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Association of Primate Veterinarians' Position Statement: Cerebrospinal Fluid Aspiration for Nonhuman Primates in Biomedical Research

Background

Cerebrospinal fluid (CSF) analysis is a powerful tool that can augment detection of various processes occurring within the central nervous system. Examples include hemorrhage, inflammation, infection, neoplasia and other clinical conditions. In addition, serial evaluation of compounds within the CSF such as hormones, medications, neurotransmitters, biomarkers, metabolites, and viruses may be extremely useful in both basic and translational research.

Purpose

The Association of Primate Veterinarians (APV) recognizes that CSF collection may be required for both clinical and research purposes in nonhuman primates (NHP). Because there are inherent risks associated with the technique, the laboratory animal veterinarian should determine the need and utility of CSF collection for clinical evaluation. CSF collections for research purposes must be scientifically justified and approved by the institutional animal care and use committee (IACUC) or equivalent regulatory body hereafter referred to as IACUC. The following recommendations provide basic information for IACUCs, researchers using nonhuman primate models, and veterinary personnel to consider when developing policies and standard operating procedures for CSF collections.

Procedural Considerations

Cerebrospinal fluid (CSF) is typically collected via puncture of the cisterna magna or lumbar vertebral space. The animal should be appropriately anesthetized, and the procedure performed using aseptic technique inclusive of hair clipping, surgical preparation of the collection site, and use of sterile materials (drapes, gloves, syringes, and needles). CSF collection is typically performed in lateral recumbency, or in a sitting position, with a slight flexion of the spine to widen the intervertebral space. Needle size and length selected should be appropriate for the species of nonhuman primate and size of the animal on which the procedure is being performed. Technique, supplies and equipment used, as well as pre-, intra- and post-operative care may vary depending on the species used and specific research aims.

Scientific justification should be provided for the number and frequency of collections performed. In the creation of this document, every effort was made to find current references and literature regarding objective numerical values for total CSF volume, limitations or recommendations for number of meningeal punctures, frequency of collections, safe volume for withdrawal and CSF replenishment rates. There is a paucity of literature in this area and our survey results collected from the APV membership indicates that facilities are successfully performing CSF collections in many different ways. We are therefore providing considerations and recommendations for CSF collection based upon the references available. Further research specific to nonhuman primates are needed in this area to facilitate the development of more prescriptive recommendations.

While few complications have been reported with CSF collections in nonhuman primates, anatomic variation as well as inappropriate or poor procedural technique can result in a compromised sample and/or complications such as hemorrhage, herniation, infection, spinal cord or nerve root damage, and animal discomfort. All of these complications, while rare, can compromise animal welfare. Other complications may be encountered when working with implantation of and collection from chronic, indwelling CSF catheters. Maintenance of chronic indwelling catheters is outside of the scope of this document, but references are provided below for more information.

Post-procedural monitoring should be provided continuously until the patient is returned to its home enclosure and able to remain consistently in an upright position without support. Patient monitoring should be done regularly for a minimum of 24 hours or as indicated in the IACUC-approved protocol.

Monitoring should include evaluation of basic NHP physiologic, behavioral, and locomotor parameters. In particular, animals should be assessed for signs of neurologic impairment including, but not limited to, lethargy, depression, obtundation, and head pressing. In human medicine spinal headache is not uncommon following CSF aspiration. In consideration of this potential sequelae in NHPs, analgesia should be provided at the time of the procedure and extended as needed based on post-operative observations for behavior associated with headache or spinal pain.

Record Keeping

IACUCs should be aware of the CSF collection logistics and all possible complications and review them at least annually. All relevant information e.g. drug doses, pre-procedural prep, CSF volume collected and post-procedural short and long term recovery should be entered in the medical record and lab logs.

IACUC Considerations

IACUCs should be aware of the CSF collection logistics and all possible complications and review them at least annually. All relevant information e.g. drug doses, pre-procedural prep, CSF volume collected and post-procedural short and long term recovery should be entered in the medical record and lab logs.

Cerebrospinal fluid can be a critical resource in a research protocol, but its collection can have consequences that impact animal welfare if the technique is not performed appropriately. The IACUC should carefully evaluate each proposal involving CSF collection and consider the following issues:

1. Are CSF collections essential to address the scientific objectives stated in the protocol?
2. Are alternative and less invasive methods of evaluating the central nervous system (such as imaging modalities)

available and, if so, have they been considered?
3. Are the personnel performing the procedures appropriately trained and do they have adequate skills?
4. Will appropriate perioperative anesthesia, and analgesia be provided? The laboratory animal veterinarian should be consulted regarding the anesthesia and analgesia plan.
5. Is the volume of CSF to be collected appropriate for the age and size of the animal?
6. Are the number and frequency of meningeal punctures appropriate for the animal and have the risks of complications been minimized? If the CSF collections are performed as part of research investigations, identifying a specific endpoint should be considered.
7. Is the plan for post-procedural monitoring adequate?
8. If chronic CSF catheters are placed, is the plan for monitoring and maintenance outlined in the protocol and is it appropriate?
9. Have all possible post-procedural complications been considered and all reasonable interventional methods inclusive of euthanasia, listed?

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