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LETTER TO THE EDITOR

Oseltamivir pharmacokinetics in Mexican obese and non-obese healthy subjects and patients. Evidence for an absence of interethnic variability

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We have read with interest the article published by Chairat and coworkers on oseltamivir population pharmacokinetics in obese patients [1]. As data on oseltamivir pharmacokinetics in Mexicans are scarce [2] and influenza cases have increased in Mexico in 2015–2016 [3], we decided to re-evaluate and contrast our observations in Mexico with those from Thailand [1]. Data correspond to the 2009 A(H1N1) influenza outbreak and were on file of at the Instituto Nacional de Enfermedades Respiratorias. All protocols were approved by the Institutional Research and Ethics Committee.

In one study we compared the bioavailability of the active metabolite oseltamivir carboxylate (OC) in 22 non-obese (BMI range 19–25 kg m^2) and 13 obese (BMI range 30–38 kg m^2) Mexican healthy volunteers. Non-obese subjects received a single 75 mg oseltamivir dose whereas obese volunteers received single doses of 75, 150 and 300 mg in three separate sessions. OC concentrations in plasma were determined as described previously and non-compartmental pharmacokinetic analysis was performed [2]. Results are shown in Table 1. OC pharmacokinetic parameters for the 75 mg dose were comparable in non-obese and obese Mexican subjects. Furthermore, OC pharmacokinetics in obese individuals appeared to be linear as both C_{max} and AUC increased proportionally with the oseltamivir dose.

We also performed a population pharmacokinetic study on 77 hospitalized patients (33 females, 44 males) with normal renal function diagnosed with A(H1N1) influenza treated with oseltamivir every 12 h. The study was performed at steady-state. Population analysis was performed using NONMEM assuming one compartment kinetics [4]. CL/*F* and *V*/*F* for OC were (mean ± SD) 28.8 ± 5.26 l h^{-1} and 324 ± 35.8 l, respectively. These values are slightly higher than those observed in healthy volunteers (Table 1). These differences are probably due to experimental design. In the case of patients, the number and timing of samples varied from one patient to other to accommodate to the needs of the clinical staff, while complete plasma concentration–time curves were constructed for volunteers according to a standardized protocol. OC exposure, however, was comparable between patients and healthy subjects. Moreover, values of all obtained pharmacokinetic parameters in Mexican healthy volunteers and patients were within the range reported in previous studies [5]. Covariates such as gender (male *vs*. female), route of administration (nasogastric tube *vs*. oral), formulation (capsule *vs*. solution) and body mass index (above or below 30 kg m^2) did not allow to identify any distinct subpopulation.

OC pharmacokinetic parameters in Mexican patients and healthy volunteers, either obese or non-obese, are similar to those reported for other populations, including Caucasians from North America and Europe, as well as Thai and Japanese subjects [1, 5]. However, studies specifically addressing oseltamivir pharmacokinetics in subjects of African origin are still wanting. We confirm that oseltamivir dosing need not be adjusted in obese patients [1] and that oseltamivir pharmacokinetics do not appear to exhibit interethnic variability [5]. Our data therefore suggest that dosing regimens can be extrapolated among populations.

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Table 1

Pharmacokinetic parameters of oseltamivir caboxylate in subjects without obesity receiving a single oral oseltamivir 75 mg dose and in subjects with obesity receiving oral oseltamivir single doses of either 75, 150 or 300 mg

Subjects	Without obesity	With obesity		
Dose	75 mg	75 mg	150 mg	300 mg
C_{max} (ng ml^{-1})	309 ± 80	306 ± 104	617 ± 223	1207 ± 227
t_{max} (h)	3.8 ± 0.9	4.0 ± 1.1	4.1 ± 1.1	3.5 ± 0.7
AUC(0,∞) (ng ml^{-1} h)	3489 ± 788	3113 ± 923	6336 ± 1262	12 623 ± 2264
Half-life (h)	7.5 ± 1.9	6.5 ± 1.8	6.2 ± 1.8	6.3 ± 1.4
V_d/F (l)	236 ± 52	237 ± 83	197 ± 73	221 ± 54
CL/F (l h^{-1})	22.6 ± 5.2	26.0 ± 6.27	28.0 ± 11.2	24.0 ± 4.3

Data are presented as mean ± SD. AUC(0,∞) is the AUC value extrapolated to infinity.

Competing Interests

GC-H has received consultancy fees form Amgen, Abbvie, Astra-Zeneca, Bayer, Boehringer-Ingelheim, Eli-Lilly, Janssen-Cilag, Liomont, Sophia, Medix, Merck-Serono, Merck, Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi and UCB. FJF-M has received consultancy fees from Roche and Psicofarma and grants from Psicofarma, Medix and Emifarma.

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