

Clinical characteristics of patients with liver injury induced by flucloxacillin and co-amoxiclav

M. A. Alshabeeb^{1,2}, G. P. Aithal³, A. K. Daly¹. ¹Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UNITED KINGDOM, ²Medical Genomics, King Abdullah International Medical Research Center (KAIMRC), Riyadh, SAUDI ARABIA, ³NIHR Nottingham Digestive Diseases Biomedical Research Unit, Nottingham University Hospitals and University of Nottingham, Nottingham, UNITED KINGDOM.

Introduction: Rare but serious liver injury may occur as a result of using the antimicrobials flucloxacillin or co-amoxiclav. This study aimed to analyse the clinical, laboratory and histologic data of the affected patients to further assess non-genetic risk factors for these forms of drug-induced liver injury (DILI).

Method: 155 cases of flucloxacillin DILI and 165 co-amoxiclav DILI cases were collected retrospectively and prospectively in several Northern European countries but mainly from centres throughout the United Kingdom (279 UK cases) based on defined criteria for DILI (1).

Results: A summary of the main findings is provided in Table 1.

Table 1. Comparison of clinical features of DILI due to flucloxacillin and co-amoxiclav

	Flucloxacillin (n=155)	Co-amoxiclav (n=165)	p value
Mean age of onset	62.6 ± 13.4	63.1 ± 12.8	0.73
% female cases (95% CI)	69.7 (62.47-76.93)	47.9 (40.28 - 55.52)	0.0001
Mean peak ALT (U/l)	400.4 ± 253.9	420.4 ± 422.7	0.61
Mean peak ALP (U/l)	569.6 ± 668.5	516.8 ± 393.4	0.39
Mean peak bilirubin (umol/l)	264.3 ± 227.1	221.4 ± 161.8	0.051
Days on drug	10.3 ± 6.2	9.2 ± 10.4	0.26
Time to DILI onset (days)	23 ± 18	20 ± 20	0.087
% cholestatic or mixed	91.6%	83.6%	0.042
% with jaundice	91.6%	90.9%	0.85

The most striking difference was a considerably higher percentage of females in the flucloxacillin

group ($p=0.0001$). Both groups showed an age of onset of more than 60 years and for both drugs liver biochemistry values were very abnormal with a high incidence of mixed or cholestatic phenotype which was significantly higher for flucloxacillin DILI compared with co-amoxiclav ($p=0.042$). These phenotypic findings were in line with a previous report (2). For flucloxacillin DILI, 84.5% were positive for *HLA-B*57:01*. There were no obvious differences in clinical phenotype between those positive and negative for *HLA-B*57:01*. Significant age differences were noted ($p=0.022$) between patients who used flucloxacillin for more than 10 days and others who were drug-exposed for 10 days or less (mean age \pm SD= 66.28 \pm 12.17 vs 60.90 \pm 13.62, respectively). For co-amoxiclav, the mean age at the time of DILI was significantly lower in females (60.2 years) compared with males (65.7 years) ($p=0.006$). Males were also found to be at higher risk of developing jaundice due to co-amoxiclav than females (OR=4.96, 95% CI=1.34-18.28; $p=0.013$).

Conclusion: Apart from the very significant gender difference, the clinical presentation and incidence of the two forms of DILI appear quite similar, though the genetic risk factors for both forms of DILI are different (3).

References:

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3. Urban TJ et al. (2014). Semin Liver Dis **34**(02): 123-133.