Dexamethasone use in normal weight and obese hospitalized COVID-19 patients: An observational pharmacokinetic study

Kenza Abouir[1,2], Pauline Gosselin[3], Stéphane Guerrier[2,4], Youssef Daali[1,2,5], Jules Desmeules[1,2,5], Jean-Luc Reny[3], Olivier Grosgurin[3], Caroline Samer[1,5], Alexandra Calmy[6], Kuntheavy Roseline Ing Lorenzini[1]

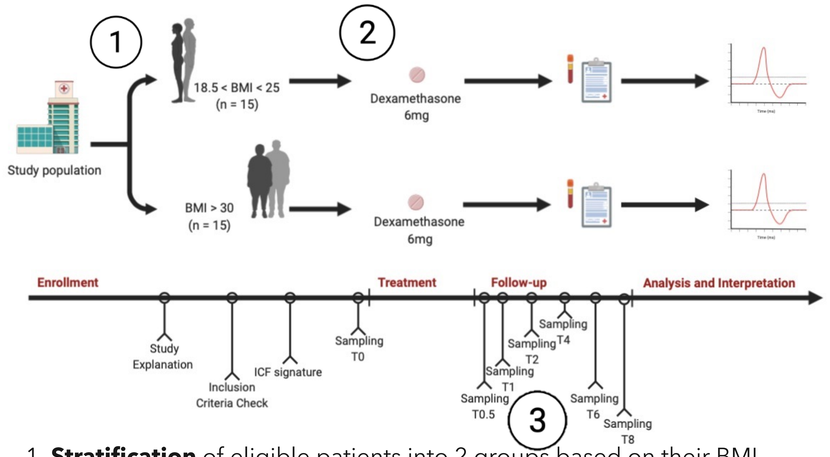
1. Division of Clinical Pharmacology and Toxicology, Geneva University Hospitals, Switzerland - 2. School of Pharmaceutical Sciences, University of Geneva, Switzerland - 3. Department of General Internal Medicine, University Hospital of Geneva , Switzerland. - 4. Geneva School of Economics and Management, University of Geneva, Switzerland - 5. Swiss Centre for Applied Human Toxicology (SCAHT), Geneva, Switzerland - 6. Division of Infectious Diseases, Geneva University Hospitals, Geneva, Switzerland

Introduction

Low-dose dexamethasone (DEX) has been shown to be beneficial in ventilated COVID-19 patients (RECOVERY study[1]) and **obesity** is a known independent risk factor for developing severe forms of COVID-19. Little information is available in the literature on DEX **dose adjustment** according to body mass index (BMI) or body weight.

We conducted a **prospective observational, exploratory, single-center study** at Geneva University hospitals (February-April 2021) **to assess the impact of weight on DEX PK** in 15 normal-weight versus 15 obese/morbidly obese patients hospitalized for COVID-19.

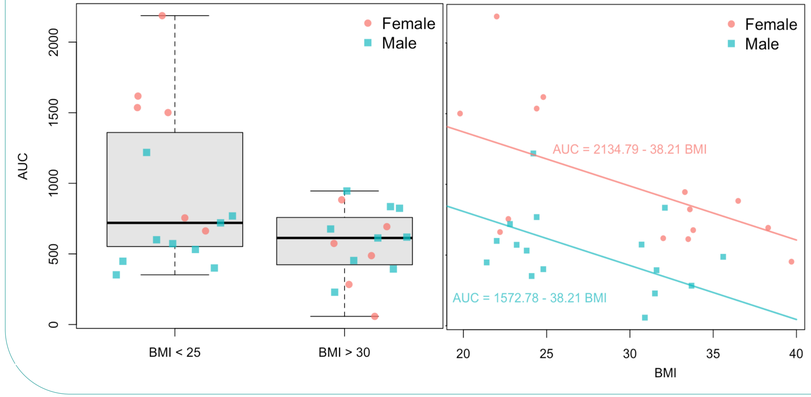
Methods



1. **Stratification** of eligible patients into 2 groups based on their BMI
2. **Administration** of DEX (6 mg) orally on the day of the study session
3. **Assessment of DEX PK** by capillary blood samplings over eight hours and using LC-MS/MS.

Results

DEX pharmacokinetics



Summary of the demographic, pharmacokinetic and exploratory outcomes data

	Normal weight (n=15)	Obese (n=15)
Demographics		
Female (n)	6 (40 %)	8 (53%)
Age (years)	65 (±12)	62 (±9)
BMI (kg/m²)	23 (±2)	34 (±2)
Weight (kg)	68 (±11)	94 (±13)
Dexamethasone pharmacokinetics		
AUC (ng.h/ml)	926 (±552)	572 (±258)**
C_{max} (ng/ml)	203 (±126)	139 (±68) *
T_{max} (h)	1.7 (±1.1)	1.9 (±1.6)
$T_{1/2}$ (h)	4.6 (±1.3)	4.3 (±1.6)
Exploratory outcomes		
Days spent at the hospital	12 (±5)	12 (±5)
Days spent in intermediate care	2 (±4)	2 (±2)
Days spent in intensive care	1 (±2)	0 (±2)

Welsh t-test with alternative hypotheses that the means decreased in obese -P-value : *<0.01 , **<0.001
all values are expressed as arithmetic means with 95 % confidence intervals

Results of regression test based on gender, BMI and intercept

(Intercept)	1628.46	2.64^{e}-05***
Gender	583.86	0.000125***
BMI	-39.78	0.001631**

$$AUC_i = 1628.46 + 538.86 * gender_i - 39.78 * BMI_i$$

i : individual

Conclusions

BMI and **weight** had a **significant impact on DEX AUC and C_{max}.**
DEX AUC was **statistically significantly higher in women than in men**
Dose adjustment may be required to achieve comparable DEX exposure in obese and/or female patients hospitalized with COVID-19.

References

1. Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, et al. Dexamethasone in Hospitalized Patients with Covid-19. The New England journal of medicine. 2021 Feb 25;384(8):693-704.

Contact: Kenza.Abouir@hcuge.ch

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