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Total Intravenous Anesthesia (TIVA) of Propofol in Beagle Dogs

Soo Han, Lee*

Department of veterinary internal medicine, college of veterinary medicine, Konkuk University

Introduction: Propofol is short-acting, rapidly metabolizable intravenous agent which is characterized in human by a virtual lack of any cumulative effect and rapid recovery after its administration in bolus doses or by continuous infusion. These studies were carried out to apply total intravenous anesthesia technique with propofol to veterinary medicine.

Materials and methods: In experiment Ⅰ 5 beagle dogs were allotted to each of three experimental groups, which were tiletamine-zolazepam(TZ) group, xylazine-ketamine(XK) group and propofol(PI) group. Animals were anesthetized with tiletamine-zolazepam(10mg/kg, i.v. administered, followed by a intermittent infusion of half dose which just previously administered), xylazine-ketamine(2.2mg/kg, 10mg/kg, i.v. administered, followed by a intermittent infusion of half dose which just previously administered) and propofol(6mg/kg, i.v. administered, followed by a intermittent infusion of 3mg/kg). The chages in heart rate (HR), arterial pressure, SpO_2, rectal temperature(RT), respiratory rate(RR), pain score, and quantitative EEG(95% SEF & MF) of animals in 3 groups during 60 minutes of intermittent infusion and 40 minutes of recovery period were compared. RT was significantly more stable in PI group($p<0.05$) than other groups during recovery period. HR was significantly lower in XK group($p<0.05$) than other groups during sedation. RR was showed similar tendency in all groups. SpO_2 value of PI group was more stable during anesthesia and significantly higher($p<0.05$) than others groups during recovery period. Systolic arterial pressure(SAP) was significantly lower in XK group($p<0.05$) than PI group during sedation and recovery period. Lower analgesic effect occurred in PI group compared with other groups. With changes of 95% SEF and MF, combination of ketamine and xylazine depressed CNS more potently than ketamine alone. And, low doses of propofol had a disinhibitory effect on CNS.

In experiment Ⅱ 5 beagle dogs were allotted to each of three experimental groups, which were propofol(PRO) group, isoflurane(ISO) group and propofol plus fentanyl plus ketamine(PFK) group. Animals were anesthetized with propofol(5mg/kg, i.v. administered, immediately intubated and followed by apropofol infusion beginning at 0.4mg/kg/min), isoflurane(inducted by mask, immediately intubated and followed by a isoflurane maintenance beginning at 2.5% concentration) and propofol plus fentanyl plus ketamine(fentanyl 0.005mg/kg, i.v. administered, after 5 min, propofol plus ketamine 3mg/kg, i.v. administered, immediately intubated and followed by propofol and ketamine infusion beginning at

0.2mg/kg/min). The changes in hemodynamics, arterial pressure, SpO_2, RT, RR, pain score, 95% SEF, and MF of the animals in 3 groups during 60 minutes of sedation and 40 minutes recovery period were compared. In addition recovery times(extubation, head lift, sternal position, righting reflex and walking) after 60 minutes of sedation were alsocompared. Rectal temperature was significantly lower in ISO group($p<0.05$) than PRO group from 10 to 100 minutes. Heart rate was significantly lower in ISO group($p<0.05$) than PRO groupat 40, 50 and 60 minutes. RR was significantly lower in PRO and PFK group($p<0.05$) at induction and 70 minutes. SpO_2 was similar in all groups. SAP was significantly lower in ISO group($p<0.05$) during anesthesia. The changes of 95% SEF and MF was similar in all groups. The correlation of 95% SEF and pain score was significant(positive, $p<0.05$) in all groups. Emergence was also similar in all groups.

In experiment Ⅲ the changes of plasma propofol concentration and 95% SEF in the animals of PRO group in experiment Ⅱwere measured to calculate the pharmacokinetic(PK) and pharmacodynamic(PD) parameter of propofol. The correlation of plasma propofol concentration and 95% SEF was significant(negative, $p<0.05$). Simultaneous PK-PD modeling was carried out by sequential fitting for individual parameter with NONMEM® software. PK of propofol in this study was best described by 2 compartment model. The PK parameters obtained by modeling were summarized as follows: $t_{1/2}a$=8.92min, $t_{1/2}b$=172.82min, V_{dss}=6.296L/kg, CL=76.66±8.17ml/kg/min, V_1=1346.54±3.14ml/kg, K_{10}=0.057±0.03/min, K_{12}=0.02±0.036/min, K_{21}=0.006±0.008/min. The PK parameters obtained by modeling were summarized as follows: E_{max}=9.89±0.12Hz, baseline of effects=35.20±0.00Hz, EC_{50}=1.12mg/ml, g=2.93±0.0718.

Results: In conclusion, the sedation by intermittent bolus infusion with propofol has advantages of stabilizing RT, SpO_2 and hemodynamics during anesthesia and provides fast recovery in beagle dogs. But it has disadvantage of low analgesic effect. Therefore, more studies on the simultaneous infusion with analgesics should be followed. TIVA with propofol has also advantage in stabilizing RT and SAP during anesthesia over inhalation anesthesia, and provides fast and stable recovery in beagle dogs. Future studies will be required to obtain more precise PK and PD parameters, especially Ke_0 through the proper modeling in order to develop prototype of target-controlled infusion(TCI) delivery system for dogs. And studies will be required to evaluate performance of the TCI system.

*Corresponding author: chungbh@konkuk.ac.kr