**BACKGROUND**

- Clevidipine is a novel dihydropyridine calcium channel antagonist with an ultra short half-life (t1/2 ~ 2 min) that can be quickly titrated.
- The effect of clevidipine on CNS physiology will determine the clinical utility of clevidipine in patients with neurologic pathology.

**OBJECTIVES**

- Determine clevidipine’s impact on:
  1. Cerebral Blood Flow (CBF) as assessed by mean Middle Cerebral Artery (MCA) blood flow velocity.
  2. Cerebral vascular reactivity to hypocapnia in healthy human volunteers using TCD.

**STUDY DESIGN**

Baseline 1 – Normocapnea, No Infusion
Patient Hyperventilation
Baseline 2 – Normocapnea, No Infusion
Clevidipine to Decrease MAP 15%
Clevidipine to Decrease MAP 30%
Clevidipine to Decrease MAP 30% +Hyperventilation
Baseline 3 – Normocapnea, No Infusion

**RESULTS**

**Table 1.** Mean middle cerebral artery blood flow velocities at baseline and in presence of intermediate (Clev-15%, 20 mg/hr) and high dose (Clev-30%, 32 mg/hr) clevidipine infusion in 6 healthy volunteers.

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<table>
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<th>Subject</th>
<th>Clevidine Dose</th>
<th>MAP</th>
<th>CBFV</th>
<th>MAP</th>
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<th>MAP</th>
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<td>Baseline</td>
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<td>49</td>
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<td>52</td>
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<td>76</td>
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<td>Clev-30%</td>
<td>32 mg/hr</td>
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</table>

*Percent change in CBFV from Baseline was not significant; -2.2% p=0.93 and +2.1% p=0.45, respectively.
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**Figure 1.** Mean MCA blood flow velocity by TCD before (control) and during clevidipine infusion. The mean percent change in CBFV from Baseline were not significant; -2.2% p=0.93 and +2.1% p=0.45, respectively.

**Figure 2.** The response of Mean MCA blood flow velocity to change in arterial carbon dioxide before (control) and during clevidipine infusion. CBF and baseline are indicated by a decrease in MCA blood flow velocity. CO2 Reactivity 0.84 +/-0.04 and 0.92 +/-0.03 (% Change CBF/mm Hg CO2), respectively, p=0.12.

**METHODS**

- Six healthy human volunteers were enrolled and each received a radial arterial line for (1) Mean Arterial Pressure (MAP) monitoring, and (2) arterial blood gas sampling to determine arterial carbon dioxide concentration (P,CO2).
- Bilateral Transcranial Doppler Ultrasound (TCD) probes were placed and manipulated to find an appropriate signal over the temporal insolation window to determine Mean Cerebral Blood Flow Velocity (CBFV) in the middle cerebral artery (MCA).
- After baseline recordings of hemodynamic variables, including mean CBFV in the MCA, each subject received clevidipine infusions at doses of 20 and 32 mg/hr to decrease MAP by ~15% and ~30%, respectively.
- Subjects hyperventilated until their P,CO2 was 20 mmHg both at baseline and in the presence of a maximal clevidipine infusion in order to assess carbon dioxide responsiveness.
- No anesthetics were administered

**CONCLUSIONS**

Clevidipine does not appear to cause clinically significant direct cerebral vasodilation in healthy human volunteers, even at the FDA recommended dosing limit. Similarly, cerebral vascular reactivity to hypocapnia is preserved in this population.

**REFERENCES**
