Responders and non-responders to NSAI drug interactions - a neglected problem?

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Side-effects of Anti-inflammatory Drugs. Rainsford, KD and Velo, GP (eds)

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SIDE-EFFECTS OF ANTI-INFLAMMATORY DRUGS

I. INTRODUCTION

It has been shown that non-steroidal anti-inflammatory drugs (NSAID's) through their inhibition of prostaglandin synthesis, can attenuate the effects of anti-hypertensive and diuretic agents. The clinical relevance and therapeutic implications of these findings are not clear at the present time due to the fact that there are large discrepancies between the findings themselves and their interpretation by the respective authors. There is, particularly, very little mention of the fact that there are responders and non-responders to that drug interaction, and very little attention has been given to protocol details that may be necessary to explain the effects observed.

This chapter discusses the discrepancies between different authors, and by the inclusion of our own data tends to support the view that subjects or patients may respond quite differently to coadministration of NSAID's to diuretic or anti-hypertensive agents. Particular attention will be given to a critical analysis of protocols, data analysis, statistics and interpretation.

II. INTERACTION OF NSAID's WITH THE ANTI-HYPERTENSIVE ACTION OF BETA-BLOCKERS AND DIURETICS IN PATIENTS WITH HIGH BLOOD PRESSURE

A. Interaction of indomethacin with pindolol and propranolol

The first clinical report of a significant drug interaction between NSAID's and beta-blockers has been described by Durao et al. In their study they could only analyse the results of seven out of fifteen patients originally in the study. Four patients used pindolol and three received propranolol. All patients were good responders to beta-blocker treatments. Indomethacin was the NSAID studied for potential interaction; it was administered for a period of 10 days. Placebo was included in that single blind study. All but one patient had normal renal function. The blood pressure before beta-blocker treatment was highly abnormal, six of the seven patients had blood pressure of WHO-class 3.

Indomethacin blunted or even abolished the anti-hypertensive effects of either beta-blocker. The authors concluded from their data that, as in previous animal work conducted by them, beta-blockers seem to exert their action through prostaglandins, which when blocked can no longer lower blood pressure. The limitations of that study is certainly the small number of patients studied and the heterogeneity of the patients where two out of the seven patients studied had pyelonephritis, with the other five patients being essential hypertensives. The anti-hypertensive equivalence of 15 mg pindolol and 160 mg propranolol was not demonstrated, nor were literature data given to prove this equivalence. The question of circadian variation of blood pressure and the importance of the time of blood pressure measurement during the day, was obviously not addressed, since no information is available on that in the paper. This limits the value of this investigation significantly. It is also the only paper, in which analysis of the individual data