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In Vitro Evidence for Potential Clopidogrel-Propofol Interaction

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***SUMMARY*. Drug-drug interaction was evaluated between cardiovascular disease treatment drug clopidogrel and intravenous anaesthetic agent propofol. Both of these two drugs have narrow therapeutic window, and drug-drug interaction easily affects the plasma concentration which might exceed the minimal toxicity concentration and induce adverse effects. The present study aims to evaluate the potential clopidogrel-propofol interaction through determining the inhibition of clopidogrel on the glucuronidation of propofol and the inhibition of propofol on the hydrolysis of clopidogrel. The results showed that clopidogrel noncompetitively inhibited the human liver microsomes (HLMs)-catalyzed glucuronidation of propofol. Mechanism analysis showed the similar inhibition extent of clopidogrel on the recombinant UGT1A9-catalyzed glucuronidation of 4-methylumbelliferone. In the contrary, 100 μM of propofol did not show the inhibition towards HLMs-catalyzed hydrolysis metabolism of clopidogrel. In conclusion, close monitoring of the drug-drug interaction between clopidogrel and propofol should given.**

RESUMEN. Se evaluó la interacción fármaco-fármaco entre la droga para el tratamiento de la enfermedad cardiovascular clopidogrel y el agente anestésico intravenoso propofol. Ambos fármacos tienen un margen terapéutico estrecho, y la interacción fármaco-fármaco afecta fácilmente la concentración en plasma que podría exceder la concentración mínima de toxicidad e inducir efectos adversos. El presente estudio tiene como objetivo evaluar el potencial de interacción clopidogrel-propofol a través de la determinación de la inhibición de clopidogrel en la glucuronidación de propofol y la inhibición de propofol en la hidrólisis de clopidogrel. Los resultados mostraron que el clopidogrel inhibe no competitivamente glucuronidación de propofol catalizada por microsomas de hígado humano (HLMs). El análisis del mecanismo mostró un grado de inhibición similar de clopidogrel en la glucuronidación de 4-metilumbeliferona catalizada por UGT1A9 recombinante. Por el contrario, 100 μM de propofol no mostró inhibición hacia la hidrólisis de clopidogrel catalizada por HLMs. En conclusión, debe monitorearse estrechamente la interacción fármaco-fármaco entre clopidogrel y propofol.

KEY WORDS: clopidogrel, drug-drug interaction, glucuronidation, hydrolysis, propofol.

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