INTRODUCTION

A number of medical conditions (e.g. lower back pain) or interventions (e.g. lower limb surgeries) require epidural or intrathecal injections in patients. Regulatory toxicology studies to assess drug candidates delivered with these routes require the same administration method in the animals to mimic the clinical conditions and assess local tolerance. Intrathecal and epidural injections have been extensively used in toxicology studies using Beagle dogs but a paucity of data exist in minipigs. Beagle dogs and Göttingen minipigs underwent fluoroscopy-guided epidural or intrathecal injections of sterile saline (0.2-0.8 mL/kg). Separate animals were administered a contrast agent to assess the optimal dose volume for both routes in both species. A spinal needle was used for intrathecal injections while a Tuohy needle was used for epidural administration.

The procedure was performed using a short inhaled anesthesia (isoﬂurane). Fluoroscopy imaging permitted precise evaluation of lumbar vertebra anatomy, which facilitated spinal or Tuohy needle positioning and durotomy for intrathecal delivery. The L5-L6 intervertebral space was considered optimal in both Beagle dogs and Göttingen minipigs. Animals were euthanized after recovery from the last administration and no observable macroscopic or microscopic finding related to the administration was noted at necropsy. In conclusion, Beagle dogs and Göttingen minipigs were considered comparable non-rodent species for epidural and intrathecal dosing in toxicology studies using these routes.

METHODOLOGY

Beagle dogs (8-15kg) and Göttingen minipigs (7-17kg) were used to compare epidural and intrathecal injections in both species. For epidural injections a 20g 3 ½ inches Tuohy needle was used (BD, Ref. 405028). For intrathecal injections, a 20g 3 inches spinal needle was used (BD, Ref. 405182). Sterile saline volumes of 0.2-0.8 mL/kg with a maximum of 10 mL/animal were used for both species for epidural injections while intrathecal administrations were limited to 0.2 mL/kg.

RESULTS AND DISCUSSION

The weight of Beagle dogs was considered an important factor to ensure the success of the procedure as lighter dogs were associated with a narrow intervertebral space which increased the difficulty of the technique. In Göttingen minipigs, the intervertebral space could be accessed easily irrespective of the body weight of the animal (Fig. 1). A caudocranial needle angle perfectly aligned with the midline was optimal for both types of injections in the animals to mimic the clinical conditions and assess local tolerance. Intrathecal and epidural saline administrations were performed fluoroscopy-guided minimally invasive epidural or intrathecal injections for repeat toxicology studies: comparison of Beagle dogs and Göttingen Minipigs.

Similarly, an intrathecal volume of 0.2 mL/kg was not associated with any neurological abnormalities in both species. As reported in the literature, epidural injections at dose volumes up to 0.2 mL/kg were successfully used for a single collection in Gottingen minipigs but repeated puncture and intrathecal dosing have been extensively used in toxicology studies using Beagle dogs but a paucity of data exist in minipigs. Beagle dogs and Göttingen minipigs underwent fluoroscopy-guided epidural or intrathecal injections of sterile saline (0.2-0.8 mL/kg). Separate animals were administered a contrast agent to assess the optimal dose volume for both routes in both species. A spinal needle was used for intrathecal injections while a Tuohy needle was used for epidural administration.

The procedure was performed using a short inhaled anesthesia (isoﬂurane). Fluoroscopy imaging permitted precise evaluation of lumbar vertebra anatomy, which facilitated spinal or Tuohy needle positioning and durotomy for intrathecal delivery. The L5-L6 intervertebral space was considered optimal in both Beagle dogs and Göttingen minipigs. Animals were euthanized after recovery from the last administration and no observable macroscopic or microscopic finding related to the administration was noted at necropsy. In conclusion, Beagle dogs and Göttingen minipigs were considered comparable non-rodent species for epidural and intrathecal dosing in toxicology studies using these routes.

METHODOLOGY

Beagle dogs (8-15kg) and Göttingen minipigs (7-17kg) were used to compare epidural and intrathecal injections in both species. For epidural injections a 20g 3 ½ inches Tuohy needle was used (BD, Ref. 405028). For intrathecal injections, a 20g 3 inches spinal needle was used (BD, Ref. 405182). Sterile saline volumes of 0.2-0.8 mL/kg with a maximum of 10 mL/animal were used for both species for epidural injections while intrathecal administrations were limited to 0.2 mL/kg.

RESULTS AND DISCUSSION

The weight of Beagle dogs was considered an important factor to ensure the success of the procedure as lighter dogs were associated with a narrow intervertebral space which increased the difficulty of the technique. In Göttingen minipigs, the intervertebral space could be accessed easily irrespective of the body weight of the animal (Fig. 1). A caudocranial needle angle perfectly aligned with the midline was optimal for both types of injections in both species. As reported in the literature, epidural injections at dose volumes up to 0.8 mL/kg with a maximum of 10 mL/animal were used for both species for epidural injections while intrathecal administrations were limited to 0.2 mL/kg.

CONCLUSION

The current evaluation confirmed that the Göttingen minipig is an appropriate non-rodent species for non-clinical toxicology studies requiring epidural and intrathecal delivery. The anatomy of the Göttingen minipig is considered superior to the Beagle dog for both routes (i.e. epidural or intrathecal administration), however, repeat CSF sampling by cisterna magna puncture in minipigs is not recommended.

REFERENCES

4. Simon Authier 1, 2, Julius Haruna 1, Eric Troncy 2, Roy Forster 1 and Raluca Kubaszky 1
1 CiToxLAB in North America, Laval, QC, Canada - 2 Faculty of Veterinary Medicine, University of Montreal, 3200 Scottia, St-Hyacinthe, QC, Canada

www.citoxlab.com