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LETTERS TO THE EDITOR

Pentoxifylline's Theoretical Efficacy in the Treatment of Fibromyalgia Syndrome

To the Editor:

Fibromyalgia is a syndrome characterized by chronic, widespread pain in combination with tenderness to palpation at specific tender point sites on the body, in the absence of otherwise apparent organic disease [1]. Given the unclear etiology of fibromyalgia, and the heterogeneous presentations of the disease, it has become clear that no one therapy is broadly efficacious. Drugs known to attenuate glial activation and secretion of proinflammatory cytokines such as naltrexone have already been tested and found efficient in the reduction of fibromyalgia symptoms [2]. Glial cell activation and subsequent secretion of cytokines constitute one of the theories underlying fibromyalgia syndrome. Glial cells, long thought to be metabolically inactive support cells in the nervous system, are now recognized as playing a substantial role in modulating pain signaling [3]. Glial cells and astrocytes are activated by stimuli that induce pain, such as nerve trauma, subcutaneous irritation, and intraperitoneal inflammation, and by neurotransmitters involved in pain signaling [3,4]. Glial cells release many neuroactive substances upon activation by painful stimuli, including nitric oxide, prostaglandins, leukotrienes, nerve growth factors, excitatory amino acids, and reactive oxygen species [5]. Activated glia upregulate release of substance P and other excitatory amino acids from primary afferent neurons in the spinal cord and enhance the excitability of pain transmission neurons. In addition, microglia and astrocytes release proinflammatory cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) [6]. Blocking the actions of these cytokines prevents or reverses exaggerated pain states [4]. In addition to naltrexone, pentoxifylline is a nonspecific cytokine inhibitor that has been shown to attenuate glial cell activation and that is known to inhibit the synthesis of TNF-α, IL-1β, and IL-6 [7]. Some studies have demonstrated that pentoxifylline influences the development of neuropathic pain behavior in rats and mice, and that when injected in a preemptive analgesia schema, it reduces postoperative pain in patients [7–9]. The antinociceptive effects of pentoxifylline are correlated with the reduction of the production of TNF-α, IL-1β, and IL-6 through inhibition of nuclear factor-κB (NF-κB), and stimulation of interleukin 10 (IL-10) expression in the spinal cord and brain [7,10]. Glial cell activation is one of the several other possible pathophysiologic mechanisms underlying the development of fibromyalgia syndrome by contributing to central nervous system sensitization to nociceptive stimuli [11]. Providing this fact, attenuating glial cell activation via the administration of pentoxifylline to individuals suffering from fibromyalgia syndrome might theoretically be efficient in ameliorating their symptoms without being a globalist therapeutic approach targeting all possible pathophysiologic mechanisms of development of the syndrome. In addition, the administration of pentoxifylline for fibromyalgia syndrome shares its rationale with the administration of this drug to other central sensitization-related chronic pain diseases such as chronic tension-type headache, chronic fatigue syndrome, chronic low back pain, and chronic whiplash associated disorders [12–15]. Moreover, other glial activation attenuating agents such as propentofylline and minocycline exist and, like pentoxifylline, have not been tested in the treatment of fibromyalgia syndrome and many other central sensitization-related chronic pain diseases [16]. Accordingly, randomized controlled studies are needed in order to evaluate the efficacy of pentoxifylline and/or other glial activation attenuating agents in the treatment of fibromyalgia syndrome and other related syndromes.

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