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No effects on linezolid pharmacokinetics by erythromycin

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Objectives

As part of routine therapeutic drug monitoring a case with sudden increase in Linezolid exposure after adding Erythromycin for prokinetic purpose was observed. Furthermore a recently published study investigating the influence of Clarithromycin, another macrolide antibiotic agent, on pharmacokinetics of Linezolid, showed a significant increase of linezolid-AUC by combined therapy. The purpose of this investigation was to evaluate whether there is an influence of Erythromycin on single dose pharmacokinetics of Linezolid.

Methods

The six authors of the abstract acted as healthy volunteers. To compare AUCs with and without Erythromycin intake one tablet of Linezolid 600 mg was taken on day one and on day three, combined on day three with three oral doses of Erythromycin 500 mg, 12 hours and 2 hour before and 3 hours after Linezolid intake. Blood samples were collected 2, 4 and 7 hours after Linezolid intake on day one and day three of the study and Linezolid levels were determined by high performance liquid chromatography with UV-detection subsequently after sampling. Linezolid pharmacokinetic parameters were calculated using non-compartmental methods.

Results

Mean AUC24 of Linezolid on day one was 130 (range 102-163) h*mg/l, not significantly different to the AUC24 on day three with 129 (range 80-168) h*mg/l. Also no significant differences (day 1 (range)/ day 3 (range)) in 7 hour levels (7.50 (6.02-9.05)/ 7.19 (4.84-9.72) mg/l), volume of distribution (0.52 (0.47-0.62)/ 0.56 (0.48-0.67) l/kg), half-life (5.75 (3.5-9.0)/ 5.99 (3.6-8.8) h) and clearance (4.78 (3.68-5.89)/ 4.98 (3.58-7.52) l/h) were observed.

Conclusions

Although a recently published study described a significant increase of the AUC24 of Linezolid with a concomitant intake of 500 mg of Clarithromycin, Erythromycin has no influence on Linezolid exposure in this investigation of six healthy volunteers with a single dose schedule. The postulated inhibition of p-glycoprotein as cause for the altered pharmacokinetics with Clarithromycin doesn't seem to have the same effect with Erythromycin. Further studies addressing this topic under the conditions of critical illness and in longer treatment periods are needed to fully exclude a potential pharmacokinetic interaction.