Pregabalin for fibromyalgia

(APRIL 2009)

TO THE EDITOR: The article by Kim et al regarding the use of pregabalin (Lyrica) in fibromyalgia is interesting and timely.[1] We would like make some additional comments.

They claim that "many hail pregabalin as an important advance in our understanding of the pathogenesis of fibromyalgia and how to treat it," but they fail to cite who those "many" are. We contend that aside from the pharmaceutical company's representatives, physicians on its speaker's bureau, and those participating in paid drug studies, it would be difficult to substantiate this statement.

The authors' historical overview discusses Gowers' description of fibrositis but misinterprets his discussion. Gowers did not believe that "inflammation of muscles" was a problem, but that fibrous tissue itself was inflamed (thus the term "fibrositis," not "myositis") and could thus produce pain such as pharyngitis and sciatica, as well as "muscular rheumatism."[2]

The authors review functional abnormalities in central nervous system processing as an etiology of pain. Russell et al are cited as elucidating the role of substance P in the process.[3] Although they showed that substance P was three times higher in the cerebrospinal fluid of fibromyalgia patients compared with normal controls, the cited paper also notes that there was an inverse relationship between substance P levels and tenderness. Substance P also did not correlate with the Visual Analogue Scale self-assessment of pain severity or "with any other clinical variable."[3] A question of whether appropriate controls were chosen for the study has to be raised as well, since 25 of 32 fibromyalgia patients and only 3 of 30 controls had "possible depression."[3]

The discussion of other therapies has limitations. The authors rely on two meta-analyses and a review to suggest that the efficacy of tricyclics is supported by a variety of studies. We don't disagree, but as we previously noted, long-term studies don't support prolonged efficacy of these drugs, which raises questions of treatment of a chronic illness.[4] Duloxetine (Cymbalta) and milnacipran (Savella) are briefly mentioned. The authors should have used at least a sentence for each drug to indicate that the drugs have their own substantial shortcomings.

Finally, the authors conclude their article by asking, "What role for pregabalin?" A careful reading of that section does not appear to provide an answer. We recently presented a study suggesting that pregabalin and standard therapy were equally effective (or equally not effective), suggesting that pregabalin neither represents a major pharmaceutical advance in therapy nor is likely to "advance our understanding of the pathogenesis of fibromyalgia."[5] We do agree with the authors that medications are only part of a comprehensive program of therapy, and further point out that fibromyalgia undoubtedly represents the end point of a variety of etiologic insults and is unlikely to be one specific syndrome.

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IN REPLY: We would like to thank the Drs. Abeles for reading our paper[1] and providing valuable input. We are, however, surprised by their question as to who the "many" people are who believe that pregabalin is an important advance in the treatment of fibromyalgia. Anyone who is involved in taking care of fibromyalgia patients would know that several patients regularly report being helped by this medication to a varying degree. These patients rightly believe that this drug—the first drug approved by the US Food and Drug Administration for their oft-misunderstood condition—has started a much-needed dialogue in the medical community, and that in itself is a major advance.

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We accept that Gowers, in his original paper on "fibrositis," believed that fibrous tissue and not muscle was the source of inflammation in this condition.

We do believe that the paper by Russell et al[2] was one of the many investigations that helped establish the role of central sensitization or abnormalities in pain processing in the central nervous system as the root cause of fibromyalgia pain. However, we do not believe our paper on pregabalin was the right place to discuss the merits or shortcomings of that paper in any more detail.

As we mentioned in our paper, therapies for fibromyalgia have limitations, and duloxetine and milnacipran are no exceptions. However, both these drugs were approved after our review was completed. We believe that the role of pregabalin in the treatment of fibromyalgia is going to be limited simply because medications overall form a small part of the comprehensive program of therapy for this condition.

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