

21. Others

Reference

Sato Y, Katagiri F, Itoh H, et al. Bushi-richu-to raises calcitonin gene-related peptide, substance P, somatostatin, and vasoactive intestinal polypeptide levels in human plasma. *Journal of Health Science* 2007; 53: 615-21. Ichushi Web ID: 2008127570 [J-STAGE](#)

1. Objectives

To elucidate the mechanism of bushirichuto (附子理中湯) activity in raising gut-regulated peptide levels.

2. Design

Randomized crossover controlled trial (RCT-cross over).

3. Setting

Department of Clinical Pharmacy, Oita University Hospital, Japan.

4. Participants

Five healthy male volunteers recruited at the facility mentioned above, n=5.

5. Intervention

Arm 1: Kanebo Bushirichuto (附子理中湯) Extract Fine Granules (EK-410) 4.5 g was orally administered with 100 mL of water for 4 weeks.

Arm 2: placebo was orally administered with 100 mL of water for 4 weeks.

Each subject was administered these drugs with an interval of four weeks.

6. Main outcome measures

Blood samples were obtained before administration, and at 20, 40, 60, 90, 120, 180, and 240 min after administration of the test substances, and plasma levels of calcitonin gene-related peptide (CGRP), substance P, vasoactive intestinal polypeptide (VIP), somatostatin, and motilin-like immunoreactive substance (IS) were measured by enzyme immunoassay (EIA).

7. Main results

One dose of bushirichuto significantly increased CGRP, somatostatin, and VIP levels (which peaked at 40–60 min) and significantly increased substance P level (which peaked at 180 min). CGRP level increased 5.7-fold at 40 min (85.2 ± 58.7 pg/mL in arm 1 vs. 14.9 ± 1.9 pg/mL in arm 2) ($P < 0.01$), somatostatin level increased 2.1-fold at 60 min (20.2 ± 6.1 pg/mL in arm 1 vs. 9.8 ± 2.1 pg/mL in arm 2) ($P < 0.01$), VIP level increased 2-fold at 60 min (16.9 ± 7.0 pg/mL in arm 1 vs. 8.3 ± 1.4 pg/mL in arm 2) ($P < 0.01$), and substance P increased 2-fold at 180 min (68.5 ± 18.7 pg/mL in arm 1 vs. 34.3 ± 17.9 pg/mL in arm 2) ($P < 0.01$). On the other hand, plasma motilin-like IS level was unaffected during observation for 240 min after administration.

8. Conclusions

Administration of bushirichuto may reduce sensitivity to cold, gastrointestinal discomfort, and gastrointestinal dysfunction *via* increasing plasma levels of CGRP, somatostatin, VIP, and substance P.

9. From Kampo medicine perspective

The authors suggest that the taste and smell of bushirichuto may affect the kinetics of gut-regulated peptides.

10. Safety assessment in the article

Not documented.

11. Abstractor's comments

Although this investigation had only a small number of subjects, the results helped us to reveal the mechanism of bushirichuto activity. As bushirichuto is an “*onchu-sankan*” (温中散寒) medicine which contains herbs (Aconiti tuber [附子] and Zingiberis siccatur rhizome [乾姜]) with strong anti-coldness (“*sankan*”) activity, it is used for patients with “*hie*” (or a feeling of coldness in the body). However, the authors did not reveal whether the male volunteers had *kan-sho* (寒証, cold pattern). Most subjects treated with bushirichuto in clinical practice are frail women. From that point of view, to minimize the discrepancy between bushirichuto use in actual clinical practice and experimental study, clinical studies of “*sho*” in women with and without symptoms, and having the same study design as this trial, are awaited.

12. Abstractor and date

Ushiroyama T, 19 December 2008, 1 June 2010, 31 December 2013.