An exploratory study on a potential neuroprotective agents for post-cardiac arrest encephalopathy using drug repositioning approach

○Takahiro NIIMURA[1], Yoshito ZAMAMI[1,2], Yuki IZAWA-ISHIZAWA[3], Masaki IMANISHI[2], Kenshi TAKECHI[4], Keijo FUKUSHIMA[5], Yuya HORINOUCHI[3], Yasumasa IKEDA[3], Hiromichi FUJINO[5], Koichiro TSUCHIYA[6], Toshiaki TAMAKI[3], Keisuke ISHIZAWA[1,2]

[1]Dept. of Clin. Pharm. and Ther., Inst. of Bio. Sci., Tokushima Univ. Grad. Sch., [2]Dept. of Pharmacy, Tokushima Univ. Hosp., [3]Dept. of Pharm., Inst. of Bio. Sci., Tokushima Univ. Grad. Sch., [4]Clin. Trial Center for Dev. Ther., Tokushima Univ. Hosp., [5]Dept. of Mol. Pharm., Inst. of Bio. Sci., Tokushima Univ. Grad. Sch., [6]Dept. of Med. Pharm., Inst. of Bio. Sci., Tokushima Univ. Grad. Sch.

OBJECTIVE: In this study, we sought a potential drug for treatment of post-cardiac arrest encephalopathy using a drug repositioning approach. **METHODS:** First, candidate drugs having an action related to neuroprotective effect were extracted using "TargetMine", a drug discovery tool. Next, the association between administration of drugs on a month after cardiac arrest and survival to discharge was estimated by multivariable logistic regression using the claim data of cardiac arrest cases obtained from the Japan Medical Data Center. Furthermore, the odds ratio adjusted using the propensity score were calculated for drugs indicated to be effective in the multivariable logistic regression. For drugs suggested to be efficacious in adjusted odds ratio, the cytoprotective effect under hypoxia / low glucose was evaluated by WST-8 assay using HT22 cells. **RESULTS:** We extracted 300 of candidate drugs using TargetMine. Then, we selected five injection drug that used in over 50 cases with cardiac arrest. As a result of evaluating the association between administration of these five drugs and survival to discharge, a significant difference was found only in thiopental, and the survival to discharge rate of thiopental administered group was significantly higher (odds ratio, 1.66; 95% CI, 1.03-2.67). In the in vitro experiment, thiopental significantly improved the HT22 cell viability in hypoxia / low glucose conditions. **CONCLUSIONS:** The current study indicate that thiopental is a potential neuroprotective agents for post-cardiac arrest encephalopathy.