Abstract:

Psoriasis is a chronic papulosquamous disorder with remissions and exacerbations. Varied estimates of the population prevalence of the disease in different parts of the world range from 0.1 - 3%. It is not uncommon in our country. Although there are no treatment options offering a complete cure, a number of options exist for providing symptomatic relief, inducing as well as prolonging remission. Various systemic therapies such as methotrexate, acitretin, cyclosporine, and biologic agents can be used. A review of pharmacokinetics, safety and a discussion of relapse rate establish acitretin, an aromatic retinoid as an efficacious, convenient, oral monotherapy for initial and maintenance of severe psoriasis. A prospective clinical trial was conducted to find out the efficacy and safety of acitretin as monotherapy in the treatment of moderate to severe plaque type psoriasis (PASI range 10-42). Thirty two clinically diagnosed cases of moderate to severe plaque type psoriasis attending the Skin and VD out patient department of Faridpur Medical College Hospital, Faridpur were selected randomly. Majority (46.9%) were between 61 to 80 years of age and only 3.1% patients were in the <20 years age group. The average age was 57.3 years and range was 19-90 years. Majority (68.8%) of the patients were male and 31.2% patients were female. The male female ratio was 2.2:1. After 8 weeks of treatment with acitretin PASI 50 and PASI 75 response rates were 55% and 24% respectively and after 12 weeks of treatment, PASI 50 and PASI 75 response rates were 75% and 50% respectively. As side effects of the treatment, 4(12.5%) patients developed alopecia, each of xerophthalmia and cheilitis was seen in 3(9.37%) patients, each of fatigue and pruritus was seen in 2(6.25%) patients and only 1(3.12%) patient developed myalgia. This study demonstrates that acitretin as monotherapy is effective and safe in the treatment of moderate to severe plaque type psoriasis.

Key words: Acitretin, Psoriasis, PASI.

Introduction:

Psoriasis is a long-lasting autoimmune disease which is characterized by patches of abnormal skin. These skin patches are typically red, itchy, and scaly. They may vary in severity from small and localized to complete body coverage. There are five main types of psoriasis: plaque, guttate, inverse, pustular, and erythrodermic. Plaque psoriasis, also known as psoriasis vulgaris, makes up about 90% of cases. It typically presents with red patches with white scales on top. Areas of the body most commonly affected are the back of the forearms, shins, around the navel, and the scalp.

Psoriasis is generally thought to be a genetic disease which is triggered by environmental factors. In twin studies, identical twins are three times more likely to both be affected compared to non-identical twins; this suggests that genetic factors predispose to psoriasis. Symptoms often worsen during winter and with certain medications such as beta blockers or NSAIDs. Infections and psychological stress may also play a role. Psoriasis is not contagious. The underlying mechanism involves the immune system reacting to skin cells.

There is no consensus about how to classify the severity of psoriasis. Mild psoriasis has been defined as a percentage of body surface area (BSA) ≤10, a Psoriasis Area Severity Index (PASI) score ≤10, and a dermatology life quality index (DLQI) score ≤10. Moderate to severe psoriasis was defined by the same group as BSA >10 or PASI score >10 and a DLQI score >10.4

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While no cure is available for psoriasis, many treatment options exist. Topical agents are typically used for mild disease, phototherapy for moderate disease, and systemic agents for severe disease. Non-biologic systemic treatments frequently used for psoriasis include methotrexate, ciclosporin, hydroxyurea, fumarates such as dimethyl fumarate, and retinoids. Methotrexate and ciclosporin are drugs that suppress the immune system; retinoids are synthetic forms of vitamin A. Biologics are manufactured proteins that interrupt the immune process involved in psoriasis. Unlike generalized immunosuppressive drug therapies such as methotrexate, biologics target specific aspects of the immune system contributing to psoriasis.

Acitretin, an aromatic retinoid, has been a valuable option for the treatment of psoriasis since the late 1980s. Retinoids primarily act by normalizing keratinocyte differentiation, thus decreasing epidermal proliferation; moreover, the drug exerts immunomodulatory and anti-inflammatory effects without a direct immunosuppressive effect. Acitretin has been proven to be effective in psoriasis, both as monotherapy as well as in combination with phototherapy or other systemic agents, without significant loss of efficacy over time. As monotherapy, acitretin is considered to be more effective in pustular and erythrodermic psoriasis compared with chronic plaque-type psoriasis.

Materials and Methods:

The efficacy of acitretin was evaluated prospectively in randomly selected thirty two patients with moderate to severe (PASI- Psoriasis Area and Severity Index range 10-42) psoriasis attending the Skin and VD outpatient department of Faridpur Medical College Hospital, Faridpur. The study was carried out from September 2017 to August 2018. Those who were >_ 18 years of age and affected with plaque type psoriasis with a PASI >_10 were included in the study. Informed consent was taken from the patients to take part in the study. Patient's data were recorded on predesigned case record forms. Patients were treated at an initial dose of 25 mg/day acitretin for 4 weeks followed by an 8 week phase of dosage adjustment according to therapeutic response. Efficacy was measured by PASI 50 and PASI 75 response at the end of 8 and 12 weeks of treatment. PASI 50 and PASI 75, refer to the percentage of patients achieving a 50% or 75% improvement in baseline PASI score. Throughout the treatment duration, additional local moisturizing or emollient products expected to hydrate the affected skin and to relieve itching were allowed. Patients with severe renal or hepatic dysfunction, hepatitis, pregnancy, breastfeeding, desire to have children and insufficient guarantee of effective contraception were excluded from the study.

Table I: Distribution of the patients by age (n=32).

| Age (in years) | Frequency | Percentage |
|---------------|-----------|------------|
| <20           | 1         | 3.1        |
| 21-40         | 4         | 12.5       |
| 41-60         | 11        | 3.3        |
| 61-80         | 15        | 46.9       |
| >80           | 1         | 3.1        |
| Total         | 32        | 100        |

Table-I shows the age of the patients of psoriasis, where majority (46.9%) cases were between 61 to 80 years and only 3.1% patients were in the <20 years age group. The average age was 57.3 years and range was 19-90 years.

Table-II: Distribution of patients by sex.

| Sex  | Number | Percentage |
|------|--------|------------|
| Male | 22     | 68.8       |
| Female | 10   | 31.2       |
| Total| 32     | 100        |

Table-II shows that majority (68.8%) of the patients were male and 31.2% patients were female. The male female ratio was 2.2:1.

Fig-1. Treatment response at 8th week (PASI 50 and PASI 75)

Fig-1. Shows that after 8 weeks of treatment with acitretin, PASI 50 and PASI 75 response rates were 55% and 24% respectively.
Fig-2. Shows that after 12 weeks of treatment with acitretin, PASI 50 and PASI 75 response rates were 75% and 50% respectively.

Table III shows that 4(12.5%) patients developed alopecia, each of xerophthalmia and cheilitis was seen in 3(9.37%) patients, each of fatigue and pruritus was seen in 2(6.25%) patients and only 1(3.12%) patient developed myalgia.

Discussion:

The efficacy of acitretin as monotherapy was evaluated prospectively in randomly selected thirty two patients with moderate to severe (PASI- Psoriasis Area and Severity Index range 10-42) psoriasis attending the Skin and VD outpatient department of Faridpur Medical College Hospital, Faridpur. The study was carried out from September 2016 to August 2017. Patients those fulfilled the inclusion criteria were included in the study. Patients were treated at an initial dose of 25 mg/day acitretin for 4 weeks followed by an 8 week phase of dosage adjustment according to therapeutic response. Efficacy was measured by PASI 50 and PASI 75 response at the end of 8 and 12 weeks of treatment. PASI 50 and PASI 75, refer to the percentage of patients achieving a 50% or 75% improvement in baseline PASI score.

The study showed that majority (46.9%) cases were between 61 to 80 years and only 3.1% patients were in the <20 years age group. The average age was 57.3 years and range was 19-90 years (Table-I), which correlates with the study done by Borghi A et al\textsuperscript{17} where average age was found as 61.4 years and range was 28-90 years. Majority (68.8%) of the patients were male and 31.2% patients were female in our study and the male female ratio was 2.2:1(Table-II), whereas it was 3:1 in the study done by Borghi A et al\textsuperscript{17} and 2:1 in the study done by Murray HE et al\textsuperscript{18} which is very much similar.

The study showed that after 8 weeks of treatment with acitretin, PASI 50 and PASI 75 response rates were 55% and 24% respectively (Fig.1) which is consistent with the findings of the study done by Kragballe K et al\textsuperscript{19} where it was 57% and 24% respectively.

It showed that after 12 weeks of treatment with acitretin, PASI 50 and PASI 75 response rates were 75% and 50% respectively. It was 66% and 34% respectively in the study done by Murray HE\textsuperscript{18} and 85% and 52% respectively in the study done by Kragballe K et al\textsuperscript{19} which are more or less similar to the result of our study.

Regarding side effects, 4(12.5%) patients developed alopecia, each of xerophthalmia and cheilitis was seen in 3(9.37%) patients, each of fatigue and pruritus was seen in 2(6.25%) patients and only 1(3.12%) patient developed myalgia. The rate of occurrence of adverse events in our study was lower than in other reported experiences\textsuperscript{20-23}. The low mean daily dosage administered in our population may account for this finding. But the side effects are accordance with the findings of the study done by Borghi A et al\textsuperscript{17}.

Conclusion:

The main limitation of this study is the lack of an age and psoriasis severitymatched control group. The relatively small number of patients were studied (n = 32) for a short period. In conclusion, due to the need for prolonged, and usually life-long, therapy of patients with psoriasis, our experience indicates that acitretin is a suitable treatment option, as it results in clearing in most patients while minimizing the risk of side-effects and toxicities. Based on our findings, a low initial dosage, escalating stepwise is recommended; once the minimal effective dose has been achieved it is possible to reduce the dose slightly in order to maintain clinical efficacy and improve tolerance long-term.

It needs further elaborative study on a larger number of patients over a longer period of time and comparing with in control group. Side effects need further evaluation. Still it could be concluded that acitretin is safe and effective monotherapy in the treatment of moderate to severe plaque type psoriasis.
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