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Study Letter Case Series

Apremilast in psoriasis: A single centre treatment experience

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Sir,

Apremilast is a phosphodiesterase-4 inhibitor that received FDA approval for the treatment of moderate-to-severe plaque psoriasis and psoriatic arthritis in 2014.[1] It offers a novel therapeutic option in patients with significant hepatic and metabolic derangements. The drug modulates the proinflammatory mediator release that plays a pivotal role in the pathogenesis of psoriasis.[2] Apremilast not only alleviates the symptoms of the disease but also improves the quality of life of patients. Although no significant derangements in laboratory values were observed in any of the trials with the drug, limited data exist on the side effect frequency and adverse events in real-world practice.[3] Dose adjustment of the drug is advocated only in severe renal impairment.[2]

We report our experience on the effectiveness and tolerability of apremilast when given in both regular and lower dosages in psoriasis, in the Department of Dermatology, Government Medical College Alappuzha, during 10 months from March to December. The drug was given to a total of 13 patients. All had moderate-to-severe psoriasis assessed with both body surface area >10% and psoriasis area severity index (PASI) >10 as per the rule of ten. Data on adverse effects and dose adjustments were recorded during regular follow-up visits of the patients.

The mean age of patients and the mean duration of psoriasis were 41.46 ± 18.13 years and 6.23 ± 12.8 years, respectively. There were only two females (15.38%) and the rest were males (84.61%). Apremilast was given for unstable psoriasis in 3 (23.07%) patients, chronic plaque psoriasis in 9 (69.2%) patients, and for exfoliative psoriasis in 1 (7.6%) patient. The mean PASI of subjects was 35.98 ± 26.06. Apremilast was added as an adjunct to methotrexate and phototherapy in 10 (76.9%) patients as a substantial improvement as expected was not obtained in those patients. This drug was the only systemic agent prescribed in 3 (23.07%) patients as two of them had chronic liver disease and one had moderate pulmonary fibrosis contraindicating methotrexate.

The dosage of apremilast given for patients during the earlier and later phases of the study was different and decided based on our experience with the side effect profile noted from patients. The drug was given in a graded dosage as recommended starting at 10 mg OD up to a maximum of 60 mg for the first 8 (61.53%) patients whom we saw in the earlier part of the study. In five patients (38.4%), whom we saw in the later phase, the drug was given only up to a maximum dose of 45 mg daily (30 mg in the morning and 15 mg in the evening) and the patients were followed up.

We found that 75% (6/8) of the patients, who were given the full dosage of the drug, reported at least one adverse effect of the drug while 25% (2/8) patients tolerated the 60 mg dosage comfortably. Side effects were observed in an average of 7.33 ± 3.55 days after attaining the full dosage.

Diarrhea (66.66%) and headache (50%) were the most common side effects. Other events included abdominal pain (33.3%), nausea (33.33%), dizziness, and non-specific gastrointestinal symptoms (12.5%

each). Apremilast causes diarrhea by activating chloride channel in the intestine leading to fluid secretion into the lumen. Headaches may be possibly due to the accumulation of cyclic adenosine monophosphate in susceptible patients.[4]

Of those who had adverse events, the drug was completely stopped in four (out of six) patients while in the other two subjects; the dose was reduced to 45 mg. The drug was restarted in those four patients in whom it was stopped after 2 months and slowly increased up to 45 mg. No appreciable modifications were made in the adjunct treatment received by all these patients during this period. Disease had a good and comparable remission in terms of reduced erythema, scaling and size of lesions, with excellent tolerability of drug at this dosage in all cases. Remission could also be maintained during the follow-up visits. Hence, the dose was not further increased to 60 mg.

In the next five patients who were given a lower dose of apremilast, an appreciable remission in disease without developing any significant side effects was observed. The response in two of the patients in this group who had apremilast as the only systemic agent was also very good. The maximum beneficial effect was observed in an average of 4.48 ± 0.96 weeks. Nonresponders to the drug were nil. The hemogram, liver, and the renal function tests of all patients were normal on follow-up visits.

In real practice, apremilast was withdrawn from patients in a greater proportion than that reported in clinical trials in the treatment of psoriasis due to many factors.[5,6] Tolerability of the drug at 60 mg dosage is always questionable.[5] Our observation adds onto the daily experience with the drug in a tertiary care center. The main limitations of our observations are the small sample of patients and the nonuniformity in drug/adjunct selection accepting the individualized treatment of physician for each patient in our center. Our vital observation despite the limitations is that clinical response of psoriasis to apremilast remains good or unaltered at a lower dosage recommending it as a good option to tackle the gastric side effects seen at higher dosages.

Studies analyzing the efficacy and adverse effects of apremilast at lower dose regimens are warranted to create a robust understanding of the drug characteristics.

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Conflicts of interest

There are no conflicts of interest.

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