MR-Based Quantification of CSF Leakage Following Intracisternal Magna Tap in Nonhuman Primates

Andy Carlson, Jason Winsor, Maggie Mohr, Eva Wembacher-Schroeder, Jen Sweet, Mark Johnson

Northern Biomedical Research

Contact: Andy Carlson, andy.carlson@nbrlab.com

INTRODUCTION

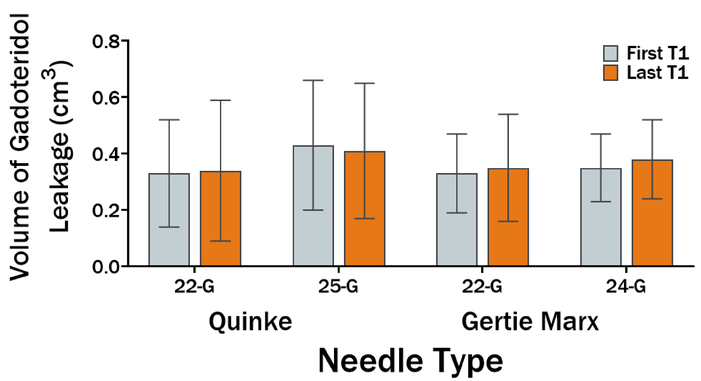
Central delivery into the cisterna magna (CM) via percutaneous administration with spinal needles is vital for a variety of therapeutics tested in non-human primates (NHP). Correct administration can be affected by multiple factors: animal position, experience and technique of the dose administrator, needle type (e.g., Cutting, pencil point), needle gauge, cerebrospinal fluid (CSF) collection, or volume of therapeutic. Cerebrospinal fluid leakage during and after dose administration is a concern. The effect that the type and gauge of spinal needle had on leakage was evaluated using magnetic resonance imaging.

METHODS

Five cynomolgus NHPs were anesthetized and prepared for CM dose administration. Induction was performed using ketamine (5mg/kg), dexmedetomidine (0.025mg/kg), and buprenorphine (0.02mg/kg). Anesthesia was maintained with a mixture of oxygen (1L/min) and isoflurane (1-3%). Buprenorphine ER (0.2mg/kg) and Meloxicam ER (0.6mg/kg) were administered in recovery.

22-G Quinke (Q), 25-G Q, 22-G Gertie Marx (GM) and 24-G GM spinal needles were evaluated. Selection of needle type and gauge varied between animals on dosing days. Dose administrator and holder remained consistent throughout the study to reduce variability. 1.0 mL of CSF was collected immediately prior to administration of 2.0 mL of 2mM Prohance (gadoteridol) in Phosphate Buffered Saline. Immediately following administration, T1-weighted and FLAIR scans were obtained with the MRI (Philips Achieva Quasar 3.0T MR). Continuous scanning occurred for ~30 minutes. The animals were recovered and allowed a two-week washout period prior to the next dose/needle type. Gadoteridol distribution volume outside the CSF space was considered as CSF leakage and was quantified by Brainlab (Brainlab AG, Munich, Germany). For volumetric assessment, a customized algorithm for segmentation of the gadoteridol distribution by subtracting the baseline images from the first and the last post infusion T1-weighted MR images was applied. (Figure 2).

RESULTS



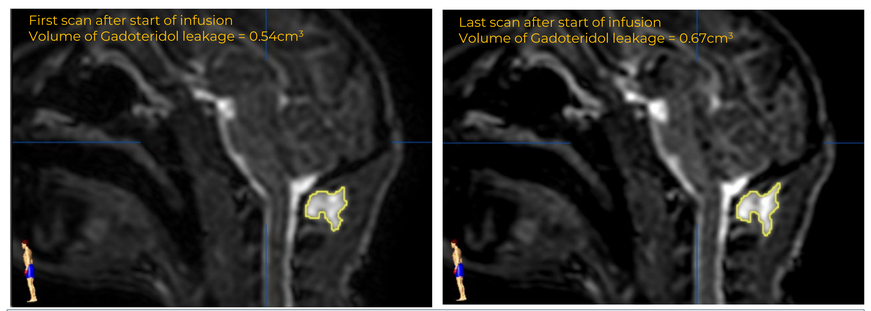


Figure 2. Screenshots showing the gadoteridol distribution volume (yellow) determined at the first scan after start of infusion (left) and at the end of infusion (right) overlaid on sagittal view T1-weighted MR).

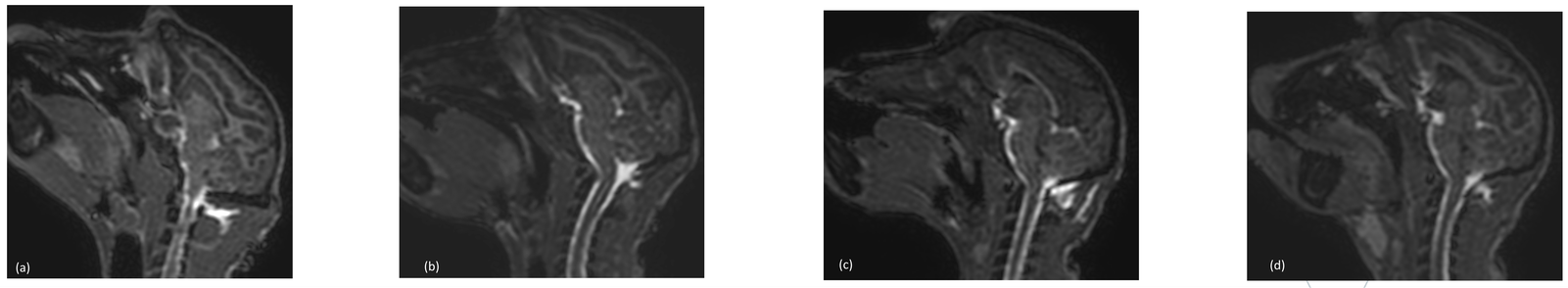


Figure 3. Screenshots of representative T1-weighted MR images. (a) 22-G Q, (b) 25-G Q, (c) 22-G GM, and (d) 24-G GM.

The 22-G Q, 25-G Q, and 22-G GM were used for CSF collection and dose administration on five animals each, while the 24-G GM was used on four animals. The first scan mean leakage (cm^3) of gadoteridol was 0.33 (22-G Q), 0.43 (25-G Q), 0.33 (22-G GM), and 0.35 (24-G GM). The final mean leakage (cm^3) of gadoteridol was 0.34 (22-G Q), 0.41 (25-G Q), 0.35 (22-G GM), and 0.38 (24-G GM). Gadoteridol leakage into muscular and or subcutaneous planes was observed with all needles tested. There was no statistical significance between the four needles tested.

Figure 1. Tip of Gertie Marx (left) and Quinke (right) spinal needle tips.

CONCLUSION

Based on this study, there is no statistically significant difference in CSF leakage between Quinke and Gertie Marx needles via percutaneous cisterna magna dose administration. Our comparison of a cutting needle to a pencil point needle with different gauges failed to show one option as superior to any other. Multiple variables may have confounding effects on the results. The possibility of the needle opening being on the cusp of the dura and imperceptible movement of the needle during the procedure are the two most likely causes of leakage due to human error.

ACKNOWLEDGEMENTS

A special thanks to Leslie Minnema and the surgical technicians.