SUMMARY

Food drug interactions are being reviewed periodically and are found to be an interesting area of research with a profound potential for the scientific community. The interactions are clinically significant in the case of drugs which are (i) drugs with a narrow therapeutic window of absorption in the intestine, (ii) drugs in which peak plasma concentration ($C_{\text{max}}$) achieved determines their efficacy or toxicity and (iii) drugs in which the time above a critical plasma concentration determines their efficacy or toxicity or lack of it. Cefaclor is a good candidate in the third category.

It's a well known fact that food does not alter the extent of absorption of cefaclor but show a delay in rate of absorption thereby causing an increase in $T_{\text{max}}$ and a decrease in $C_{\text{max}}$. But there are also some instances where it was reported that the bioavailability of cefaclor is lowered in fasting state as compared to fed state therefore, it’s a controversial topic and needs a further insight.

Hence, this study was planned to investigate the effect of 4 dietary treatments viz., high fat vegetarian, low fat vegetarian, high fat non vegetarian and low fat non vegetarian diets on the bioavailability of cefaclor. The bioavailability was also determined under fasting condition and it was used as reference for comparison.

The study was designed as open label, balanced, randomized, five period, five sequence, single dose, cross over bioavailability study on cefaclor (Keflor®) in 20 healthy, adult, male, human volunteers. A wash out period of 7 days was maintained between the five periods. One subject dropped out in the third period and one more subject dropped out from the study in the fifth period. The remaining 18 volunteers completed all the five periods of the study.

The analysis was carried out by an HPLC method which was validated for selectivity, linearity, accuracy, precision, recovery and stability (including bench top and in injector stability). The chromatograms were processed using class VP/LC10 software and the pharmacokinetic analysis was done using Win Nonlin Software Version 1.5 (SCI, USA). Statistical analysis was performed on the pharmacokinetic parameters using SAS software version 6.12 (SAS Institute Inc., Cary NC, USA).
All diets produced a significant decrease in $C_{\text{max}}$ but it was highly significant only for high fat vegetarian diets, indicating the role of dietary fat.

Only high fat non vegetarian diet (recommended by US: FDA for bioavailability studies) produced a significant decrease in the extent of absorption (AUC) of cefaclor, indicating the role of source of food.

All diets except high fat non vegetarian diet, significantly the time above MIC$_{50}$ level of plasma cefaclor concentration, as compared to the fasting state. The effect of low fat vegetarian diet on these pharmacodynamic parameters was significantly greater, as compared to high fat non vegetarian diet.

The fat non vegetarian diet also produced greatest prolongation of time to reach MIC$_{50}$ plasma levels of cefaclor.

The results obtained in the present study indicate that cefaclor may conveniently and advantageously (therapeutic efficacy) be administered after food. The therapeutic implication of this finding for the vast majority of Indian population especially the poor are considerable.

The recommendation of US: FDA to use high fat non vegetarian food for bioavailability studies in fed state needs a re-look, as far as cefaclor is concerned. Further studies in this area i.e. time dependent antimicrobials-food interactions are warranted.


References


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