Erasmus MC
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Population pharmacokinetics of dexamethasone in critically ill COVID-19 patients: does inflammation play a role?

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CONCLUSION

Our study showed that the pharmacokinetics of dexamethasone could be adequately described by a two-compartment model. The dexamethasone PK parameters of ICU COVID patients were quite different from those come from non-ICU individuals. Inflammation might play an important role in dexamethasone clearance and the dosing should be more individualized in order to achieve best therapeutic effect in ICU patients

RATIONALE

One of the common causes of COVID-19 related death is acute respiratory distress syndrome (C-ARDS). Dexamethasone is the cornerstone in the treatment of C-ARDS and reduces mortality probably by suppressing inflammatory levels in ICU patients. Its anti-inflammatory effects may be concentration-dependent. However, no pharmacokinetic studies of dexamethasone have been conducted in ICU patients.

AIM

We designed a population pharmacokinetic study to gain a deeper understanding of the pharmacokinetics of dexamethasone in critically ill patients in order to identify relevant covariates that can be used to personalize dosing regimens and improve clinical outcomes.

METHODS

Erasmus MC
18 ICU COVID-19 patients

1~3 samples per patient
86 samples in total

Run NONMEM

PARTICIPANTS

Erasmus Medical centor

18 pt retrospective study

D0 giving dexamethasone D3 and D4 for sampling
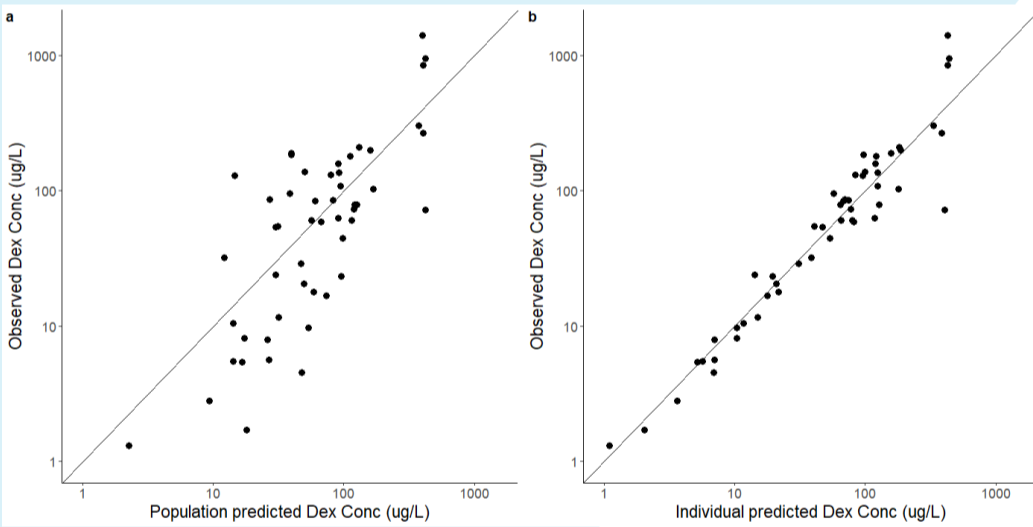
1-3 blood samples per pt to draw PK curves

RESULTS

Model diagnostics: Goodness of fit plot

Model diagnostics: Visual predictive check

97.5 percentile Conc.

Median Conc.

2.5 percentile Conc.
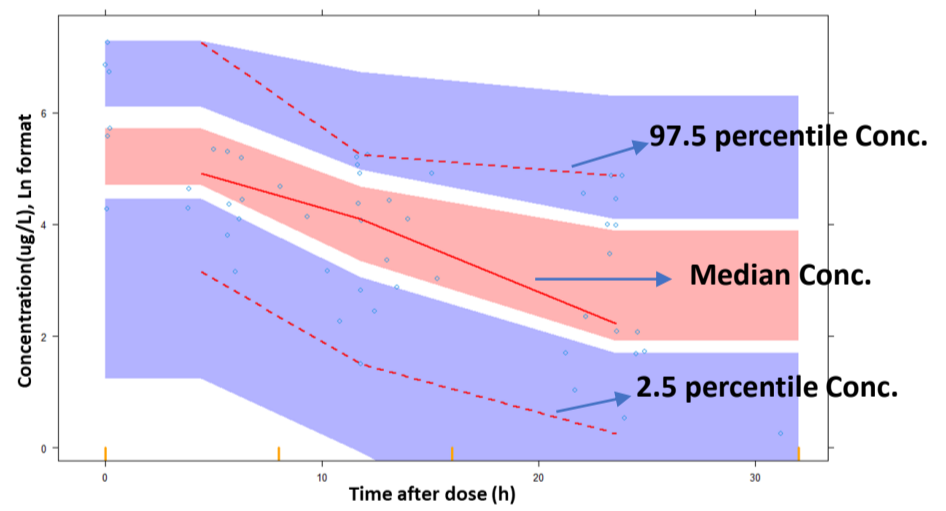
CRP as covariate influence Clearance

Dexamethasone clearance decreases with increasing CRP levels
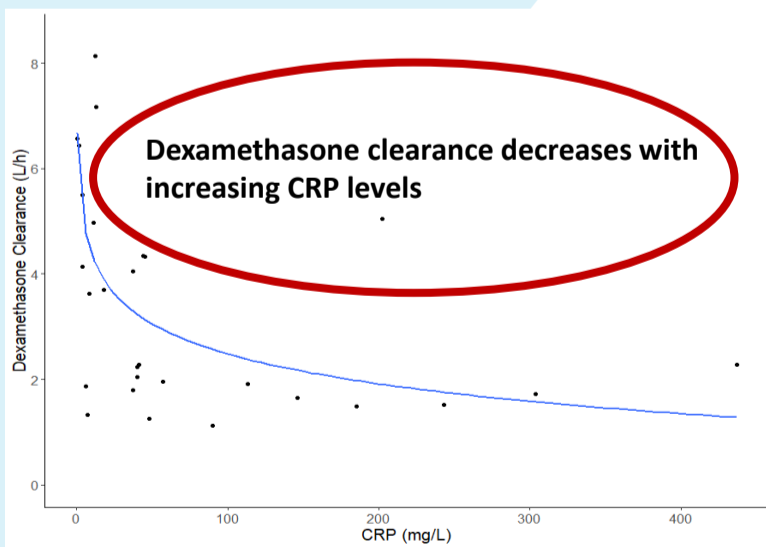
Effect of CRP on Dexamethasone trough levels by simulation

CRP levels
5
20
50
100

Dexamethasone exposure will increase with increasing CRP levels
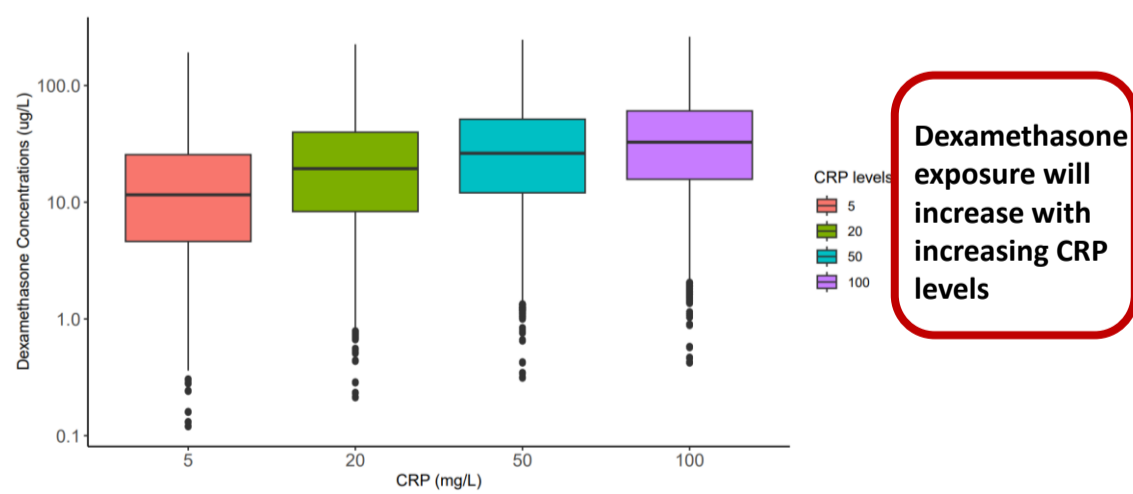
Discussion

Inflammation and steroids: ebb and flow

Dex exposure increase

Increase anti-inflammatory

CRP decreased

Dex clearance increase

Dex exposure decrease

Inflammation progress

CRP increase

Dex clearance decrease

Dex CL

CRP levels

One dose fit all?

Same dose full treatment?