

学 位 論 文 の 要 旨

氏名 森田照美

学 位 論 文 名 Effects of Rikkunshito (TJ-43) on Esophageal Motor
Function and Gastroesophageal Reflux

発 表 雑 誌 名 Journal of Neurogastroenterology and Motility
(巻, 初頁～終頁, 年) (18: 181–186, 2012)

著 者 名 Terumi Morita, Kenji Furuta, Kyoichi Adachi, Shunji Ohara,
Takashi Tanimura, Kenji Koshino, Tomochika Uemura,
Kohji Naora, Yoshikazu Kinoshita

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a disease frequently encountered in gastroenterology clinics in both western countries and Japan. Decreased esophageal motor function is one of the most important factors for occurrence of GERD. The powder extract of the herbal medicine rikkunshito has been reported to be effective in improving various upper gastro-intestinal symptoms. Rikkunshito, extracted from a mixture of *Atractylodis Lanceae* Rhizoma, *Ginseng Radix*, *Pinelliae Tuber*, *Hoelen*, *Zizyphi Fructus*, *Aurantii Nobilis Percarpium*, *Glycyrrhizae Radix*, and *Zingiberis Rhizoma*, is manufactured and distributed as TJ-43. Several studies have demonstrated that TJ-43 stimulates gastric motor activities and accelerates gastric emptying. However, its effects on esophageal motor functions have not been examined. We conducted the present double-blind crossover study to clarify the effects of TJ-43 on esophageal motor functions and gastroesophageal reflux events.

MATERIALS AND METHODS

The study protocol was approved by the ethical committee of Shimane University Faculty of Medicine.

The study subjects were 10 normal male volunteers (22.8±2.0 years old). Esophageal motor function and post-prandial gastroesophageal reflux were determined after a 7-day administration of TJ-43 or a placebo in random order using a double-blind crossover design. TJ-43 at 2.5 g was administered 3 times per day (commonly used for adult patients in Japan with GERD and functional dyspepsia (FD) symptoms) 30 minutes before each meal. Lactose was used as the placebo drug. Lower esophageal sphincter (LES) pressure and esophageal body peristaltic contractions were examined using high-resolution 36-channel manometry. Post-prandial gastroesophageal reflux was also determined using a multi-channel impedance pH dual monitor.

RESULTS AND DISCUSSION

Effects of TJ-43 on Esophageal Motor Function

Resting LES pressures in sitting and supine positions during administration of TJ-43 or a placebo were measured. There was no statistically significant difference in LES pressure values determined during the administrations of TJ-43 and the placebo in the sitting position, whereas those in the supine position were significantly different. Esophageal body peristaltic contractions were also measured at each segment (1, 2, 3 from the proximal to the distal segment) of the esophagus in the sitting and supine positions. In both positions, segment 3 (lowest) showed the highest peak contraction pressure. In addition, contraction pressures were higher in the supine position in all of the segments. TJ-43 administration did not augment esophageal peristaltic contraction pressure in any of segments in either the sitting or supine position.

Effects of TJ-43 on Post-prandial Gastroesophageal Reflux

There was no statistically significant difference between the number of total post-prandial

3-hour reflux episodes during the TJ-43 and placebo administrations, though the number of reflux episodes tended to be higher during TJ-43 administration. Liquid only was the most frequently observed type of reflux in each post-prandial period, followed by the mixture of gas and liquid. There were also no significant differences for the ratios of weakly-acid and non-acid reflux between liquid only and mixed reflux events during administration with TJ-43 and the placebo. Furthermore, there were no significant differences between TJ-43 and the placebo regarding the percentage of esophageal acid (pH <4.0) exposure time during the 3-hour post-prandial period. On the other hand, bolus clearance time of the gastroesophageal refluxate tended to be shorter during TJ-43 administration.

In the present study, we conducted a detailed investigation of the effects of TJ-43 at a standard dose on esophageal motor activity and gastroesophageal acid/non-acid reflux. However, we did not find evidence of its efficacy as an anti-reflux agent. On the other hand, TJ-43 elevated resting LES pressure in a supine position, and tended to accelerate esophageal bolus clearance and increase post-prandial reflux, though that latter finding is contrary to a previous report regarding the effect on esophageal motor function in pediatric GERD patients. We employed a placebo-controlled double blind design in the present study, and also utilized highly sensitive and reliable methods to determine esophageal motor activity and gastroesophageal reflux. Therefore, the efficacy of TJ-43 for adult patients with GERD may not be related to augmentation of esophageal motor function, while increased gastric motor function caused by administration of TJ-43 may relieve GERD symptoms. Investigation of the effects of TJ-43 on esophageal sensory and perception mechanisms in a future study will be important.

CONCLUSION

No significant effect of TJ-43 on esophageal motor activity or gastroesophageal reflux events was revealed in the present double-blind crossover study. Further investigations are needed to clarify its effects in patients with GERD.