

O247

Oral Session

New old antibiotics: safety and efficacy

FLUOROQUINOLONES AND QT PROLONGATION IN THE CLINICAL SETTING: STUDY OF THEIR IMPACT IN THE HEAVILY PREDISPOSED HOSPITALIZED POPULATION.

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Objectives:

QTc interval changes remain challenging for the practicing internist. Abundant literature data exist in animal models and healthy volunteers. In the clinical setting, however, with 'real-time' patients in the extremes of age carrying predisposing factors, sparse data exist. The scope of our 5-year prospective trial was to study the clinical significance of this effect and to identify the risk factors that might enhance it.

Methods:

228 patients hospitalized in the internal medicine ward and deemed to receive fluoroquinolone intravenously, were enrolled in the study. Patient's clinical characteristics, biochemical profile, antibiotic regimen, dosing and infection site were recorded. All patients underwent an ECG on admission. 72-hours post fluoroquinolones' initiation both ECG and biochemical profile were reevaluated. QTc values of both ECGs were calculated and the difference between them (Dqt) was registered. All cardiac events during hospitalization were recorded. SPSS17 was used for the statistical analysis.

Results:

Median age was 70 years. There were 119(52.2%) men. 52(22.8%) patients suffered from ischemic heart disease (CHD). 24(10.5%) reported chronic heart failure (CHF). 53(23.2%) had renal failure and 15(6.6%) liver failure. 70(30.7%) patients were diabetics. 58(25.4%) already received medications reported to interfere with QTc. 35(15.4%) patients received moxifloxacin, 121(53.1%) levofloxacin and 67(29.4%) ciprofloxacin. 86(37.7%) suffered from urinary tract infection, 84(36.8%) from respiratory tract infection.

QTc baseline was estimated at a mean of 349.4ms (297minimum, 449maximum) and at 72-hours at 366.7ms (307minimum, 455maximum). DQTc was calculated at 17.36(-41ms minimum, 85ms max). When studying each subgroup in separate, QTc difference was calculated at 19.06ms for the moxifloxacin group, at 15.12ms for levofloxacin and at 20.49ms for ciprofloxacin, which shows a trend toward statistical significance(p=0.104) for the ciprofloxacin group and thus merits further study with a larger sample. This is in accordance to our previous smaller series. No difference in DQTc could be demonstrated when comparing different genders, age groups, presence or absence of CHD or CKD, but a larger sample might be necessary. Heart failure shows a trend toward QTc prolongation(p=0.11). Only four patients (1.8%) experienced supraventricular arrhythmia. In these patients, however, DQTc was significantly prolonged.

Conclusions: Our study confirms that QTc is significantly prolonged among fluoroquinolones, probably more with ciprofloxacin. This effect however is not translated to serious clinical adverse events, not even in the predisposed in-hospital population. This must be explained by the 'double hit' theory: although fluoroquinolones interfere with IKr and therefore carry the capacity to prolong QT they, unlike macrolides, lack 'metabolic liability' which would enhance QT prolongation. Only with altered pharmacokinetics can this become apparent. Our study confirms this effect. However, it shows that, even in altered pharmacokinetics (CKD, CHD, electrolyte derangements), this is not translated in serious adverse events rendering quinolones a safe option in the hospitalized population.