

PHARMACOKINETICS OF INDOMETHACIN IN CHRONIC MIGRAINE PATIENTS AFTER WITHDRAWAL OF THE OVERUSED COMBINATION OF INDOMETHACIN, PROCHLORPERAZINE, AND CAFFEINE

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The combination of indomethacin, prochlorperazine and caffeine (IPC) is often overused by migraine patients who develop medication-overuse headache (MOH), a secondary chronic headache that recovers after withdrawal of the overused medication. In a previous study (1) we showed that indomethacin clearance was lower in chronic migraine patients overusing IPC combination than in migraine patients only occasionally taking this combination. **Objective:** to verify if the reduced clearance of indomethacin reverts to normal after withdrawal of the overused IPC. **Methods:** we repeated the study of indomethacin pharmacokinetics in 9 female headache patients after 6 months from inpatient withdrawal of the IPC combination. In each patient indomethacin pharmacokinetics had been already studied before withdrawal treatment. The IPC combination (indomethacin 50mg, prochlorperazine 8mg, caffeine 150mg) habitually taken was administered by rectal route to each patient. Blood samples were drawn before dosing and at the following post-dose times: 0.5, 1, 2, 3, 4, and 6 h. Indomethacin concentrations were measured by HPLC method. Pharmacokinetic parameters were calculated by means of the P K Solutions 2.0 program. **Results:** the pharmacokinetic parameters of indomethacin in 4 patients (group A) who relapsed in IPC overuse were similar to those observed before withdrawal treatment; on the other hand (Table 1) in 5 patients (group B) who steadily discontinued IPC combination, indomethacin disposition was significantly different from that observed before withdrawal treatment.

Table 1. Pharmacokinetic parameters of indomethacin in group B.

Parameter	Before withdrawal	After withdrawal
Half life (h)	2.74±0.98	1.45±0.34 *
AUC _{0-t} (µg/h/ml)	13.02±6.62	5.36±2.36 *
Cl (ml/h/Kg)	64.05±30.16	123.98±39.91 *

*P <0.05 (paired Student' t-test)

Conclusions: in headache patients who discontinued IPC overuse, indomethacin clearance increased and reverted to values previously obtained in occasional IPC users (1).

1. Ferrari A., Savino G., Gallesi D., Pinetti D., Bertolini A., Sances G., Coccia C.P.R., Pasciullo G., Leone S., Loi M., Sternieri E. (2006) Pharmacol. Res. 542: 142-149.