Review Article

Unconventional treatment options in psoriasis: A review

Shekhar Neema, Sunmeet Sandhu[1], Ankan Gupta[2], Soumya Jagadeesan[3], Biju Vasudevan

Department of Dermatology, Armed Forces Medical College, Pune, Maharashtra, [1]Department of Dermatology, Command Hospital Air Force, Bengaluru, Karnataka, [2]Department of Dermatology, Christian Medical College, Vellore, Tamil Nadu, [3]Department of Dermatology, Amrita Institute of Medical Sciences, Cochin, Kerala, India

Abstract

Psoriasis is a common skin disease that affects 1–3% of the general population. The treatment depends on body surface area involved, quality of life impairment and associated comorbidities. The treatment options include topical therapy, phototherapy, conventional systemic therapy (methotrexate, cyclosporine and acitretin), biologics and oral small molecules (apremilast and tofacitinib). Despite the availability of newer therapies such as biologics and oral small molecules, many a time, there is a paucity of treatment options due to the chronic nature of the disease, end-organ toxicity of the conventional drugs or high cost of newer drugs. In these scenarios, unconventional treatment options may be utilized as stand-alone or adjuvant therapy. In this review, we have discussed these uncommonly used treatment options in the management of psoriasis.

Key words: Psoriasis, therapeutics, therapy, treatment

Introduction

Psoriasis is a common T-cell mediated disorder seen in approximately 1–3% of the general population.[1] Once considered a skin disease alone, psoriasis is now considered to be part of a multi-system inflammatory disorder. Moreover, the chronicity of the disease has a significant psychosocial impact and affects the quality of life of the patient and their caregivers. Hence, adequate treatment of the disease is of utmost importance to stop the "psoriatic march."[2]

Lifestyle modifications, assessment of comorbidities and removal of precipitating factors need to be part of the therapy. Conventional pharmacotherapy includes topical agents, phototherapy, first-line systemic therapy (methotrexate, cyclosporine and acitretin), biologics and oral small molecules such as apremilast. The choice of the systemic drug depends on the patient's age, comorbidities, prior response to treatment, severity and stability of the disease and the cost of treatment.[3] It is not uncommon to come across "difficult to treat" psoriasis patients who have not responded, not tolerated or have depleted all well-established treatment options because of comorbidities, adverse effects or high cost of the drugs. This leaves clinicians with only a few options to choose an alternative strategy for the management of psoriasis. In this review, we will discuss the non-pharmacological measures, drugs and treatment strategies that are considered unconventional and have not been approved by regulatory agencies for the management of psoriasis. The treatment options are classified in Table 1.

Thiazolidinediones (TZD)

Peroxisome proliferator-activated receptors (PPAR) are expressed on keratinocytes and induce differentiation of keratinocytes, inhibit terminal growth and reduce inflammatory response. Thialzolidonediones are anti-diabetic drugs which activate nuclear peroxisome proliferator-activated receptors and could help in the management of psoriasis. Pioglitazone and rosiglitazone are available thialzolidonediones, of which pioglitazone has been better studied for its effect on psoriasis. Pioglitazone has a dose-dependent effect with higher percentage of patients achieving 75% reduction in the Psoriasis Area and Severity Index (PASI) score (PASI75) with a 30 mg daily dose as compared to 15 mg once a day. A pilot trial of pioglitazone 15 mg, 30 mg and placebo found mean PASI reduction of 41.1%, 47.5% and 21.6%, respectively.[4] A placebo-controlled trial conducted by Hafez *et al*. found 21% (5/24) patients achieving PASI75 in pioglitazone 30 mg group as compared to placebo (1/24) at ten weeks.[5] Other studies found pioglitazone in

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Corresponding author: Dr. Shekhar Neema, Associate Professor, Department of Dermatology, Armed Forces Medical College, Pune, Maharashtra, India. shekharadvait@gmail.com

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Table 1: Classification of unconventional therapeutic options in the management of psoriasis

General lifestyle measures	Weight loss, smoking cessation, moderating alcohol consumption, exercise and yoga
Nutrition	Supplements: Vitamin D, folic acid and probiotics Diet: Gluten free, very low-calorie ketogenic diet, intermittent fasting
Prevention of triggers	Antibiotics, tonsillectomy, staphylococcal decolonization
Immunomodulators	Mycophenolate mofetil, azathioprine, leflunomide, hydroxyurea, tofacitinib
Anti-neutrophilic drugs	Dapsone, colchicine
Drugs intended to improve metabolic parameters	Peroxisome proliferator-activated receptors agonists, biguanides, glucagon like peptides
Procedures	Radiotherapy/Grenz Ray, bariatric surgery
Others	Somatostatin, bevacizumab, sulfasalazine, low-dose naltrexone, intravenous immunoglobulin

combination with methotrexate or acitretin to be superior to methotrexate or acitretin as monotherapy.[6,7] A recent meta-analysis concluded that pioglitazone alone or in combination with methotrexate, acitretin or phototherapy is safe and effective for management of plaque psoriasis as compared to placebo. Adverse effects such as nausea, raised liver enzymes and weight gain were noticed with the use of pioglitazone but were not found to be statistically significant. Serious adverse effects including hypoglycemic events were not reported in any studies included in meta-analyses.[8,9] Pioglitazone also improved metabolic parameters in patients with psoriasis.[10]

Glucagon-like Peptide (GLP), Biguanide and Dipepidyl Peptidase 4 (DPP IV) Inhibitors

Glucagon like peptide 1 (GLP-1) is a hormone required for glucose homeostasis. These receptors are identified in immune cells, inhibit tumor necrosis factor-α (TNF-α) and have anti-inflammatory effects; they are also expressed in psoriasis plaques.[11] Liraglutide is a Glucagon like peptide 1 agonist available as a multidose pen; the dose varies from 0.6 to 1.8 mg subcutaneous once a day. A patient of psoriasis with Type 2 diabetes mellitus showed improvement in an isolated case study.[12] A study conducted in glucose tolerant obese patients with psoriasis showed significant weight loss but no improvement in psoriasis as compared to controls at eight weeks.[13] A prospective cohort study showed significant improvement in PASI, waist circumference, weight reduction and glycosylated haemoglobin (HbA1c) levels at 12 weeks in patients of psoriasis with Type 2 diabetes .[14]

Dipeptidyl peptidase 4 (DPP IV) inhibitors also known as gliptins are oral hypoglycemic drugs that act by increasing the level of glucagon-like peptide 1. The commonly used drugs available in this class are sitagliptin, linagliptin and vildagliptin. They can improve keratinocyte differentiation and decrease T cell activation.[15] A randomized controlled trial in patients without Type 2 diabetes mellitus comparing sitagliptin and narrow band ultraviolet B (NBUVB) with NBUVB alone found significant improvement in PASI in combination group without significant adverse effects.[16]

Metformin is a biguanide oral anti-diabetic drug used commonly in the management of Type 2 DM. It inhibits keratinocyte proliferation and release of pro-inflammatory cytokines through mammalian target of rapamycin (mTOR) pathway and activation of mitogen-activated protein kinase signaling pathway.[17] In a placebo-controlled open label study using metformin 1000 mg/day for 12 weeks, improvement in metabolic parameters and erythema, induration and scaling was reported in the treatment group.[18] A cross-sectional study found significantly improved quality of life in patients receiving metformin and methotrexate combination as compared to methotrexate alone.[19] A recent meta-analysis on antidiabetic medicine found that metformin is not very effective in management of psoriasis. This may be due to lack of available data as only one study was available.[20]

Probiotics

The skin and gut microbiota are complex ecosystems and remain in symbiosis with the host. The gut microbiome influences host immune system, enables immune tolerance of environmental antigens and protects against potential pathogens. The alterations in this ecosystem, also known as dysbiosis, is found to be associated with skin diseases such as psoriasis, atopic dermatitis and acne vulgaris.[21] In psoriasis, the gut microbiome is altered, with decrease in symbiont bacteria such as *Lactobacillus* spp., *Bifidobacterium* spp. and Faecalibacterium prausnitzii.[22] The role of *Streptococcus* in the pathogenesis of guttate psoriasis is well known. The colonization of skin by *Staphylococcus aureus*, *Malassezia* and *Candida albicans* exacerbates psoriasis. Almost 10% patients with inflammatory bowel disease are diagnosed with psoriasis indicating a strong association of psoriasis with gut inflammation.[23]

Probiotics are viable bacteria with beneficial effects. Various strains have shown beneficial effects in psoriasis in experimental and clinical studies. Mice fed with *Lactobacillus pentosus showed* decreased pro-inflammatory cytokines (tumour necrosis factor (TNF)-α, interleukin (IL)-17, IL-6 and IL-23) and developed milder imiquimod induced psoriasis as compared to controls.[24] The evidence for the use of probiotics in patients with psoriasis is limited but encouraging. Groeger *et al*. demonstrated improvement in inflammatory biomarkers (c-reactive protein, TNFα and IL-6) in patients who were administered *Bifidobacterium infantis* 35624 as compared to controls at eight weeks.[25] A randomized controlled trial (RCT) using probiotic mixture showed improvement in PASI and physician global assessment in probiotic group as compared to placebo at 12 weeks but the difference was not statistically significant.[26] The evidence for the use of probiotics as an adjunct in management of psoriasis is limited and needs larger studies.

Bariatric Surgery

Psoriasis is found to be significantly associated with obesity. Obesity may co-exist, predate, or develop after diagnosis of psoriasis.[27] Increased body-mass index is associated with more severe and refractory disease and weight loss results in better control of the disease.[28] Bariatric surgery is a surgical procedure performed on gastrointestinal system that helps in body weight reduction; it consists of various procedures such as gastric

banding, gastric bypass, sleeve gastrectomy and biliopancreatic diversion with duodenal switch. Gastric bypass was found to be associated with reduced risk and improved prognosis of psoriasis and psoriatic arthritis, in a population-based cohort study.[29] A study on morbidly obese patients with psoriasis who underwent gastric bypass also reported improvement in psoriasis in 39.4% (13/33) patients; the degree of post-operative weight loss and type of procedure (Roux-en-Y gastric bypass) was significantly associated with the improvement in psoriasis.[30] Another study on ten patients showed that 70% of patients remained in remission for psoriasis six months after surgery; three out of four patients on systemic therapy discontinued medications resulting in significant improvement in the quality of life.[31] There is a significant weight loss following surgery which may result in improvement in comorbidities; however, improvement in psoriasis is seen even before weight loss begins and may be related to glucagon-like peptide 1. Its level increases up to 20 times after gastric bypass surgery but not during restrictive surgeries such as gastric banding; hence, glucagon-like peptide 1 may be responsible for the improvement in psoriasis.[32] Bariatric surgery, especially gastric bypass may be a useful option in patients with morbid obesity and refractory psoriasis.

Bevacizumab

Vascular endothelial growth factor (VEGF) is an important mediator of angiogenesis. Vascular phenomena such as vascular dilatation, elongation and increased capillary permeability are parts of psoriasis pathogenesis and Vascular endothelial growth factor A is highly expressed in lesional psoriatic skin. A transgenic mouse model that expressed Vascular endothelial growth factor A developed skin lesions resembling psoriasis which improved by blocking Vascular endothelial growth factor A.[33] Bevacizumab is a monoclonal antibody that acts against Vascular endothelial growth factor. There are reports of improvement in co-existent psoriasis in patients of metastatic renal cell carcinoma and colon carcinoma treated with bevacizumab.[34,35] The exact place of this drug in the management of psoriasis is not yet defined; it seems to be a promising drug in the management of psoriasis, especially in presence of co-morbidities where bevacizumab is used as a primary indication, such as in diabetic retinopathy.

Colchicine

Colchicine is a naturally occurring alkaloid derived from the plant, *Colchicum autumnale*. It inhibits micro-tubule polymerisation and cell division, as well as migration and signal transduction, especially in leukocytes. There are clinical studies that have shown improvement in psoriasis with oral colchicine. A study involving 22 patients with psoriasis in the dose of 0.02 mg/kg for two–four months showed improvement in eight out of nine patients with thin plaques and in all patients (8/22) who suffered from arthralgia. Patients with thick, chronic stable plaque psoriasis did not show much improvement.[36] An RCT comparing 2.1 mg colchicine per day with methotrexate 7.5 mg/week showed a mean reduction in PASI of 45 ± 7.56% in the colchicine group as compared to 52.25 ± 8.93% in the methotrexate group.[37] The use of colchicine in palmoplantar pustulosis is more common and is supported by many studies. A case series of 32 cases treated with colchicine 1–2 mg daily showed complete resolution of pustulation in 13 and significant improvement in 14 patients.[38] Colchicine has also been used in management of generalized pustular psoriasis in a few cases and recently, it has been used in combination with guselkumab.[39,40] Gastrointestinal adverse effects are common and dose limiting.

Immunomodulators

Azathioprine

Azathioprine is a thiopurine and works by inhibiting purine synthesis required for the proliferation of cells, especially leukocytes. An RCT on 50 patients comparing methotrexate 10 mg weekly with azathioprine 1–3 mg/kg found that excellent and good response was seen in 27% and 55% of patients in the azathioprine group at eight weeks.[41] In an open label study involving 50 patients using azathioprine 300 mg weekly for 24 weeks; 42% (21/50), 36% (18/50) and 22% (11/50) patients achieved PASI75, PASI90 and PASI100, respectively.[42] It can also be used in the management of concomitant psoriasis and bullous pemphigoid.[43]

Mycophenolate mofetil (MMF)

It is a prodrug of mycophenolic acid which blocks de-novo purine synthesis, thereby interfering with T cell proliferation. An RCT involving 38 patients comparing mycophenolate mofetil 2 g/day to methotrexate 7.5 mg/week found a reduction in PASI score from 16.46 ± 5.29 to 3.17 ± 2.35 in the methotrexate group and 17.43 ± 7.42 to 3.97 ± 5.95 in patients treated with mycophenolate at 12 weeks ($P > 0.05$).[44] This means that both the treatments showed efficacy in treatment of psoriasis, but there was no statistically significant difference between methotrexate and mycoohenolate mofetil.Another open-labeled study involving 23 patients with moderate to severe psoriasis using mycophenolate 2–3 g/day showed a 47% reduction in PASI at 12 weeks.[45] It has also been used in combination with low-dose cyclosporine (2.5 mg/kg) in patients who failed previous systemic therapies. Seven out of nine patients showed good disease control without any evidence of additional toxicity.

Hydroxyurea

It is an antimetabolite used in the management of hematologic and solid organ malignancies. It works by inhibiting DNA synthesis and reducing cell turnover and is effective in the management of psoriasis. Due to the narrow therapeutic window and the availability of other agents, it is used only for the management of recalcitrant psoriasis. In a study involving 85 patients, where it was used in the dose of 0.5–1.5 g daily; 51 (60%) and 68 (80%) patients showed complete and good to moderate response, respectively. Adverse effects occurred in 37 (43%) patients and the drug was discontinued in six patients.[46] In another study with 31 patients of recalcitrant psoriasis; 70% reduction in PASI score was observed at eight weeks. The dose used was 1–1.5 g/day and none of the patients required therapy discontinuation.[47]

Tacrolimus

It is a calcineurin inhibitor and the mechanism of action is similar to cyclosporine, though it is considered 100 times more potent inhibitor of T cell activation. A European multicentric study involving 19 patients in a dose ranging from 0.05 to 0.15 mg/kg orally found 70% or more reduction in PASI at

nine weeks in 12 (63%) patients.[48] Another study involving 26 patients in a dose of 0.1 mg/Kg orally, reported PASI75 in 73.1% (19/26) and PASI90 in 42.3% (11/26) patients.[49]

Tofacitinib

It is an oral small molecule which inhibits Janus kinase (JAK) 1 and 3 signaling. It is approved for the treatment of psoriatic arthritis, but not plaque psoriasis. A randomized controlled trial found that PASI75 was achieved in 39.9%, 59.2% and 6.2% with twice daily tofacitinib 5 mg, 10 mg and placebo respectively at week 16.[50] In a study on Japanese patients, it was found that 62.8% and 72.7% patients achieved PASI 75 at 16 weeks with 5 mg and 10 mg twice a day dose, respectively and efficacy was maintained throughout 52 weeks.[51] A recent meta-analysis of RCT's including 3743 patients found tofacitinib (5 mg or 10 mg) to be more effective than placebo but with higher incidence of adverse effects.[52] Upadacitinib is selective JAK1 inhibitor and is approved for treatment for psoriatic arthritis in the dose of 15 mg/day.[53]

Leflunomide

It is an immunosuppressant which inhibits T cell activation and proliferation by inhibiting pyrimidine synthesis. It is Food and Drug Administration (FDA)-approved to treat rheumatoid arthritis. A placebo-controlled trial for the treatment of psoriatic arthritis found that it is effective in the management of skin disease.[54]

Miscellaneous Drugs

Sulfasalazine

It is an anti-inflammatory agent, used in the management of inflammatory bowel disease. An RCT reported moderate to marked improvement in 82% of patients at eight weeks.[55] A placebo-controlled trial for psoriatic arthritis reported significant improvement in joint symptoms and morning stiffness at eight weeks compared to placebo.[56]

Dapsone

It is a sulfone drug and has antimicrobial and anti-inflammatory actions. The anti-inflammatory action is due to inhibition of neutrophil myeloperoxidase and impaired neutrophil chemotaxis. It has been reported to be effective in the management of pustular psoriasis in various case reports. A case series involving five patients with treatment-resistant pustular psoriasis showed good response in four patients.[57] There are reports of improvement in therapy-resistant generalized pustular psoriasis and inverse psoriasis with dapsone.[58,59]

Isotretinoin

It is a first-generation systemic retinoid used in the management of acne. A randomized study involving 60 patients who received either isotretinoin or etretinate at the dose of 1 mg/kg with psoralen-UVA therapy concluded that isotretinoin is as effective as etretinate for psoriasis management.[60] It has also been used for the management of generalized pustular

Table 2: Adverse effects of various discussed therapeutic modalities

S. No.	Drug	Dose	Common adverse effects
1.	Pioglitazone	15–30 mg OD	Edema, nausea, raised liver enzymes, weight gain/loss, hypoglycemia
2.	Liraglutide	0.6 mg SC per day for 1 week; followed by 1.2 mg OD	Nausea, diarrhea, vomiting, dyspepsia, headache, injection site reaction
3.	Metformin	1000 mg per day	Gastrointestinal adverse effects (Nausea, vomiting, abdominal distension, constipation, dyspepsia), flatulence, hypoglycemia, asthenia, lactic acidosis (rare)
4.	Sitagliptin	100 mg per day	Hypoglycemia, nasopharyngitis, headache
5.	Colchicine	1–2 mg per day	Nausea, vomiting, diarrhea, myelosuppression, rhabdomyolysis
6.	Azathioprine	1–3 mg/kg/day	Myelosuppression, liver toxicity, hypersensitivity syndrome, opportunistic infections
7.	MMF	2–3 g/day	Dose-dependent gastrointestinal effect such ass nausea, vomiting, diarrhea and infections
8.	Hydroxyurea	0.5–1.5 g/day	Myelosuppression, renal toxicity, infections, cutaneous adverse effects (alopecia, dermatomyositis such as eruption, hyperpigmentation of skin/nails and leg ulcers)
9.	Tacrolimus	0.05–0.15 mg/kg	Diarrhea, abdominal pain, acral paraesthesia, altered fasting blood sugar levels, hypertension and deranged serum creatinine
10.	Tofacitinib	5–10 mg BID	Nasopharyngitis, upper respiratory tract infection, diarrhea, headache, hypertension, increased cholesterol levels, gastroenteritis, anemia, nausea, serious infection and venous thromboembolism
11.	Leflunomide	100 mg/day X 3 days; 20 mg OD	Diarrhea, infections, agranulocytosis, hepatitis
12.	Sulfasalazine	2–3 g per day Start with 0.5 g TDS	Gastrointestinal intolerance Leukopenia and agranulocytosis Exanthem, SJS/TEN
13.	Dapsone	50–100 mg/day	Hemolytic anemia, methemoglobinemia, leukopenia, agranulocytosis, DRESS, TEN and exanthem peripheral neuropathy
14.	Isotretinoin	1–2 mg/kg/day	Xerosis, desquamation, photosensitivity, pyogenic granuloma, staphylococcus infections, dry eyes, deranged lipid profile, pseudotumor cerebri, hepatotoxicity and teratogenicity
15.	Somatostatin	250 µg/h for 96 h	Infusion reaction, abdominal pain, steatorrhea, diarrhea, malabsorption and gall stone formation
16	Fumaric acid esters	upto 1.2 gms per day	Gastrointestinal intolerance, leukopenia, lymphopenia, flushing

OD: Once a day, BID: Twice a day, TDS: Thrice a day, SC: Subcutaneous, MMF: Mycophenolate mofetil

Table 3: Level of evidence and place in management

S. No.	Drug	Level of evidence	Place in management
1	Pioglitazone	1a	Patients with metabolic syndrome (MS)
2	Liraglutide	4	Obese patients with Type 2 DM
3	Metformin	2b	Psoriasis with metabolic syndrome
4	Sitagliptin	2b	Psoriasis with Type 2 DM
5	Probiotics	2b	As an adjunct to conventional treatment
6	Bariatric surgery	4	Morbid obesity with psoriasis
7	Bevacizumab	4	Not defined; use for primary indication
8	Colchicine		
	Palmoplantar pustulosis	1b	First line
	Psoriasis	2b	Adjunct to systemic treatment in patient with thin plaque
	GPP	4	Not well defined
9	Azathioprine	2b	Psoriasis with bullous pemphigoid
10	MMF	2b	Adverse effect to first line treatment
11	Hydoxyurea	2b	Recalcitrant psoriasis; unavailability of other options
12	Tacrolimus	2b	Same indications as cyclosporine with better adverse effect profile
13	Tofacitinib	1a	Psoriatic arthritis with psoriasis
14	Leflunomide	5	Psoriatic arthritis with psoriasis
15	Sulfasalazine	1b	Psoriatic arthritis with psoriasis
16	Dapsone	4	Palmoplantar pustulosis
17	Isotretinoin	4	With phototherapy in women of child bearing age when acitretin cannot be used
18	Somatostatin	4	Not defined
19	FAE	1a	Can be used as first line therapy in moderate to severe psoriasis.
20	Dietary measures	2b, 3b, 4	Can be tried in all patients

1a: Systematic review of RCT, 1b: RCT with narrow confidence intervals, 2a: Systematic reviews of cohort disease, 2b: Individual cohort study and low quality RCT, 3a: Systematic review of case-controlled studies, 3b: Case-controlled studies, 4: Case-series and poor-quality cohort and case-controlled studies, 5: Expert opinion

psoriasis.[61] Isotretinoin has a shorter half-life and may play a role in management of psoriasis in women of child-bearing age. It may be used in case acitretin is contraindicated, like in women of childbearing age. Acitretin and etretinate have similar problem of requirement of long-term contraceptives.

Antibiotics

There is evidence to suggest that bacterial infection can trigger or exacerbate psoriasis especially guttate psoriasis. Various antibiotics have been used for management of various forms of psoriasis. Guttate psoriasis is the most common psoriasis variant in which antibiotics are used. RCTs comparing penicillin for two weeks with placebo found no treatment benefit.[62] An RCT comparing rifampicin 600 mg/day for 60 days with placebo found significant improvement in rifampicin group.[63] In chronic plaque psoriasis, long-term benzathine penicillin (every two weeks for 12 weeks) and azithromycin 500 mg per day for four weeks showed significant improvement in PASI.[64,65] Most studies suggest that antibiotics are effective in psoriasis only if they are used for long-term (four weeks and more) and not as short course.

Somatostatin

It is a human growth factor inhibitor. Somatostatin has variable efficacy in the management of psoriasis. In a study involving 20 patients with severe and recalcitrant psoriasis; somatostatin infusion (250 µg/h for 96 h) resulted in significant improvement in psoriasis and psoriatic arthritis with the infusion being well tolerated.[66] Another study showed complete or partial remission in psoriasis in 22 out of 26 patients and rapid reduction in joint pains in all four patients.[67]

Other rarely used drugs include low-dose naltrexone which has been recently used in one patient with erythroderma.[68] Intravenous immunoglobulin has also been used in the management of treatment refractory psoriasis in the pre-biologic era in the dose of 2 g/kg over three days with beneficial effects.[69]

Fumaric acid esters (FAE)

Fumaric acid esters are derivative of fumaric acid and has been used in treatment of psoriasis since long time specially in Germany. It has anti-inflammatory and immuno-modulatory effects. The available drug is a combination of dimethylfumarte and monoethyl fumarate. The highest recommended dose is 1.2 gms per day and the dose is built up slowly to reduce gastrointestinal tolerance. PASI75 is achieved in 50-60% at 16 weeks in patients treated with fumaric acid esters.[70]

Dietary Measures

Dietary measures have been used in the management of psoriasis as adjunctive therapy with variable efficacy. Weight loss in patients with psoriasis improves disease control and better treatment response. Dietary modification is commonly undertaken by psoriasis patients in the hope of improved response. Various types of diets have been used in the management of psoriasis and they possibly work by reducing pro-inflammatory cytokines.

Ketogenic diet is a high fat, adequate protein and low carbohydrate diet. A case report described restoration of treatment response to adalimumab after four weeks of a very-low calorie ketogenic diet (VLCKD).[71] An open label clinical trial involving this diet as induction (four weeks) followed by a hypocaloric, balanced Mediterranean-like diet (six weeks) showed PASI 50 and PASI 75 in 36 (97%) and 24 (64.9%) patients, respectively, at ten weeks.[72] Mediterranean diet contains a high amount of fruits, vegetables, cereals and olive oil with a restriction on consumption of dairy products, red meat and alcohol except wine. There is no causal relationship between this diet and the severity of psoriasis, but studies have found an association of severe psoriasis, psoriatic arthritis and cardiovascular risk factors with poor adherence to the Mediterranean diet.[73,74]

Celiac disease is more common in patients with psoriasis and elevated antigliadin anti IgA antibody is seen in psoriasis patients even in the absence of celiac disease.[75,76] A gluten free diet resulted in improvement in psoriasis, even in those without celiac disease. The presence of antigliadin antibody may act as a prognostic marker for response to gluten free diet.[77]

Intermittent fasting (IF) is a type of eating pattern in which there is no consumption of food for a fixed duration. The most

common type of IF is 16:8 in which fasting time is 16 h and feeding time, eight hours. This fasting time may be extended. There is some evidence to suggest that IF improves metabolic parameters and longevity and reduces the incidence of obesity and cancer.[78] The data regarding the effectiveness of IF on improvement in psoriasis are limited; one study showed beneficial effects of Ramadan fasting on psoriasis.[79]

The adverse effect and place in the management of various treatment modalities are discussed in Table 2 and level of evidence for various modalities is tabulated in Table 3.

Conclusion

To sum up, though newer anti-psoriatic drugs are being developed, evaluated and incorporated into clinical practice on a regular basis, there is a sub-set of patients in whom we need to look beyond biologics or the conventional first-line systemic agents. The unconventional therapeutic strategies that we have discussed here are less well-known in the treatment of psoriasis. Many of them can complement the first-line agents or can replace them when the patients do not tolerate or respond to conventional agents or cannot afford them. The current evidence for their use in psoriasis as well as the strengths and weaknesses of such therapies have been highlighted to help the clinician make an informed choice.

Declaration of patient consent

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Conflicts of interest

There are no conflicts of interest.

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