KINETIC ANALYSIS OF THE TRANSPORT OF A NOVEL PROSTAGLANDIN DERIVATE, ONO-8815, ACROSS THE HUMAN PLACENTA

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The transplacental transfer of drugs to the fetus is one of the great concerns of the pharmacotherapy during pregnancy. In this study, we aimed to evaluate the transplacental transfer of a novel prostaglandin derivate (ONO-8815) with potent inhibitory effects against the spontaneous uterine contraction by using human placental perfusion technique. Term placentas were obtained after vaginal or cesarean section deliveries of term pregnancies. All experiments were conducted in a dual perfusion system. ONO-8815 and antipyrine were simultaneously perfused to the maternal or fetal circulation in a manner of single pass. The time profiles of drug concentration in the perfusate were analyzed by a newly developed pharmacokinetic model. ONO-8815 was rapidly transported across the placenta from the maternal to fetal circulation. However, the transfer index for ONO-8815 was a half of that for antipyrine. Furthermore, ONO-8815 rapidly disappeared from the fetal perfusate and placental tissues after the perfusion with drug free buffer. Since ONO-8815 is more lipophilic than antipyrine, these results suggest that the placenta functions as an effective barrier to reduce the fetal exposure of ONO-8815. Moreover, the developed pharmacokinetic model could adequately explain the transplacental transfer of the drugs. The model may enable us to predict quantitatively the transplacental transfer and fetal distribution of ONO-8815 in vivo.