European Journal of Clinical Pharmacology (2018) 74:1095
https://doi.org/10.1007/s00228-018-2475-8

LETTER TO THE EDITOR

Extracorporeal circulation systems in coronary artery bypass surgery can affect pharmacokinetics of drugs: may altered CYP-mediated liver function be a possible reason?

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Received: 13 March 2018 / Accepted: 2 May 2018 / Published online: 9 May 2018

Dear Editor,

An interesting paper titled "How do different extracorporeal circulation systems affect metoprolol bioavailability in coronary artery bypass (CABG) surgery patients" by Kokki et al. (2018) reports a markedly decreased bioavailability of metoprolol in the early phase after CABG surgery patients [1]. The study mainly focuses on the effects of different modalities of CABG surgeries namely cardiac surgery and conventional extracorporeal circulation (CECC), miniaturized ECC, and off-pump surgery (OPCAB) and demonstrates no significant difference among the mentioned methods. The same research group published a similar finding on decreased metoprolol bioavailability in their earlier study [2].

Here, we would like to emphasize another confounding factor that may be associated with a possible alteration in drug metabolism during the bypass surgery. Metoprolol is mainly metabolized by cytochrome P450 2D6 (CYP2D6) and suggested as a probe drug for this enzyme in phenotyping [3, 4].

We previously have demonstrated that cardiopulmonary bypass procedure during cardiac surgery altered CYP2C9 activity [5] using losartan as a phenotyping probe drug [6]. We showed a markedly reduced activity of CYP2C9 (assessed as urinary losartan/E-3174, an active metabolite of the parent drug) shortly after the CABG procedure as compared to the activity before the surgery. This decreased activity returned to normal levels about 1 week after the surgery [5].

In the paper by Kokki et al., the effects of three different bypass surgery methods on metoprolol bioavailability have been well described while not much was accounted for altered cytochrome P450-mediated metabolism during the surgery [1]. It is of importance to emphasize that not only metoprolol but also other drug substrates of CYP2D6 [7] such as other beta adrenoceptor blockers, antidepressants, antipsychotics, and other drugs may be similarly affected especially in the subjects with poor metabolizer status for CYP2D6. We would like to draw attention to possible inhibitory effects of CABG procedure on CYP-mediated drug metabolism particularly in the liver.

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