TITLE: DOUBLE-BLIND ULTRASONOGRAPHIC DEMONSTRATION OF MORPHINE-INDUCED SPASM OF THE COMMON BILE DUCT

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<u>Introduction</u>: Although increase in common bile duct pressure has been repeatedly demonstrated in experimental animals and humans, this is the first double-blind study designed to demonstrate the spasm of the common bile duct as a result of i.v. administration of morphine in surgical patients by direct visual observation utilizing the novel ultrasonographic technique of Sigel.

Methods: Twelve patients scheduled to undergo cholecystectomy were investigated in a double-blind randomized study design. The study was approved by the Institutional Review Board. Written valid consent was obtained from each patient. Seven patients (F = 6; M = 1) with a mean  $\pm$  S.E.M. age of 43.3  $\pm$ 7.9 yrs. and weight of 65.1  $\pm$  5.6 kg received 0.2 mg/kg morphine, whereas 5 patients (F = 4; M = 1) with a mean age of  $43.6 \pm 6.9$  yrs. and weight of 78.0 ± 6.4 kg received a saline placebo. Premedication consisted of either midazolam or triazolam with glycopyrrolate, but no narcotic was given 12 hrs. prior to the study. Anesthesia was induced with thiopental and intubation was facilitated by succinylcholine. Isoflurene with N20:0, was used for maintenance of anesthesia. After exposure of the common bile duct and appropriate imaging by ultrasound, the unknown drug was injected in 30 seconds into a continuously running i.v. drip. The caliber of the common bile duct was determined before and 2, 4, 8 and 10 min. after the drug administration. ANOVA program was utilized for statistical analysis of the data by student t-test. P< 0.05was considered significant.

Results: No significant change in common bile duct caliber was observed after placebo administration, since the caliber was 0.75  $\pm$  0.20 cm before and 0.74  $\pm$  0.15, 0.74  $\pm$  0.15, 0.73  $\pm$  0.18 and 0.77  $\pm$  0.14 cm at 2, 4, 8 and 10 min. after placebo. Morphine caused a significant reduction in the caliber of the common bile duct at 8 min. when the peak effect was observed. Before morphine the caliber was 0.95  $\pm$  0.13; after morphine at 2, 4, 8 and 10 min. 0.82  $\pm$  0.10, 0.72  $\pm$  0.10, 0.58  $\pm$  0.10 and 0.66  $\pm$  0.12 cm. Figure shows the percentage changes in the caliber of common bile duct at 8 min. after morphine or placebo.

<u>Discussion</u>: This is the first report on ultrasonographic confirmation of the spasmotic effect of morphine on the common bile duct caliber, although many previous studies showed indirect evidence of spasm by demonstrating changes in biliary duct pressure following morphine administration. In conclusion, morphine should not be used either for premedication or supplementation of anesthesia in patients in whom spasm of the common biliary duct and cholestasis ought to be avoided.

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% CHANGES IN BILE DUCT CALIBER BEFORE AND AFTER PLACEBO OR MORPHINE ADMINISTRATION

