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Points of View

Proposal to use pentoxifylline and Lyprinol therapy for chronic inflammatory diseases

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Our research group read with enthusiasm the article by Whitehouse recently published in this journal (Whitehouse, 2004). He proposed the therapeutic use of pentoxiphylline (PTX) associated with Lyprinol for a few chronic inflammatory diseases. PTX reduces the production of TNF-α and Lyprinol, a mussel extract, inhibits lipoxygenase. He showed clear evidence of the usefulness of this association in experimental models of animal "chronic" inflammatory disease. There was a clear synergism with the two agents. Whitehouse lists a series of benefits of this combination compared with present therapeutic approaches. In the last decade, our laboratory pioneered the understanding of the contribution of cytokines to the development of inflammatory pain. We described (in rats and mice) a cascade of hypernociceptive cytokines which starts with TNF-α and ends with IL-1β and KC (CINC) releasing prostanoids and sympathomimetic amines, respectively (Cunha *et al*., 1992, 2005; Poole *et al*., 1999). Recently we have shown that TNF-α released by inflammatory stimuli was inhibited by PTX (Vale *et al*., 2004) or thalidomide (Ribeiro *et al*., 2000), inhibition that was strictly related with anti-nociception. On the other hand, we described in two series of experiments of persistent or "chronic" inflammatory tests that in the late phase the importance of prostaglandins for the development of hypernociception was overshadowed by the participation of lipoxygenase metabolites (Tonussi and Ferreira, 1999; Canetti *et al*., 2001; Cunha *et al*., 2003). Thus, our experiments fully support Whitehouse's proposal to introduce the combination of PTX and Lyprinol for therapy of some chronic diseases. This combined therapy is certainly of lower cost than engineered TNF-α antibodies or

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receptor antagonists, since PTX is out of patent and Lyprinol is a natural product (classified as food). We agree with Whitehouse that there is little industrial interest in developing therapeutics of low profit return. I would expect, however, the Public Health System of undeveloped countries like mine, Brazil, would be sensible and invest in clinical trials of this low-cost and far-reaching therapeutic strategy.

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