Biotrofix

ACUTE STROKE NEUROPROTECTION MODEL

MODEL: **PERMANENT SUTURE OCCLUSION (FILAMENT OCCLUSION) OF MIDDLE CEREBRAL ARTERY (MCA)**

TEST NUMBER: BTFX-A01

CATEGORY: Permanent focal ischemia model

SPECIES: Mature Wistar or Sprague-Dawley rats

APPLICATION: Testing neuroprotective agents in a model of acute focal stroke (permanent occlusion)

METHOD: Mature rats are allowed free access to food and water before surgery. Animals are anesthetized with halothane or isoflourane by inhalation or chloral hydrate by i.p. injection. Rectal temperature is maintained at 37.5 ± 0.5° C using a heating blanket connected to a temperature controller. Blood pressure and blood gases can be monitored though the femoral artery.

Under the operating microscope, the bifurcation of the right common carotid artery is exposed through a midline incision in the neck. A 4-0 monofilamnent nylon suture with its tip rounded near a flame is introduced into the right external carotid artery and advanced into the internal carotid artery for a length of 17~20 mm from the bifurcation. These methods place the tip of the suture at the origin of the anterior cerebral artery, thereby occluding the middle cerebral artery. The suture is left in place until death.

Following MCA occlusion, animals are allowed to awaken from anesthesia. Surgical mortality is <10% in this model.

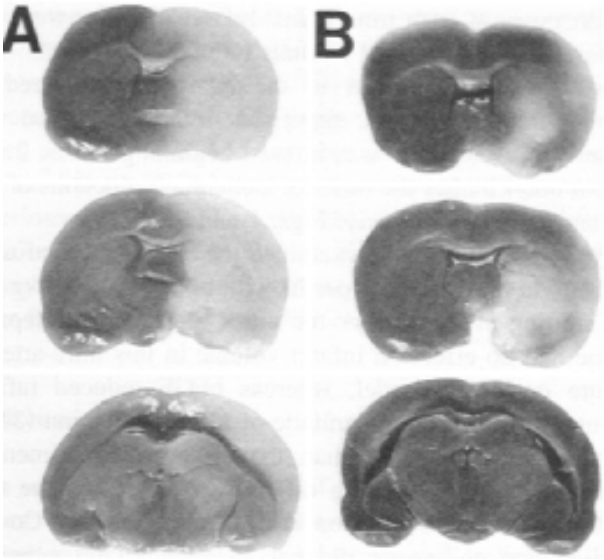
At 24 h after ischemia, animals are assessed by a brief rating scale for neurological dysfunction. Animals are then killed by an overdose of chloral hydrate, and brains are removed for infarct volume assessment.

ENDPOINTS: Infarct volume; short-term behavioral studies

DESCRIPTION OF INFARCTION:

This method produces a large infarction in the distribution of the MCA, involving a large portion of the lateral cerebral cortex and underlying white matter and striatum. The cortex represents the ischemic penumbra

in this model.. Animals typically survive for only a day or two, making this model appropriate for short-term neuroprotection studies.



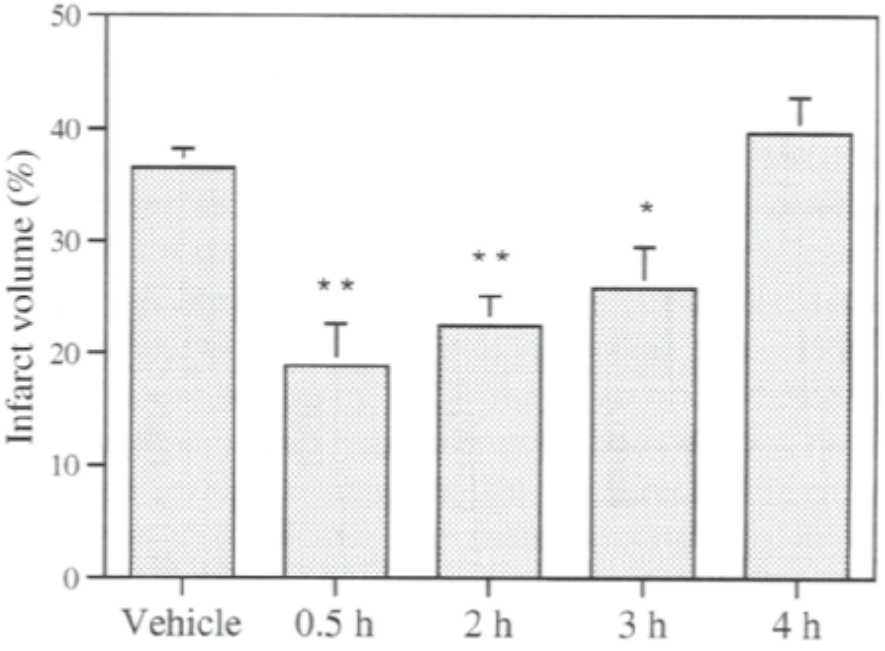


Figure 1. Example of data obtained using the permanent suture occlusion method and a neuroprotective drug (bFGF, see ref. [2]). Intravenous administration of bFGF starting at 0.5, 2, and 3, but not 4 hours significantly decreased infarct volume.

REFERENCE(S):

1. Fisher, M., M.-E. Meadows, T. Do, J. Weise, V. Trubetskoy, M. Charette and S. P. Finklestein (1995). "Delayed treatment with intravenous basic fibroblast growth factor reduces infarct size following permanent focal cerebral ischemia in rats." J. Cereb. Blood Flow Metab. **15**: 953-959.

2. Ren, J. and S. P. Finklestein (1997). "Time dependence of infarct reduction by intravenous basic fibroblast growth factor (bFGF) following focal cerebral ischemia in rats." Eur. J. Pharmacol. **327**: 11-16.