Do Case Series have a Role in an Evidence-Based Medical Culture?

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Physicians have the duty to meet the standard of care for any given condition. In the practice of medicine today, the standard of care is generally considered to involve evidence-based decisions. The art of medicine remains important, but for most disorders, evidentiary proof of a therapy's efficacy is deemed to be desirable as all interventions carry with them some risk. Both physicians and patients must weigh the risks of any proposed intervention against perceived benefits. For new drugs, the Therapeutics Products Program and Federal Drug Agency ensure that these standards are met by careful scrutiny of clinical research trials for both efficacy and safety. Older drugs being tested in the clinic for new indications lack similar scrutiny.

In the case of common disorders, many interventions have been investigated in a rigorous fashion; i.e. with randomized, double-blind, placebo-controlled, clinical trials, and evidence-based therapeutic decisions are possible. However, for rare conditions, sufficient rigorous evidence may be difficult to acquire. Thus, case studies and case series remain important for these conditions. Even when such conditions are known to remit spontaneously, anecdotal reports of treatment efficacy are published. Is an anecdotal report of response to therapy justified given that the disorder may improve without intervention? Does the suggestion of an intervention with associated risks seem appropriate in a self-limited disorder? Are the results of the report misleading? These difficult questions need to be considered when such a report appears. An historical example illustrates the pitfalls of uncontrolled reports. Corticosteroids were recommended for use in Guillain-Barré syndrome based on anecdotal reports prior to randomized, placebo-controlled trials.[1] Others found corticosteroid therapy to be deleterious,[2] and a recent review by the Cochrane group indicates lack of efficacy and recommends against the use of corticosteroids for this immune-mediated polyneuropathy.[3] Thus, anecdotal reports were misleading in this particular inflammatory polyneuropathy.

Elsewhere in this journal,[4] the use of IV methylprednisolone in 11 patients having lumbosacral radiculoplexus neuropathy (LSRPN) without diabetes is described. The therapy is considered to be beneficial for the patients. The natural history of LSRPN is one of gradual improvement, although long-term morbidity is present in most patients.[5] However, resolution of pain and improved strength are to be expected eventually in all patients having LSRPN.[5] In the case series reported, pain resolved in four patients and improved at least moderately in seven. Strength improved in nine subjects with only one out of six subjects still confined to a wheelchair following treatment. A single patient with LSRPN, with strictly unilateral lower limb disease, fulfilling the criteria presented in this publication and treated at another clinic, failed to respond in any way to this treatment. Thus, out of 12 patients with the criteria for LSRPN, 11 at one center responded to therapy and one at another center did not do so. Does this discrepancy represent bias from one center, or simply random differences in patients? Would a meta analysis of case studies and case series give a more accurate estimate of response to therapy with methylprednisolone? The authors correctly caution readers that the trial is uncontrolled and open, and that the results must be interpreted with caution. They suggest that a prospective, sham-controlled, double-blind trial would be appropriate. This conclusion seems reasonable, since a therapeutic approach to LSRPN cannot be determined from this report.

Another rationale for publication is that patients having LSRPN are currently being treated with IV methylprednisolone, and, therefore, a review of systematic intervention and reporting of the therapeutic or adverse results is warranted. The report is then valuable in presenting current clinical practice, even in the absence of rigorous scientific evidence. Endeavors designed to improve the rationale for a therapy are laudable. The weakness of the results can then be weighed against the value of initiating discussion about more appropriate studies. In this case, different standards as to inclusion of patients in the report might improve the validity of the findings. For example, the diagnosis of LSRPN becomes problematic if "patients were not excluded if they also developed some upper extremity symptoms or signs…" With inclusion of such cases in the series, the distinction of LSRPN from chronic inflammatory demyelinating polyneuropathy (CIDP) is problematic. Patients with CIDP are known to respond to corticosteroid therapy.[6,7] This blurring of diagnostic lines creates doubts as to the validity of the therapeutic response in patients having LSRPN. Finally, the presence of some perivascular inflammatory cell cuffing is not equivalent to microvasculitis implying the need for immunomodulation. In fact, such findings are considered nonspecific and certainly, nondiagnostic by many neuropathologists. Such changes can be found in noninflammatory types of neuropathy which also follow a course of spontaneous resolution such as diabetic neuropathy[8] and hereditary neuropathy.[9]

Ideally, results such as those described in this case series lead to definitive trials of therapy which may, depending on their outcome, alter practice.

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