Monitoring of Drug Effects on Intestinal Motility with MRI

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Synopsis: A non-invasive MR monitoring method to study motility effects of drugs at various sites of the gastrointestinal tract is proposed. A standardized distension method together with a positive intraluminal contrast agent were used in order to allow reproducible contraction amplitude measurements over time. Motility was measured with ultrarapid T1-w 2D-GRE sequences concomitantly in all three planes and with a 1.6s temporal resolution. Different pharmacological actions with varying degrees of pro- and akinetic effects on peristalsis were demonstrated exemplarily for Buscopan®, Paspertin® and erythromycine with follow-up times of up to 35 minutes.

Introduction: Current methods for measuring gastrointestinal peristaltic motion need intubation which is unpleasant for the patient and therefore unsatisfactory. Assessment of small gut motility has been performed successfully with MRI [1]. Prolongation of measurement time concomitantly with a three-dimensional monitoring would improve the concept and allow a much clearer description of pharmacological effects on the various functional and anatomical segments of the intestine. The ultimate goal being a pharmacological test method for monitoring peristalsis effects of drugs, first attempts with Buscopan® (hyoscine butylbromide), Paspertin® (metoclopramide) and erythromycine were to be realized.

Materials and Methods: A standardized protocol for optimal distension and strong enhancement of the gut lumen consisting of 20ml Gd-DOTA (Meglumine-gadoterate, Dotarem®, Guerbet, France) dissolved in 1500ml of water in combination with 1.0g/kg body weight of Metamucil® (Procter & Gamble, Ohio, USA) was divided into 5 doses and given in hourly intervals over 4 hours. Except additional water no other food or beverages were allowed during the study [2]. After the last intake imaging was performed using a 1.5T MR unit (Philips NT-Intera 6000) with an abdominal phase-array body coil. Gastrointestinal motion was determined with a series of sequential coronal, sagittal and axial slices (all 3 acquired within approximately 1.6 seconds) in stationary dynamic mode using a 2D gradient echo sequence (TR/TE 3.4/ 1.6 ms, flip-angle 25°, matrix 134X256, FOV 500mm, apnea with intervals, prone, 10mm slice thickness) (Fig.1). After recording “normal” motility over 2 minutes, 40mg of Buscopan® were administered intravenously as a bolus to inhibit peristaltic contractions. Prokinetic effects of 20mg i.v. Paspertin® (metoclopramide) and erythromycine were to be realized

Results: Gut motility dynamics, amplitudes and contraction/time frequencies could be obtained in single volunteers over a maximum monitoring time of 35 minutes and on all three planes (Fig.1). Normal motility with contraction frequencies of 11.0/min ± 1.88 in the proximal gut declined to an almost complete and abrupt arrest following 1.5mg/kg body weight of Metamucil® (Procter & Gamble, Ohio, USA) was divided into 5 doses and given in hourly intervals over 4 hours. Except additional water no other food or beverages were allowed during the study [2]. After the last intake imaging was performed using a 1.5T MR unit (Philips NT-Intera 6000) with an abdominal phase-array body coil. Gastrointestinal motion was determined with a series of sequential coronal, sagittal and axial slices (all 3 acquired within approximately 1.6 seconds) in stationary dynamic mode using a 2D gradient echo sequence (TR/TE 3.4/ 1.6 ms, flip-angle 25°, matrix 134X256, FOV 500mm, apnea with intervals, prone, 10mm slice thickness) (Fig.1). After recording “normal” motility over 2 minutes, 40mg of Buscopan® were administered intravenously as a bolus to inhibit peristaltic contractions. Prokinetic effects of 20mg i.v. Paspertin® (metoclopramide) and erythromycine were to be realized

Conclusions: Three-dimensional transsegmental small gut and pylorus motility may easily be depicted and assessed quantitatively with the proposed non-invasive MRI method and followed for up to 35 minutes. Varying effects on intestinal motility with differing action-sites may be monitored over long time windows and characterized qualitatively and quantitatively. MRI as a non-invasive imaging method allows to standardize a simple drug assay test for effects on peristalsis.

References