Authors' reply

Sir,

We are thankful to the author[1-2] for evincing interest in our article.[3]

1. Firstly we focused on newer approaches in scleroderma. Dexamethasone-cyclophosphamide pulse (DCP) therapy is by no means a new approach.
2. The evidence against use of steroids is overwhelming. There is a mountain of evidence from textbooks, and guidelines of medicine, rheumatolology and dermatology detailing the evidence against the use of steroids except for alveolitis, mycocarditis and sometimes for renal involvement[4–22] [Table 1].
3. Steroids have multitude of side effects which add to the already multisystem damage of scleroderma.[13–15]
4. Skin improvement, which is a tool observed by most Indian case reports, is the most nonspecific tool to monitor improvement. Steroids *per se* have no role to play in altering the skin pathology of progressive systemic sclerosis (PSS).[4-8] Glucocorticoids are not effective in improving or preventing skin induration and the progression of systemic sclerosis (SSc; also known as scleroderma).[14]
5. The most crucial aspects is that evidence-based

Table 1: Role of steroids in scleroderma

Scientific data	Use	Conclusion
Scleroderma Foundation	No use	Can be used for myocarditis, alveolitis
Evidence Based Dermatology	No use	Can be used for myocarditis, alveolitis
Cochrane Database	Not disease modifying	-
BAAD Guidelines	Not disease modifying	Can cause scleroderma renal crisis
ACR Guidelines	Not disease modifying	Can be used for myocarditis, alveolitis
American Academy Guidelines	Not disease modifying	-
European Academy Guidelines	Not disease modifying	Gives a sense of well being
Kelley's Textbook of Internal Medicine[7]	Not disease modifying	-
Scleroderma: In Samter's immunologic diseases[8]	Not disease modifying	-
ACP Medicine[9]	Not disease modifying	
Harrison's principles of internal medicine[12]	Not disease modifying	Can be used for myocarditis, alveolitis
	Should not be given	
Rheum Dis Clin North Am[13-16]	Not disease modifying	-
	Should not be given	
Oxford Textbook of Rheumatology[20]	Not disease modifying	-
	Should not be given	

Table 2: Summary of dose effect and relationship of steroids[1–8,12–16,20]

1. Low-dose prednisone (10 mg/day or less)—edematous phase (skin involvement); joint and tendon pain.
2. High-dose prednisone (20-30 mg/day) with steroid-sparing agent such as methotrexate or azathioprine—inflammatory myositis, pericarditis, early active alveolitis.
3. Glucocorticoids have been associated with the development of renal crisis.[5,6]
4. Diffuse cutaneous SSc showed a significant association between prior high-dose glucocorticoids (prednisone 15 mg/d) and the development of scleroderma renal crisis

double blinded trial has never shown steroids to be disease modifying [Table 1].[4–22]

6. To complicate the matter, the disease has a well known spontaneous resolution and the trial has to be factored in any reported trial that shows results.[8,15–18] In other words, a disease in the resolving phase will show a false response to any drug therapy.
7. The evidence for cyclophosphamide is there, but as yet the results of the largest multicentric, multiregional (SCOT) trial is awaited and only after that we can comment on the therapeutic role of cyclophosphamide.[7,12,13,15-18]

Also, all our references were of evidence-based double blinded trials, whereas the references alluded by the author[4–10] are not.

Secondly, the indexed literature does not contain references 4, 6, and 8, referred to by the author.

And case reports are not in any way considered as evidence even in the Cochrane registry of controlled trials, and most of the data reported by the author do not meet the standards of the Cochrane guidelines.

Lastly, the author has excluded two articles reporting the side-effects, which have been reported from India.[20,21] This highlights the risks involved in the indiscriminate use of this form of therapy.

In view of the huge data from scientific journals, specialty books and international guidelines,[3-17,21] the obstinate persistence of DCP pulse in scleroderma is purely a individual perception which is beyond scientific purview as its role has not been mentioned in any evidence-based data to date.

The summary guidelines on steroids gleaned from the wealth of data are given below [Table 2].

Kabir Sardana, V. K. Garg

Department of Dermatology and STD,
Maulana Azad Medical College and Lok Nayak Hospital,
Delhi, India

Address for correspondence: Dr. Kabir Sardana, 466, Sector 28, Noida, UP - 201 303, India. E-mail: kabirijdvl@gmail.com

REFERENCES

1. Pasricha JS. Systemic sclerosis and dexamethasone cyclophosphamide pulse therapy. Indian J Dermatol Venereol Leprol 2009;75:510.
2. Gupta R. Dexamethasome-cyclophosphamide pulse therapy for systemic sclerosis. Indian J Dermatol Venereol Leprol 2009;75:511.
3. Sardana K, Garg VK. Therapeutic trials for systemic sclerosis: An update. Indian J Dermatol Venereol Leprol 2008;74:436-45.
4. Sapadin AN, Fleischmajer R. Treatment of scleroderma. Arch Dermatol 2002;138:99-105.
5. Denton PC. Therapeutic targets in systemic sclerosis. Arthritis Res Ther. 2007;9:S10.
6. Rubin LJ, Black CM, Denton CP, Seibold JR**.** New therapeutic strategies for systemic sclerosis--a critical analysis of the literature. Clin Dev Immunol. 2005;12:165-73.
7. Charles C, Clements P, Furst DE. Systemic sclerosis: hypothesis-driven treatment strategies. Lancet 2006;367:1683-91.
8. Matucci-Cerinic M, Steen VD, Furst DE, Seibold JR. Clinical trials in systemic sclerosis: lessons learned and outcomes. Arthritis Res Ther 2007;9:S7. Review
9. Ruddy S, Harris ED, Sledge CB, Sergent JS, Budd RC. Kelley's Textbook of Internal Medicine, 6TH E-edition, Philadelphia: W.B. Saunders Company; 2006. p. 1326.
10. Austen KF, Frank MM., Atkinson JP, Harvey C. Samter's immunologic diseases, 6th ed. Philadelphia: Lippincott Williams and Wilkins; 2001. p. 1264.
11. Dale DC, Federman DD. ACP Medicine, WebMD,2006. p. 2754-6.
12. Hoyles RK, Ellis RW, Wellsbury J, Lees B, Newlands P, Goh NS, *et al*. A multicenter, prospective, randomized, double-blind, placebo-controlled trial of corticosteroids and intravenous cyclophosphamide followed by oral azathioprine for the treatment of pulmonary fibrosis in scleroderma Arthritis Rheum 2006;54:3962-70.
13. Vanthuyne M, Blockmans D, Westhovens R, Roufosse F, Cogan E, Coche E, *et al*. A pilot study of mycophenolate mofetil combined to intravenous methylprednisolone pulses and oral low-dose glucocorticoids in severe early systemic sclerosis. Clin Exp Rheumatol 2007;25:287-92.
14. Gilliland BC. Systemic Sclerosis (Scleroderma) and Related Disorders. In: Kasper DI, Braunwald E, Fauci AS, Hauser SI, editors, Harrison's principles of internal medicine, 16th edition, New York: McGraw-Hill; 2005. p. 1979-99.
15. Nihtyanova SI, Denton CP. Current approaches to the management of early active diffuse scleroderma skin disease. Rheum Dis Clin North Am 2008;34:161-79; 8.
16. Herrick A. Diagnosis and management of scleroderma peripheral vascular disease. Rheum Dis Clin North Am 2008;34:89-114.
17. Rubin LJ. Treatment of pulmonary arterial hypertension due to scleroderma: challenges for the future. Rheum Dis Clin North Am 2008;34:191-7.
18. Distler J, Distler O. Novel treatment approaches to fibrosis in scleroderma. Rheum Dis Clin North Am 2008;34:145-59. .
19. Pasricha JS, Ramam M, Shah S. Reversal of systemic sclerosis with dexamethasone pulses. Indian J Dermatol Venereol Leprol 1990;56:40-2.
20. Saoji VA. Premature ovarian failure due to cyclophosphamide: a report of four cases in dermatology practice. Indian J Dermatol Venereol Leprol 2008;74:128-32.
21. Ahmad QM, Shah IH, Nauman Q, Sameem F, Sultan J. Increased incidence of tuberculosis in patients of systemic sclerosis on dexamethasone pulse therapy: A short communication from Kashmir. Indian J Dermatol 2008;53:24-5.
22. Maddison PJ, Isenberg DA, Woo P, Glass DN, Breedveld F. Oxford Textbook of Rheumatology, 3rd Edition, USA: Oxford University Press, Section 6. Subsection 2004. p. 76.7.