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Fludrocortisone and chronic fatigue syndrome

In a recent study,[1] Blockmans et al cite two trials (published in 1998 and 2001) that investigated the effects of fludrocortisone as monotherapy in the treatment of chronic fatigue syndrome (CFS). They also discuss two studies (published in 1998 and 1999) finding hydrocortisone alone to be beneficial to patients with CFS. Then, they refer to the hypothesis that a combination of hydrocortisone and fludrocortisone would be better than monotherapy for treating CFS as 'our hypothesis'.[1] In truth, this hypothesis is mine and was first advanced in 1996, in *JAMA*.[2]

Blockmans et al also cite a paper of mine,[3] only to dismiss my suggestion that CFS is a mild form of Addison's disease by objecting that 'treatment with low-dose hydrocortisone and fludrocortisone should have been beneficial'.[1] Since this treatment, as I have recently reported,[4] continues to be extremely effective in suppressing all my symptoms of CFS, I cannot but surmise that there is some error in Blockmans' study.[1]

A methodological error may be revealed by the authors' statement that there was 'no difference between the active compound and the placebo in appearance or taste'.[1] The authors do not specify how they made the placebo indistinguishable from the commercial tablets of hydrocortisone and fludrocortisone. However, considering that the appearance and taste of those tablets are distinct and characteristic, it is probable that Blockmans et al[1] rendered the placebo apparently identical to the active compound by simplistically putting them into identical capsules.

Unfortunately, as I pointed out and quoted elsewhere,[5,6] the distorted effects of commercial tablets extemporaneously converted to capsules 'could severely bias the results'[7] of clinical trials. On the other hand, it is obvious that the commercial form of a drug is not random, nor changeable arbitrarily, this form being the result of a rational decision based on the pharmacokinetics and pharmacodynamics of the drug. Sublingual drugs, for example, could hardly act adequately if ingested.

If Blockmans et al[1] did hide the commercial tablets of fludrocortisone in capsules, they may have biased their results by incurring the same methodological error that led other researchers to conclude that fludrocortisone is ineffective in the treatment of CFS.[5,6] By contrast, nearly half of patients treated with fludrocortisone in its normal form of tablets reported 'complete or nearly complete resolution'[8] of CFS symptoms. This suggests that the tablets of fludrocortisone are to be allowed to display their typical instantaneous dissolution at the lingual level, which is impossible if they are trapped in capsules, whose delayed disintegration occurs tardily in the stomach.[7]

Considering that CFS and Addison's disease share 42 clinical features,[4,9] including all the diagnostic criteria for CFS,[10] and that Addison's disease is routinely treated with hydrocortisone and fludrocortisone taken in their commercial forms of tablets, Blockmans et al also should have assessed whether patients with CFS can benefit substantially from those steroids administered in their normal, original forms.

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