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Oral mini -pulse steroid therapy in the treatment of dermatological diseases: review of the literature

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Abstract

Background: Pulse therapy is a type of systemic management in which large amounts of medications are administered to patients in short time and intervals (e.g. weekly) to get the stronger effects of medication sooner and avoid long term use of them.

Objective: To determine how therapy-resistant dermatology diseases respond to oral mini-pulse steroids .

Methods: Articles with Mesh terms "pulse therapy", "dermatology" and "steroid" were searched in PubMed database .we chose case reports and clinical randomized controlled trials on oral steroid mini- pulse therapies of dermatology diseases.

Results: Most articles and case reports mentioned the successful treatment of refractory diseases like lichen planus, vitiligo and alopecia areata with oral mini -pulse steroids.

Conclusions: Oral mini pulse has stronger beneficial effects and fewer side effects than daily systemic corticosteroids. Since it is administered twice weekly , patient compliance will be better. Therefore, oral corticosteroids mini- pulse can be a good alternative to daily systemic corticosteroids in dermatologic diseases.

Introduction

Corticosteroids have been used in dermatology since a long time ago. Pulse therapy is a type of systemic management in which large amounts of medications are administered to patients in short time and intervals (e.g. weekly) to get the stronger effects of medication sooner and avoid long term use of them [1]. Pulse steroid therapy was firstly used in a patient with renal allograft in 1969 [2]. Oral mini pulse (OMP) is a type of pulse steroid therapy which is given orally in intervals to patients [1]. It is more comfortable for patients to comply with than daily systemic steroid therapy [3].

Pasricha et al. [4] used OMP in the treatment vitiligo for the first time and later it was used in other dermatological conditions such as lichen planus, alopecia areata, nail dystrophy, infantile periocular hemangioma and etc.

Our article is a short review about the clinical use of oral mini- pulse steroid in the treatment of different dermatological diseases to determine how therapy-resistant cases respond to oral steroid pulse therapy till now.

Methods:

We searched the PubMed data bank using the following MESH-terms: pulse therapy, steroid, dermatology. We limited our search for clinical trials and case reports on treating dermatologic refractory cases with only oral mini pulse steroids. We didn't have access to the most full articles so we used abstract forms of the articles. There were 7 case reports and 17 original articles found on oral mini- pulse therapy and dermatology diseases.

Results:

Lichen Planus

Lichen planus (LP) is mucocutaneous chronic inflammatory disease [3,5]. The definite treatment of LP has not yet been found, but systemic corticosteroids have been used for severe LP. Since systemic corticosteroids should not be used daily for a long time taking corticosteroids as OMP may have more efficacy and less adverse effects [3,6].

In a randomized clinical trial (RCT) on the effectiveness of OMP (betamethasone 5mg on two consecutive days) compared to triamcinolone 0.1% orabase in patients with oral LP, 68% of the patients in OMP group responded earlier [6]. In another study on patients with cutaneous LP, the majority of the patients in the OMP group (80%) who took 5mg Betamethasone on two consecutive days for 6 weeks showed complete remission in comparison to 5% in the control group [3]. Relief of itching by OMP was significantly better than control group.

In a study, 22.85% of 35 patients with LP, who took 6 mg betamethasone weekly, had 50-100% remission of the disease [7]. Moreover, Mittal et al [8] evaluated the efficacy of OMP using 5mg betamethasone twice weekly. The majority of the patients (60%) had excellent response (75-100% flattening of the Lesions) and 40% had good response (50-75% remission).

In a case report, acute generalized LP improvement was seen after taking 5 mg betamethasone on 2 consecutive days for 3 weeks. The patient did not develop any side effects and stayed in remission[9]. In another report, a case of generalized bullous LP improved after taking 5mg betamethasone twice weekly for 2 weeks [10].

Vitiligo

Vitiligo is an acquired, but sometimes inherited disorder, characterized by depigmented macules that may progress with time. Many studies showed that it is an autoimmune disease. The current treatments for this disease include: topical steroids, oral steroids, phototherapy, grafting or combination therapies [11,12,13].

Pasricha et al [14] treated extensive vitiligo with oral betamethasone pulse (5mg daily for 2 consecutive days per week). Disease progression was halted in 89% of the patients within 1-3 months and repigmentation was seen in 80% of patients within 2-4 months. Moreover, Kanwar et al[15]. evaluated the efficacy of different doses of oral mini pulse (5 mg up to 25 mg of dexamethasone on 2 consecutive days per week) on patients with unstable vitiligo. In 43.8% of the patients, progression of the disease stopped and mild to moderate repigmentation was observed, while in 56.2% no response was seen. In another study, the effectiveness of phototherapy in combination with oral mini pulse (0.1 mg/kg betamethasone on 2 consecutive days a week) was assessed. Combination therapy of narrowband UVB with oral mini pulse improved the repigmentation to 18% in comparison to phototherapy alone (8%). It was proposed that oral mini pulse might help arrest the disease progression [16]. In another study, vitiligo progression stopped in 87.7% of patients with low dose prednisolone (0.3mg/ kg daily) for 2 months. In 70.4% of cases repigmentation was seen[17]. In another study, vitiligo progression was arrested in 88% of patients treated with 10mg oral dexamethasone for 2 consecutive days per week and repigmentation was seen only in 17.2% [18]. In the study of Banerjee et al [19], vitiligo spreading was stopped in 90% of 100 patients and repigmentation was reported in 76%. The patients took low dose prednisolone daily (0.3 mg/ kg) for 4 months.

In a research by Majid et al [20], 400 children with progressive vitiligo received oral methylprednisolone (0.8mg/kg with maximum dose of 32mg) on 2 consecutive days per week for 6 months. The progression of the disease was halted in more than 90% of the children and moderate repigmentation was seen in 65.5% of the patients.

Complete repigmentation in a 5 year old girl with extensive vitiligo was reported after treatment with 2.5mg betamethasone twice weekly for 3 months, no side effects were seen [21,22].

Alopecia areata

Alopecia areata(AA) is an autoimmune disease that results in non scarring alopecia. Since it is an autoimmune disease, most treatments depend on immune modulating medications [23].

Pasricha et al [24] evaluated the effectiveness of oral mini pulse of betamethasone (5 mg daily for 2 consecutive days per week) in an 8 year old girl with alopecia totalis. Regrowth of hair on the entire scalp was reported in 3 months.

In the study of Sharma et al [25], 30 patients with extensive alopecia areata were treated with oral betamethasone (5 mg daily for 2 consecutive days per week) for 12 weeks. Complete to excellent hair regrowth was seen in 63.3% of the patients, but in 20% of patients no hair growth was observed. In another research, 75% of the patients had excellent to good response to 5mg betamethasone twice weekly [26].

Bajaj et al [27] reported that 63.3% of cases with extensive alopecia areata responded well to oral prednisolone (30 mg daily for 3 consecutive days in a week for 6 months), while 27.3% of the patients with alopecia totalis had good to average re-growth of hair. In another report, 66.6% of 15 patients with extensive alopecia areata had excellent response while 26.6% showed good response to 5mg betamethasone on 2 consecutive days a week [28].

Researchers in another study assessed the effectiveness of 0.1 mg /kg betamethasone twice weekly on 15 patients; eight patients with alopecia totalis/universalis and 4 with ophiasis. Eleven patients completely responded to treatment [29].

Miscellaneous diseases

Efficacy of OMP in the treatment of trachyonychia was evaluated in two studies. In one study, the patient responded completely, while in the other one, OMP was ineffective [30,31].

A 1 month-old infant with periocular haemangioma had 90% improvement of haemangioma after administration of 2 mg betamethasone twice a week for 12 weeks [32].

In another study, 10 patients with severe chronic urticaria treated with 16 mg methylprednisolone twice a week for 2 months showed significant improvement in terms of wheal diameters and itching sensation [33].

Side effects of oral mini -pulse therapy

Although corticosteroids have great effects on many autoimmune and dermatological diseases, they can cause serious problems which can happen even with short time use. Long term use of corticosteroids can cause adrenal suppression, avascular necrosis, osteoporosis and growth retardation. Since oral mini pulse is administered in intervals, fewer side effects are reported than daily use of low- dose corticosteroids.

Researchers showed that cortisol levels decreased significantly after the second dose of dexamethasone in a week, but returned to baseline range during the 5 days in which patient was off treatment so, OMP did not lead to adrenal suppression [18].

The most common side effect reported by researches was weight gain. Epigastric discomfort and acne flare up were other complaints. Only in one study, tinea capitis and corporis developed in 4% of patients [20].

In a study, prolonged hiccups after administration of the second dose of OMP (5 mg betamethasone) in a 22 year- old man was seen [34]. In other report, severe bradycardia after administering 125 mg methylprednisolone as mini-pulse in 2 patients was seen. Bradycardia

was reported previously by using methylprednisolone intravenously [35].

Discussion

In studies on the treatment of LP with OMP almost all patients had good response [6-10] (Table1).

	OMP	Dose (mg)	Response (%)	Side effect (%)	Total (n)
Malhotra et al. [6]	Betamethasone	5 mg/d 2 days a week	68	56	25
Rashid et al. [3]	Betamethasone	5mg/d 2 days a week	80	Not reported	40
Ramesh et al. [7]	Betamethasone	6mg/d Once weekly	22.85	57.1	35
Mittal et al. [9]	Betamethasone	5mg/d 2 days a week	100	20	10

Table1. Response of LP to OMP

In the studies about the management of unstable or generalized vitiligo with OMP or low dose daily prednisolone, all studies concluded that oral mini pulse steroid therapy is useful in improving repigmentation of the lesions and can be combined with phototherapy [14-22] (Table2).

	OMP	Dose (mg)	No progress (%)	Repigmentation (%)	ss Side effects(%)	Total (n)
Pasricha et al. ^[14]	Betamethasone	5mg/d 2 days a week	89	80	22.5	40
Kanwar et al. ^[15]	Dexamethasone	5-15mg/d 2 days a week	43.8	43.8		32
Rath et al. ^[16]	Betamethasone	0.1mg/kg/d twice weekly	90	15.5	50	20
Kim et al. ^[17]	Prednisolone	0.3mg/kg/d daily	87.7	70.4	56.7	81
Radakovic et al. ^[18]	Dexamethasone	10mg/d 2 days a week	88	17.2	69	29
Banerjee et al. ^[19]	Prednisolone	0.3mg/kg/d daily	90	76	Not reported	100
Majid et al. ^[20]	Methyl prednisolone	0.8mg/kg/d 2 days a week	90	65	25.7	400

Table2. Response of vitiligo to OMP

Six studies about the management of extensive and recalcitrant alopecia were conducted. In five studies, oral betamethasone pulse improved the condition and led to hair regrowth in most patients, but oral prednisolone pulse did not have the same effect [24,28]. (Table3).

	OMP	Dose (mg)	Response (%)	Side effects (%)	Total (n)
Sharma et al. [25]	Betamethasone	5mg/d 2 days a week	63.3	26.6	30
Khaitan et al. [26]	Betamethasone	5mg/d 2 days a week	75	43.7	16
Bajaj et al. [27]	Prednisolone	30mg 3days a week	39.2	-	22
Agarwal et al. [28]	Betamethasone	5mg/d 2 days a week	93.2	26.6	15
Deshpande et al. [29]	Betamethasone	0.1mg/kg/d 2 days a week	80%	13	15

Table3. Response of alopecia to OMP

It has been shown that OMP can lead to improvement in trachyonychia, periocular haemangioma and urticaria in some cases. Although most of the studies are in favor of OMP, but it needs further investigations.

Conclusion

Based on the satisfactory results of the above studies on the treatment of recalcitrant forms of lichen planus, alopecia areata and vitiligo, it seems that dermatologists should try oral mini- pulse therapy for some patients with resistant forms of the aforementioned diseases in order to get stronger effects of steroids in a shorter time with less side effects.

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