SPECT Imaging of Direct Nose-to-Brain Transfer of MAG-3 in Man.
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METHODS

Study Design:
Seven subjects were enrolled in this study. MAG3-99m, a technetium-99m labeled peptide, was delivered as the radiotracer. This study used a two arm cross-over design to investigate MAG3 administration with Impel’s POD nasal device in comparison with a traditional nasal pump. Imaging was performed on two separate days, one week apart. After tracer administration, 2D SPECT imaging was performed for 5 minutes. Then, 3D SPECT imaging was acquired for 8 minutes starting at 10 minutes after tracer administration. An MRI (GE Signa Excite) scan was also acquired to provide detailed anatomical information. Pixel analysis (VivoQuant) by nasal region of interest was used to quantify radioactivity in each target nasal deposition region (MATLAB). MAG3-99m in the 3D scan regions of interest was quantified using VivoQuant Software (Invicro). Regional radioactivity signal was compared using a paired two tailed Students t-test. The clinical study was conducted at Lovelace Respiratory Research Institute.

RESULTS

• The POD nasal device resulted in a large fraction of dose being deposited in the upper third of the nasal cavity after administration.
• The traditional nasal pump resulted in a majority of the dose being deposited in the vestibule portion of the nasal cavity. With the traditional nasal pump there was no observable transfer of the MAG3 peptide from the nasal cavity to the central nervous system.
• With POD administration the tracer could be observed in the basal membranes of the brain and other brain regions in a distribution pattern similar to what has been observed in several preclinical studies on nose-to-brain transport.
• No significant amount of tracer was observed in muscle tissue, indicating a direct nose-to-brain transfer.

CONCLUSIONS

The Impel POD device was superior in depositing the peptide tracer into the upper third of the nasal cavity where connections exist between the nasal cavity and the CNS. This nasal distribution appears critical to enable direct transfer of compound from the nasal cavity to the central nervous system along the nose-to-brain distribution pathways. This study indicates a nose-to-brain transport pathway in humans using SPECT imaging and validates the continued study of this pathway to deliver biologic therapeutics to the CNS.