Yet the treatment of MS with mitoxantrone early in the course of the disease is not routinely undertaken, and in fact, it is discouraged by many MS specialists. The reason, of course, is the risk of adverse events, including permanent cardiac damage resulting in congestive heart failure and leukemia. For example, a recent study of 2854 mitoxantrone-treated MS patients showed the risk of leukemia was 0.74% (about 1 in 135).\[2\]

As a result of these risks and others, mitoxantrone is generally used, if at all, in patients exhibiting breakthrough exacerbations or secondary progression of their MS, often after multiple drug failures.

So why do this study in treatment-naïve patients? The authors were treating an indigent multiple sclerosis population, without insurance and unable to afford expensive medications. In their opinion it was considered reasonable to offer a more dangerous, but much less expensive, medication to these patients. The patients understood the potential risks, as well as the potential benefits, of mitoxantrone. As a result, a number of patients received treatment for their MS that they could not have obtained otherwise.

This study highlights the ethical dilemmas in treating patients around the world. Is it best to treat patients with a less expensive, but riskier, medication, rather than not treat them at all? This question can be asked for many diseases and the dilemma undoubtedly will be the subject of discussion for many years. In the meantime, individual physicians need to treat individual patients on a daily basis. If both the physician and patient understand the benefits and risks of medication, as well as the financial issues, should treatment be denied if the safer, but less effective drug, is not affordable? Furthermore, should patients be allowed to choose a more effective, but riskier drug, even if affordability is not an issue?

This article and this review will not answer the questions posed, but should encourage both physicians and patients to participate in an unbiased, open and properly educated discussions about their disease and their medications.

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**Invited Commentary**

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Multiple sclerosis (MS) is a chronic and relentlessly progressive disorder, in the vast majority of patients affected worldwide. The data available from long-term follow-up of patients with an initial benign presentation has shown that a significant number of patients develop disabling deficits especially involving cognitive functions. There are no reliable clinical or radiological predictors of disease course in MS. In addition, pathological evidence exists of irreversible brain damage very early on in the course of disease. Therefore, there is no doubt that a disease modifying agent is needed; this agent should have an acceptable safety profile and should not only reduce relapses but also delay the progression of disease. In developing countries such as India, another factor would be affordability of this medication which has to be taken very often for indefinite periods of time. In this context, a report by Singhal et al.,[1] on the use of mitoxantrone as an initial agent in the treatment of MS, is interesting. The authors have shown reasonably good response to...
the treatment in a significant number of patients. They have, however, treated their patients, who had varying duration and stage of disease, unblinded.

Mitoxantrone, though more affordable in comparison to interferon and glatiramir acetate, does not share the safety profile of the latter. In view of potentially fatal cardio toxicity, frequent cardiological evaluations are required during the course of medications. Therapy related leukemia is another concern which has been reported up to as much as five years after treatment. Therefore, the actual benefit will fall on a select minority of patients who can be kept under stringent follow-up and are willing to consider alternative and costly disease modifying drugs (DMD) after the initial therapy with mitoxantrone. The authors have left this intriguing question unanswered. Mitoxantrone is not a ‘stand alone’ treatment modality in MS. Initial benefit with mitoxantrone is not necessarily sustained, and therefore, subjecting a patient to a drug which is cheaper but has safety issues must be carefully considered while selecting patients for this form of therapy. However, it must be acknowledged that mitoxantrone along with newer molecules such as monoclonal antibodies are being increasingly recognized as drugs which induce a quick remission. The role of combination therapy with mitoxantrone is being explored through several trials at the moment. This paper brings to focus the growing recognition that MS is not uncommon in India and that there is a real need for a safe and affordable treatment. Extending this study to include larger and more homogenous group of patients and combing with relatively less expensive disease modifying agents such as azathioprine may be worth considering in the future.

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