency of second attack, are all features paralleled by many diseases of proven infective origin ***(Bjornberg and Tegner, 2003)***. Up to 69% of patients with PR have prodromal symptoms of fever, malaise, headache, arthralgia, anorexia, nausea and sore throat before the herald patch appears ***(Bjornberg and Hellgren, 1962; Sharma et al., 2000)***.

Outbreaks of the condition occur in cluster suggesting that an infectious agent is circulating within the community. PR has been known to occur in small epidemics in fraternity houses and military establishments. In addition, it has been found a high incidence in people, either working at or

attending educational establishments ***(Messenger et al., 1982; Kempf and Burg, 2000; Bernardin et al., 2002).*** Furthermore, there have been numerous isolated reports of concurrence of the disease in the same household or through close contact ***(Bjornberg and Hellgren, 1962; Bosc, 1981; Chuh et al., 2003)***.

There is a strong association between upper respiratory infection and subsequent development of PR ***(Chuang et al., 1982)***. Furthermore, most upper respiratory infections like PR have a seasonal variation in occurrence, show increased incidence in autumn and winter with a decrease in summer ***(Hudson et al., 1981)***.

Recurrence of PR outside the acute phase is rare, suggesting that there is long lasting immunity after infection ***(Sorensen, 1990)***. In addition, higher prevalence of PR was reported during an altered state of immunity such as pregnancy or after bone marrow transplantation ***(Spelman et al., 1994)***.

Kempf and Burg, 2000 supported the concept of an infectious factor in pathogenesis of PR by treating the patients with specific convalescent plasma or pooled gamma globulin during the first week of the eruption leading to a modified form of the disease and shortening of its duration.

During the acute phase, some patients with PR show slight decrease in the number of peripheral blood T-lymphocytes and a transient increase in B lymphocytes and an elevated erythrocyte sediment-tation rate ***(Kermani-Arab et al., 1978; Kempf et al., 1999).*** In addition, ***Baker et al., 1993*** found that T-lymphocytes specific for group A streptococcal

antigens occasionally have been demonstrated in PR (as in guttate psoriasis).

Histologically, dyskeratotic cells and in particular multinucleated giant cells in the epidermis are features observed in viral infections such as Herpes simplex virus (HSV) and Varicella zoster virus (VZV) infections ***(Kempf and Burg, 2000)***.

1.3.1.1 Bacterial infection

Bacteria have been incriminated in the causation of PR by the alleged increased incidence of bacterial tonsillitis in PR patients ***(Hazen, 1931);*** and also by the observation of relative elevation in the erythrocyte sedimentation rate, relative shift to the left in the differential white blood cell count and by a relative rise in the total serum protein level ***(Bjornberg and Hellgren, 1962)***.

Mycoplasma pneumoniae has also been implicated in the causation of PR, as it is occasionally associated with a pityriasiform eruption ***(Murray et al., 1975)***. However, ***Hudson et al., 1981*** reported an insignificant rise in the titre of complement fixation tests to mycoplasma in PR. In addition, *legionella micdadei* antibodies were detected in 12 of 36 (33.3%) PR cases and in one of 19 (5.2%) controls. *Legionella micdadei* antibodies were significantly more common in PR cases than in controls. PR may be the clinical manifestations of an infection caused by legionella ***(Gjenero-Margan et al., 1995)***.