Pulse therapy - Evidence versus faith and unconditional other acceptance

Sir,

I deeply appreciate the interest shown in our comments[1] on dexamethasone cyclophosphamide pulse (DCP) therapy for pemphigus.[2] In this comment it is mentioned that we "almost dismissed" and "tried to prove the worthlessness of pulse therapy in pemphigus". I would like to point out that we did not use these words in our article, rather, we made three important points: (a) Randomized controlled trials (RCTs) are the gold standard for determining the efficacy of any treatment; (b) there are no RCTs of DCP therapy in pemphigus; and (c) the evidence presented is only case series, which considerably lags behind the gold standard, and in the case series also there are important shortcomings.

I am happy to note that the authors commenting on our article agree with our above-mentioned conclusions (a) (they write "RCTs are considered to be the highest level of evidence", and "it is true that RCTs provide the highest level of clinical evidence") and (b). But then it is written that "we do not feel the need for the same" (i.e., RCT to evaluate DCP therapy). I am unable to reconcile with these contradictory statements. With regard to our point (c), the authors write that "these drawbacks are only minor". I disagree, because both as a dermatologist and when I put myself in the patient's position, I am unable to consider the following shortcomings as only minor because these are not in the patients' interest nor in the interest of science: no mention of the patients' characteristics; use of same doses irrespective of body weight; patients receiving treatment as outpatients (no mention of admission;

patients with pemphigus, with possible exception of those with oral lesions only, require admission, due to the life-threatening nature of the disease and also due to the potential of pulse therapy to cause serious adverse events including sudden death during and after pulse administration, which necessitates close monitoring);[1] unknown number of patients with diabetes receiving pulse in 5% glucose (albeit with insulin; normal saline would have been safer); unmarried patients and those willing to have children receiving cyclophosphamide in cumulative doses of approximately 31.5 g to > 45 g; no mention of pregnancy tests and contraception advice; no mention of frequency, severity, time of occurrence, actions taken with regard to adverse events and further management of these patients; mentioning that osteoporosis does not occur without conducting dual energy X-ray absorptiometry; investigations to examine the toxicity of cyclophosphamide and high glucocorticoid doses, not performed according to standard guidelines, but after enormous intervals; no monitoring of blood pressure and electrocardiographic changes during and after glucocorticoid pulse administration; patients receiving antibiotics (including cephalosporins, which can induce or aggravate pemphigus) for several months; no mention of reasons of dropouts; no mention of causes of death when it occurred; and drawing of conclusions disregarding these dropouts and deaths. In scientific writings, only those actions or procedures, which are mentioned, are understood to have been performed. A recent case series from India has shown the life-threatening nature of pemphigus and has documented several immediate and delayed adverse effects of DCP therapy.[3]

As there is no RCT of DCP therapy and there is one in which a similar treatment, but not exactly the same, was evaluated,[4] we mentioned it. This RCT failed to find evidence of the superior efficacy of the tested pulse therapy. I do not intend to defend the shortcomings of this study, if there are any. Excessive focus on this article sidetracks us from the main issues (a), (b), and (c), as mentioned a little earlier in the text. Furthermore, the presence of shortcomings in this article does not mean the presence of evidence in favor of DCP therapy. They are different things. Many treatments that appear to be effective in personal experience and case series turn out to be less effective when examined in RCTs, hence the requirement of RCTs. A recent evidence-based systematic review of treatments for pemphigus does not mention DCP therapy because of this reason.[5]

I am surprised by the "advice" given to us "to be polite in choice of their words" and the next sentence. I am unable to find any impolite word in our article, [1] nor did any of the four referees say that we wrote impolitely. In fact, we mentioned our admiration for Dr Pasricha in our article (paragraph 7). I strongly restate that we admire and respect him. However, being respectful to someone does not mean that we cannot scientifically read and comment on someone's study. Despite this humble submission, if any impolite word in our article is pointed out to me, I will apologize for that. Following my revered teacher Albert Ellis, I practice unconditional other acceptance,[6] (accepting everyone as she or he is, although disagreeing with their certain views).

Richard Dawkins defines faith as belief without evidence.[7] Given a choice between faith and evidence, I prefer evidence. We did not "almost dismiss" or "tried to prove the worthlessness of pulse therapy in pemphigus" as mentioned in the comment on our article. Instead, we asked a scientific question: Is DCP therapy for pemphigus backed by quality evidence? The answer we got was a no.

Sanjay Singh

Department of Dermatology, Institute of Medical Sciences, Banaras Hindu University, Varanasi - 221 005, India

Address for correspondence: Dr. Sanjay Singh, C-9, New Medical Enclave, Banaras Hindu University, Varanasi-221005, India.
E-mail: sanjaye2@gmail.com

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