

August 22, 2012



Dear Jin-Lei Wang,

Thank you very much for your letter of August 12, 2013, along with the reviewers' comments. We thank the reviewers for their in-depth evaluation of our manuscript and their valuable comments. We have discussed extensively the questions that were raised by the reviewers, and these have been carefully answered point-by-point in the paragraphs shown below. The revised manuscript has been improved in accordance with the suggestions of the Editor-in-Chief. The format has been updated to meet the standards and format of the *World Journal of Gastroenterology*. Please find enclosed the edited manuscript in Word format (file name: 4612-review.doc).

Title: Anisodamine accelerates spontaneous passage of single symptomatic bile duct stones ≤ 10 -mm

Authors: Jun Gao, Xue-mei Ding, Shan Ke, Yi-ming Zhou, Xiao-jun Qian, Rui-liang Ma, Chun-min Ning, Zong-hai Xin, Wen-bing Sun

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Answers to queries from Reviewer # 1

In this study the authors performed a randomized controlled trial investigating whether Anisodamine accelerates spontaneous passage of single symptomatic common bile duct stones of 10-mm diameter or smaller. The study was well conducted and statistics are o.k. The only comment is that there was no 1 year follow up of patients successfully treated with Anisodamine or placebo to investigate for symptomatic retained stones.

Answer: The primary endpoint was the rate of spontaneous passage of CBD stones in 4 weeks. The secondary endpoints were the safety of anisodamine and dropout rate. Hence, a 1-year follow-up was not necessary to show the superiority of anisodamine for patients after CBD stones were treated successfully. Furthermore, the results after 1-year follow up would be hard to explain with consideration of the possible

recurrence of CBD stones.

Answers to queries set by Reviewer # 2

1. The author defined the spontaneous passage of CBD stone as no signs of stones by CT or MRCP. Subjectives of this study were patients with small CBD stones less than 10mm in diameter. In such instances, can CT or MRCP accurately evaluate whether stones are present or absent?

Answer: One of the inclusion criteria was a single CBD stone ≤ 10 mm in diameter confirmed by conventional CT or MRCP. For this group of patients, CT or MRCP can be used readily to evaluate spontaneous passage of CBD stones.

2. At the laparoscopic cholecystectomy, did the author perform intraoperative cholangiography? Are there any patients who were found out small CBD stones which were missed in preoperative CT or MRCP?

Answer: Spontaneous passage of CBD stones was defined as no sign of CBD stones upon CT or MRCP and normal results of liver function tests after conservative treatment. Hence, we did not undertake intraoperative cholangiography at the laparoscopic cholecystectomy.

3. In the patients who were diagnosed as having spontaneous passage of the stones, how often the symptoms and/or spontaneous elevation of liver enzymes were seen just the right time of passing stones.

Answer: All 197 patients with symptomatic CBD stones experienced one or more episodes of biliary colic during conservative treatment. Verifying whether the stone passage occurred during the colic attack or whether it occurred silently was difficult. This content was added in the RESULTS section of the revised manuscript.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Wen-bing Sun, MD

Chair and Professor

Department of Hepatobiliary Surgery

West Campus, Beijing Chao-yang Hospital

Capital Medical University

Beijing 100043, China