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Traditional Chinese Medicine in Geriatrics, Evidences, and the Guideline

Koh Iwasaki

Abstract

The average life span of Japanese is 90 years. So that Japan is an unprecedented super-aging society. However, healthy life span is 10 years shorter than life span. Many spend an average of 10 years in frailty. People become frail, and reached to “geriatric syndrome.”

Keywords: traditional chinese medicine, elderly, dementia, aspiration pneumonia, constipation

1. Geriatric syndrome

Geriatric syndromes include many symptoms caused by aging, such as dementia, depression, delirium, incontinence, vertigo, falls, spontaneous bone fractures, failure to thrive, and neglect and abuse. Geriatric syndromes are associated with reduced life expectancy. To be considered a geriatric syndrome, these conditions must interfere with a person's daily life.

In ancient China, people considered this phenomenon as Qi (氣) deficiency in Kidney organ (shen xu, 腎虛). Qi is energy and signaling using energy. Kidney in traditional Chinese medicine (TCM) is very different from Kidney in Western medicine. TCM kidney is somewhat base of life. Human inherits essence of life (jing, 精) from his/her parents and keeps it all his/her life. When jing runs out, people die. TCM kidney is the box keeping jing. When people become old, the jing in TCM kidney decreases, and the function of whole body goes down. This is the reason of aging and geriatric syndrome. These thoughts were written in the famous ancient medical text book Huan di nei jing (黃帝內經), written in BC 2nd ~ 1st century. That is to say, TCM had geriatric medicine in 2000 years ago. How can we keep jing in TCM kidney? People sought the ways, from unexpected to some herbal drugs, training methods.

Here, we introduce some evidences of TCM for geriatric syndrome and clinical practice guideline from Japan Geriatrics Society. How can we treat geriatric syndrome using traditional Chinese Medicine?

2. Dementia

In China, dementia is called as chidai (痴呆). Zhang Jing yue (張景岳) developed this term in his text book Jing yue guan su (景岳全書), in 12th century. But Zhang Jing yue considered chidai as acquired symptoms. He thought that unstable emotion induced chidai. In Qing (清) era, 19th century, Wang Qing Ren (王清任)

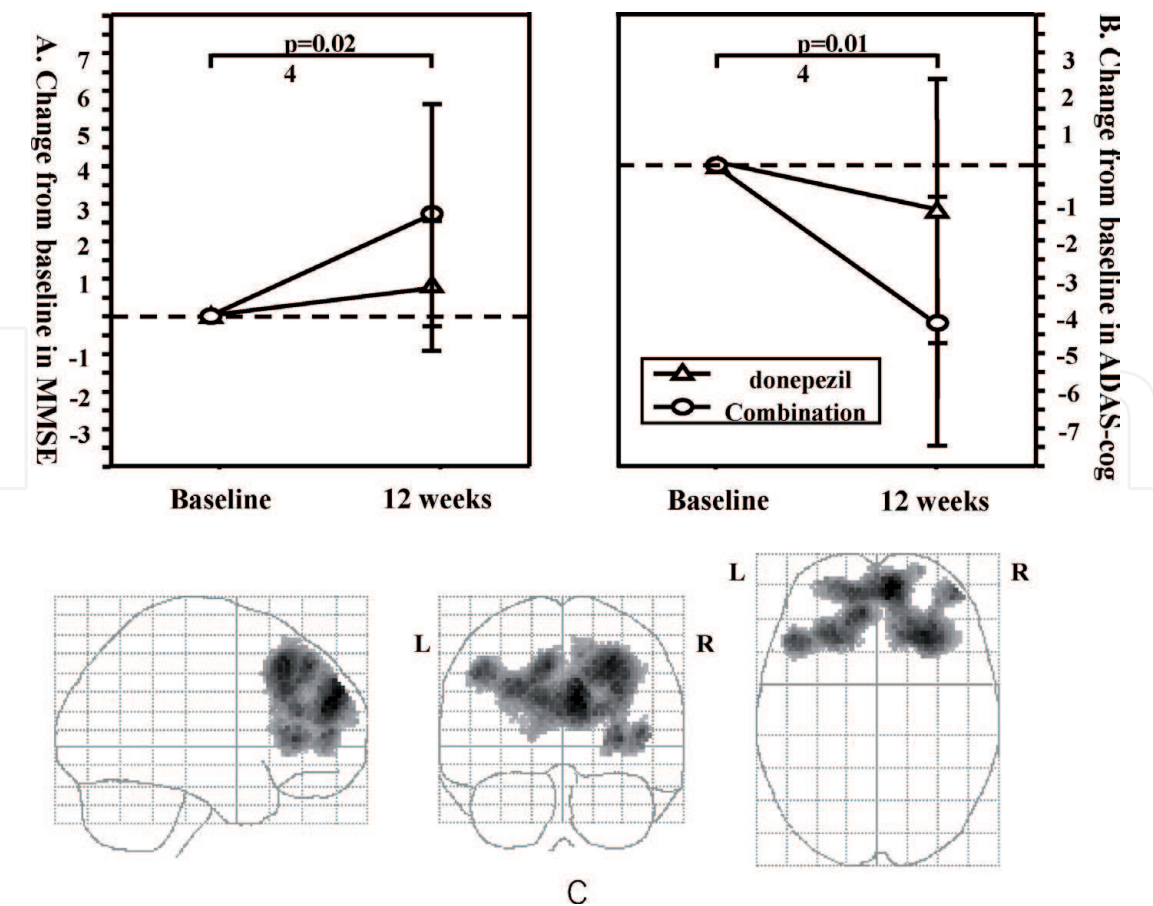


Figure 1. Change of MMSE(I_t) and ADAScog of 2 groups, donepezil plus KUT combination (○) vs. donepezil only (△). Combination group showed significant improvement to single donepezil group. Colored areas in the brain reveal areas in which significant blood flow increases in the combination group.

considered that chidai was caused by brain atrophy. Wang Qing Ren is the first man who described dementia in a scientific manner.

We demonstrated that a combinatorial use of donepezil plus Jia wei weng dan tang (加味温胆汤), was more beneficial than donepezil alone in both cognition and brain perfusion (**Figure 1**) in demented people. Although cholinergic-related adverse effects might be expected, such events did not occur in the combination group. Therefore, despite a small sample size and a short observation period study, donepezil and Jia wei weng dan tang may work synergistically in a safe fashion to enhance an availability of acetylcholine [1].

Same time, we showed that bawei dihuan wang (八味地黄丸、BDW) could improve the cognitive function of Alzheimer disease patient. **Figure 2** shows that BDW improves Mini Mental Score Examination about 2.5 in the treatment period [2]. BDW was described in the ancient text book Jin kui Yao lue (金匱要略) written by Zhan Zhong jing (張仲景) in 2nd century. He wrote that this recipe delayed aging, i.e., effective for Qi (氣) deficiency in Kidney organ (shen xu, 腎虛). Therefore, it is used for geriatric syndrome and frailty of aged people. It contains Rehmaniae Radix, Corni Fructus, Dioscoreae Rhizoma, Alismatis Rhizoma, Hoelen, Moutan Cortes, Cinnamomi Cortes and Aconi tuber.

3. Traditional Chinese medicine for behavioral and psychological symptoms of dementia (BPSD)

Behavioral and psychological symptoms of dementia (BPSD) is the serious clinical problem of dementia. Usually major tranquilizers are used, but they

MMSE change with BDW

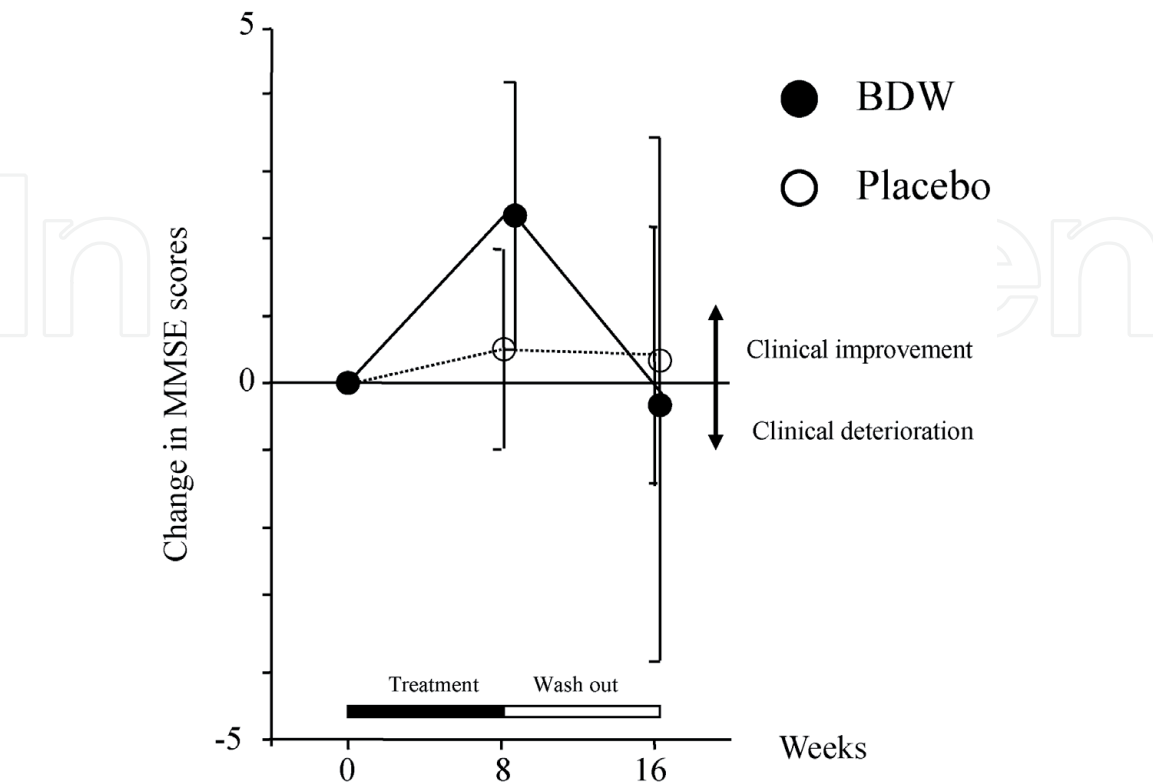
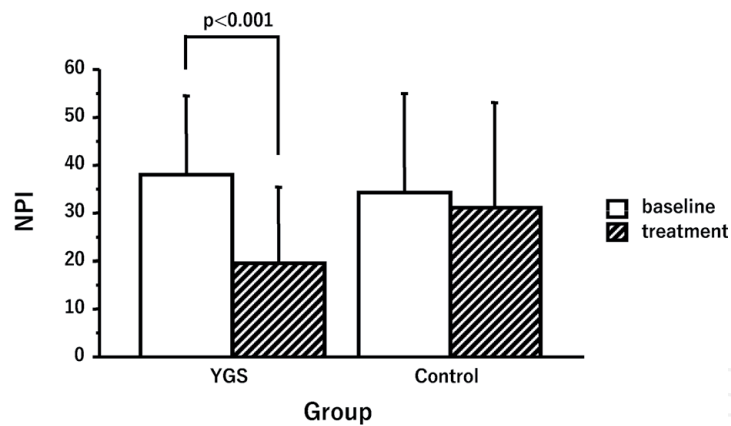


Figure 2.
Changes of MMSE of BDW and placebo groups. BDW improves mini mental score examination about 2.5 in the treatment period.

cause extrapyramidal side effects. We reported that Yigan San (抑肝散) could improve BPSD without extrapyramidal side effects [3]. Mild-to-severe demented patients who had BPSD (18 men and 34 women; age 80.3 ± 9.0 [mean \pm SD] years) were investigated. Participants were randomly assigned to the YGS group ($n = 27$) or control (drug-free) group ($n = 25$) and treated for 4 weeks. The Neuropsychiatric Inventory (NPI) test for the assessment of BPSD. Meanwhile, cognitive function was estimated by the Mini-Mental State Examination (MMSE), and ADL by the Barthel Index were tested at baseline and the end of the treatment. The frequency of extrapyramidal symptoms (EPS) and other adverse events were recorded. All participants in both groups completed the trial. In the control group, 11 patients required treatment with tiapride hydrochloride because of deterioration of BPSD.

Significant improvements BPSD (from 37.9 ± 16.1 to 19.5 ± 15.6 , mean \pm SD) (**Figure 3**) and Barthel index (from 56.4 ± 34.2 to 62.9 ± 35.2) were observed in the YGS group, but not in the control group. MMSE was not changed in both groups. EPS were not observed in either group, but dizziness and impaired postural sway were observed in 6 patients treated in control group, may be caused by tiapride hydrochloride. At the same time, we also found that Yigan San could improve typical hallucination in Dementia with Lewy Bodies (DLB), as shown in **Figure 4** [4].

Yigan San was developed by Xue Ji (薛己) in 16th century. He devised this recipe for emotional liability of children. But this recipe was not widely spread in China, and Japanese doctors in Edo era applied it to adults. They found that it is effective for persons who are easy to anger. I applied it to some demented patients who easily anger. Therefore, I carried out Randomized Control Trial (RCT) described above. Now then, we found 219 papers with key word “yokukansan (Japanese



* NPI score shows that BPSD significantly improved in Yigan San group.

Figure 3. Changes of NPI in the YGS group and control. NPI significantly improved from baseline to endpoint only in the YGS group.

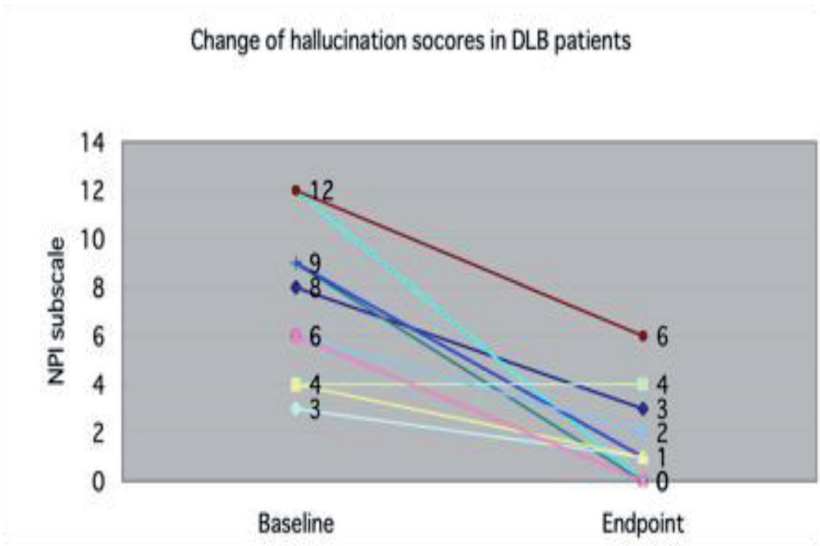


Figure 4. Change of hallucination sub score of NPI in DLB patients. Hallucination improved by YGS treatment.

name of Yigan San).” Nakatani Y et al. reported that Yigan San has a neuroprotective effect [5]. Yigan San contains Atractylodis Lanceae Rhizama, Hoelen, Cnidii Rhizoma, Angelicae Radix, Bupleuri Radix, Glycyrrhizae Radix, and Uncariae Ramulus et Uncus. Active ingredients are not sure but Ikarashi Y et al. reported that Geissoschizine methyl ether (GM) in Uncaria hook and 18β-glycyrrhetic acid (GA) in Glycyrrhiza may concern to several pharmacological actions of YiGan San [6].

4. Aspiration pneumonia

Pneumonia is now the 4th reason of death of Japanese, and most of them are aspiration pneumonia in the elderly. Absence or attenuation of the cough [7] and swallowing [8] reflex in elderly patients causes micro aspiration. We investigated the effects of Banxia Houpu Tang (半夏厚朴湯、BHT), on the swallowing [9] (Figure 5) and cough [10] (Figure 6) reflexes in elderly stroke patients. Finally, we found that BHT reduced pneumonia risk in the elderly [11]. Elderly participants

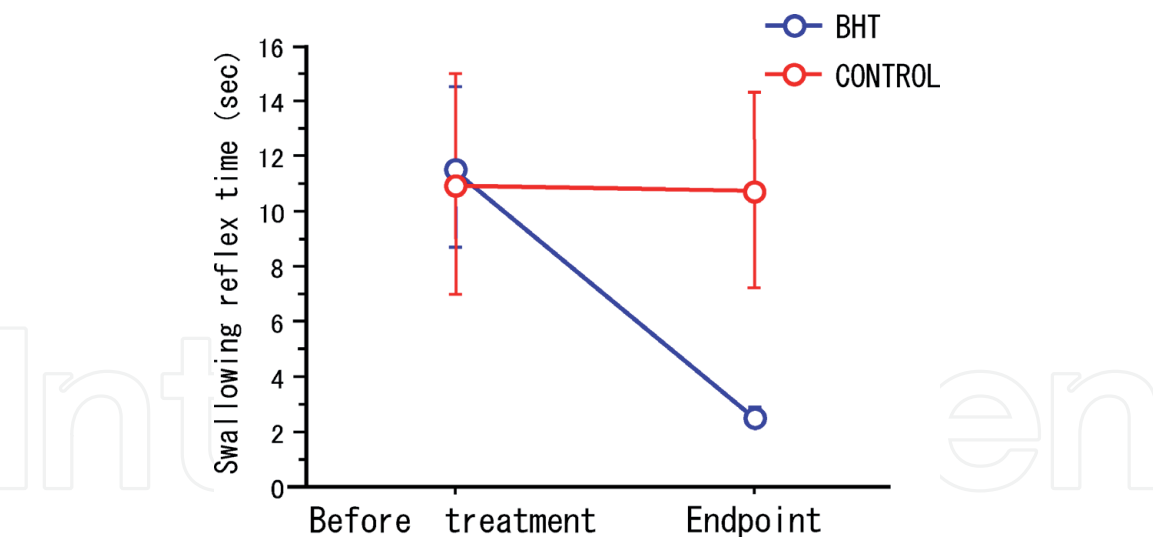


Figure 5. Changes of the swallowing reflex in BHT and the control groups. The reflex significantly improved the time (shortened) only in the BHT group.

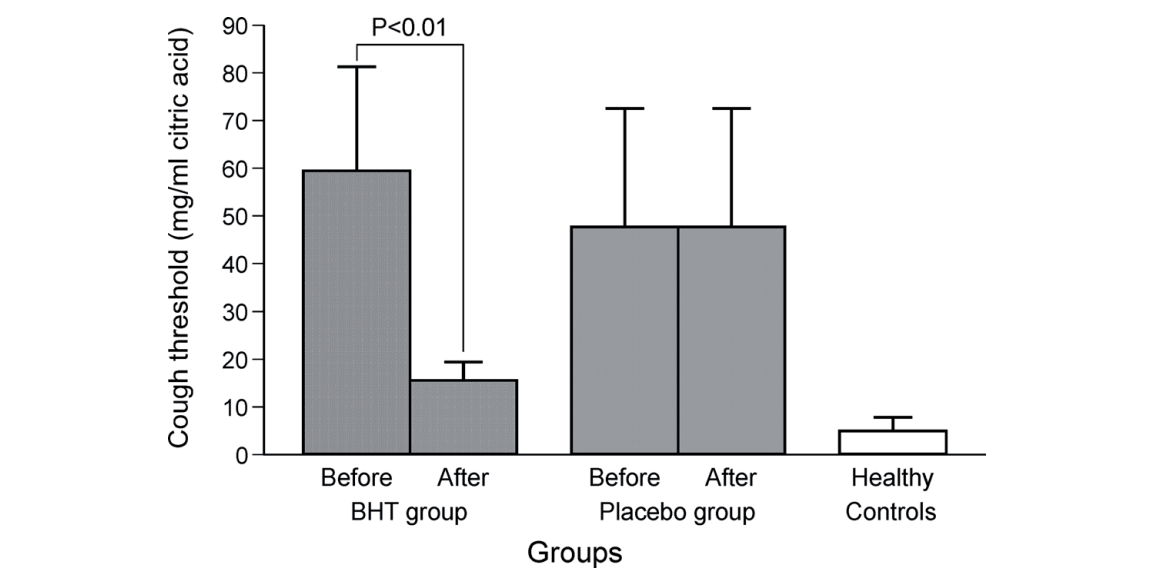


Figure 6. Change of the cough reflex in BHT treated and the control groups. The threshold of the reflex significantly shortened (improved) in the BHT group.

who had history of aspiration pneumonia (mean age 84.0, M:F = 28:67) were randomly assigned to the BHT treatment group (n = 47) or the control group (n = 48) and took BHT or placebo for 12 months. The occurrence of pneumonia, mortality due to pneumonia, and the daily amount of self-feeding were measured. As a result, four participants in the BHT group developed pneumonia, and one of them died as a result, while 14 participants in the control group developed pneumonia, and 6 of them died. There was a significant difference between the two groups in pneumonia onset ((**Figure 7**, $P = .008$), and a tendency toward significance in pneumonia-related mortality ($P = .05$). The relative risk of pneumonia in the BHT group compared with the control group was 0.51 (95% confidence interval (CI) 0.27–0.84, $P = .008$) and that of death from pneumonia was 0.41 (95% CI = 0.10–1.03, $P = .06$). No adverse events were observed from treatment with BHT. The BHT group was able to maintain self-feeding better than the control group ($P = .006$). Very recently, the suppressing effect of BHT for aspiration pneumonia was confirmed by double blind RCT [12].

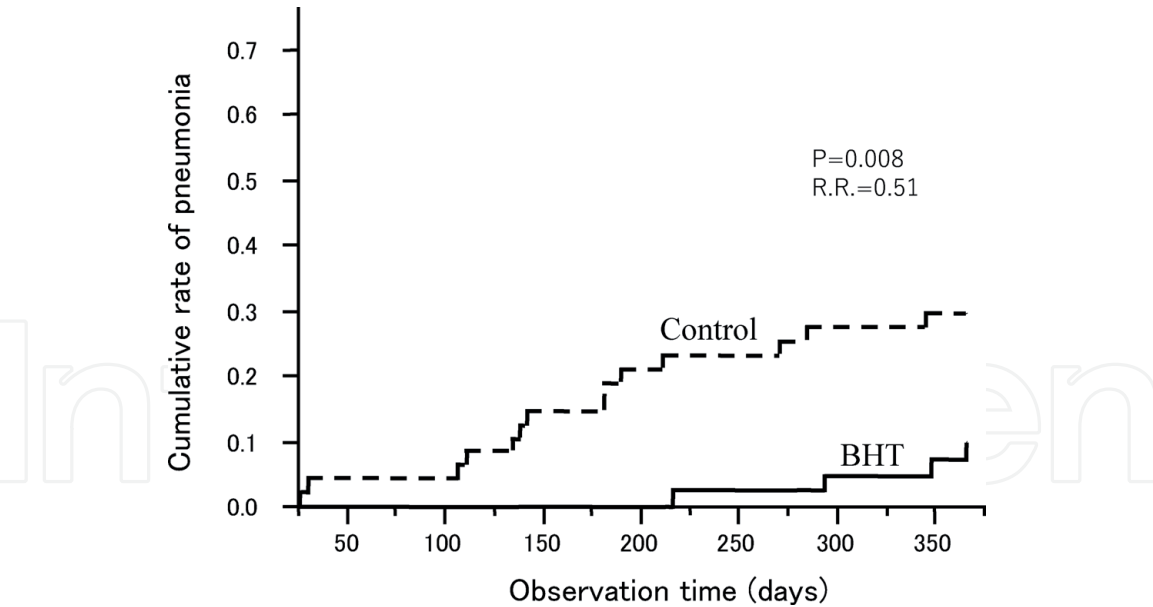


Figure 7. Cumulative rate of pneumonia in BHT treatment group and the control group. There is a significant difference in pneumonia occurrence rate between the groups.

BHT was described in Jin kui Yao lue (金匱要略) by Zhan Zhong jing (張仲景) in 2nd century. It contains Pinelliae Tuber, Hoelen, Magnoliae Cortex, Perillae Herba, and Zingiberis Rhizoma. It is written that when women feel something block her throat, try this recipe. Now it is considered as throat dysesthesia, and BHT is widely applied to neurosis, depression, and psychophysiological disorder.

5. Chronic constipation

There were over 1.34 million patients suffering from cerebrovascular diseases in 2008 reported by Ministry of Health, Labour and Welfare in Japan. Poststroke patients often cause constipation. Stratified by stroke severity on the National Institutes of Health Stroke Scale, the incidence of constipation in poststroke patients were reported from 38.9% to 88.2% [13]. Poststroke patients with functional constipation, assessed by the Rome III criteria were recruited in a study on the effects of the traditional Chinese medicine Da Jian Zhong Tang (大建中湯) on constipation. Thirty-four patients (17 men and 17 women; mean age: 78.1 ± 11.6 years) were randomly assigned to 2 groups; all patients received conventional therapy for constipation, and patients in the Da Jian Zhong Tang group received 15 g/day of Da Jian Zhong Tang for 4 weeks. We recorded Constipation Scoring System (CSS) points and the Gas Volume Score (GVS) (the measure of the intestinal gas volume calculated from plain abdominal radiographs) before and after a 4-week observation period. The total score on the CSS improved significantly in the Da Jian Zhong Tang group compared to the control ($p < 0.01$) (Figure 8). In addition, some CSS subcategories (defecation frequency, feeling of incomplete evacuation, and need for enema/disimpaction) significantly improved in the Da Jian Zhong Tang group ($p < 0.01$, $p = 0.049$, and $p = 0.03$, respectively). The GVS was also significantly reduced in the Da Jian Zhong Tang group (Figure 9, $p = 0.03$) [14]. Da Jian Zhong Tang was also described in Jin kui Yao lue (金匱要略) by Zhan Zhong jing (張仲景) in 2nd century. Zhan Zhong jing wrote that this recipe was effective for patients who felt severe abdominal pain, abdominal coldness and gut sharply moved. It is very

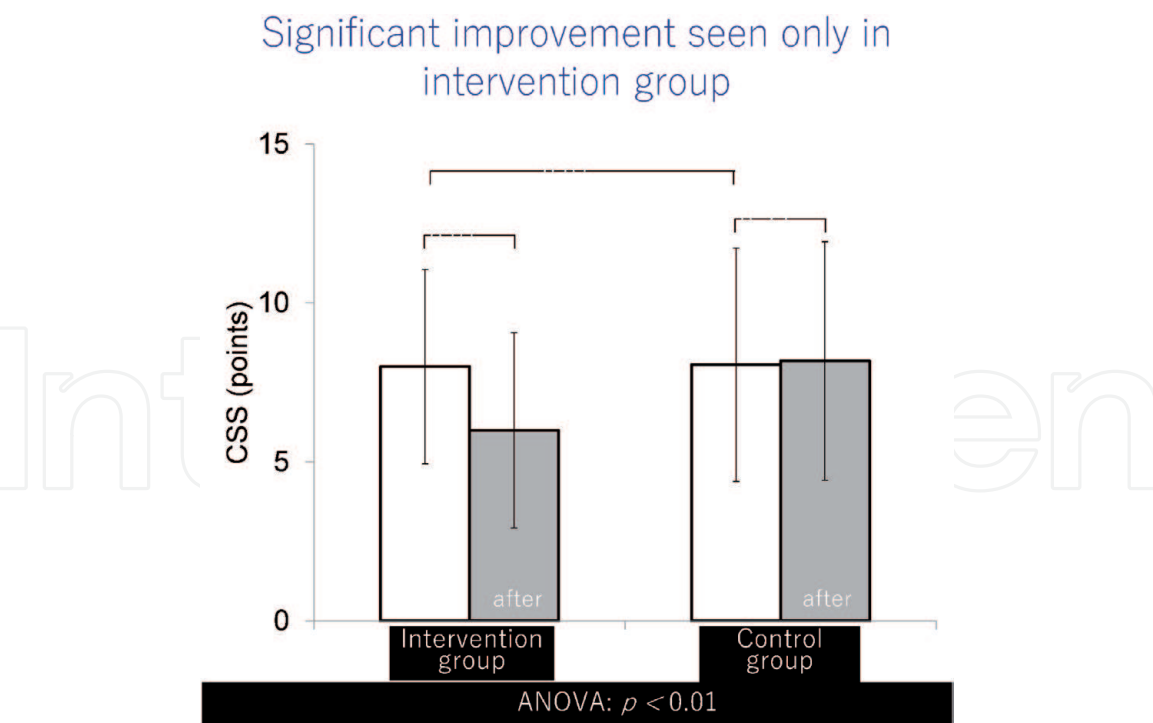


Figure 8.
Change of CCS points in the Da Jian Zhong tang treated group and the control. CSS significantly reduced (improved) in Da Jian Zhong tang group.

Reduction in Bowel Gas Volume

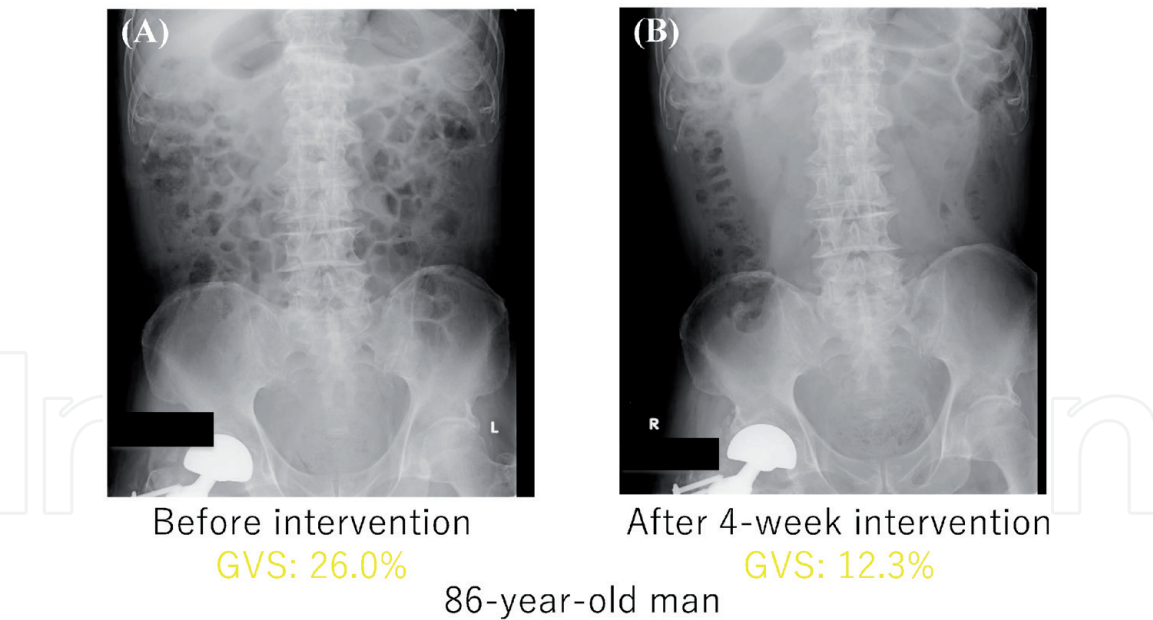


Figure 9.
Bowel gas volume at baseline and the endpoint of Da Jian Zhong tang treatment (a case).

alike to ileus, and this recipe had been used for ileus prevention after abdominal surgery. Da Jian Zhong Tang contains Ginseng Radix, Zanthoxyli Fructus, and Zingiberis Siccatur Rhizoma.

6. Guideline

Concerning these evidences, Japan Geriatric Society treated traditional medicine as the independent chapter in their guideline 2015 [15]. As a result, Yigan San,

Banxia houpu Tang, Da Jian Zhong Tang, Buzhongyiqi Tang (補中益氣湯), and Ma Zi Ren Wan (麻子仁丸) covering by Japanese national insurance, were reviewed and found to have a high Quality of evidence for the elderly (**Table 1**). In these 5 recipes, I already explained Yigan San, Banxia houpu Tang, Da Jian Zhong Tang above. Buzhongyiqi Tang was developed by Li Dong yuan (李東垣) in 13th century. He promoted the theory that disease results from the inhibition of digestive functions. In his book Pi wei lun (脾胃論), he wrote as below. Mongolian army attacked his country and closed in the capital many months. At that time, severe infectious disease spread in the capital and many people died. Doctors could not treat the disease. Then he thought that people went down because of food deficiency. Their digestion deteriorated and immune function declined so that infectious disease did not recover. Then he developed Buzhongyiqi Tang and treated many patients. Buzhongyiqi Tang was assessed in two small, open labeled RCTs [16, 17], the findings of which suggested that it improved systemic inflammation and nutritional status in elderly patients with chronic obstructive pulmonary disease and reduced systemic inflammation. It represents a unique therapeutic strategy to improve nutritional status and control chronic inflammation, something lacking in Western medicine. Buzhongyiqi Tang contains Astragali radix, Atractylodis Lanceae Rhizoma, Ginseng Radix, Angelicae radix, Bupleuri Radix, Cimicifugae Rhizoma, and Zingiberis Rhizoma.

Ma Zi Ren Wan (麻子仁丸) is purgative, very easy to use for the elderly. It was described in 2 books, Jin kui Yao lue and Shang ha lun (傷寒論), both written by Zhang Zhong jin. It contains Rhei Rhizoma, Aurantii Fructus Immaturus, Armeniaca Semen, Magnoliae Cortes, Paeoniae Radix, and Cannabidis Semen. The effect as purgative was proved the double blinded RCT [18].

Medicines	Ingredients	Effects	Attention	QoE and RS
Yigan San (Chinese), Yokukansan (Japanese), (抑肝散)	蒼朮: Atractylodis Lanceae 當歸: Angelicae Radix 茯苓: Hoelen 柴胡: Bupleuri Radix 川芎: Cnidii Rhizoma 甘草: Glycyrrhizae Radix 釣藤鈎: Uncariae Uncis Cum Ramulus	Yigan San improves the BPSD of dementia patients (AD, VD and DLB), and is particularly effective for DLB-related hallucinations.	Hypokalemia could occur in 6 % of cases.	QoE: moderate RS: strong
Banxia houpu Tang (Chinese), Hangekobokuto (Japanese), (半夏厚朴湯)	半夏: Pinelliae Tuber 蘇葉: Perillae Herba 茯苓: Hoelen 生薑: Zingiberis Rhizoma 厚朴: Magnoliae Cortex	Banxia houpu tang (BHT) reduced the aspiration pneumonia risk in elderly patients with dementia and maintained self-feeding.	None	QoE: moderate RS: strong
Dajianzhong Tang (Chinese), daikenchuto (Japanese), (大建中湯)	乾姜: Zingiberis Siccatum Rhizoma 山椒: Zanthoxyli Fructus 人參: Panacis Ginseng Radix 膠飴: Maltose	Dajianzhong Tang is effective for defecation control in post-stroke patients.	Interstitial pneumonia, and, rarely, liver dysfunction.	QoE: moderate RS: strong
Buzhongyiqi Tang (Chinese), hochuekkito (Japanese), (補中益氣湯)	黃耆: Astragali Radix 大棗: Zizyphi Fructus 蒼朮: Atractylodis Lanceae 陳皮: Aurantii Nobilis Pericarpium 人參: Panacis Ginseng Radix 甘草: Glycyrrhizae Radix 當歸: Angelicae Radix 升麻: Cimicifugae Rhizoma 柴胡: Bupleuri Radix 生薑: Zingiberis Rhizoma	Buzhongyiqi Tang improved systemic inflammation and nutritional status in patients with COPD	It contains licorice and may cause hypokalemia	QoE: low RS: weak
Ma Zi Ren Wan, (Chinese), mashiningan (Japanese), Hemp seed pill (HSP) (English) (麻子仁丸)	麻子仁: Cannabis Fructus 杏仁: Armeniaca Semen 大黃: Rhei Rhizoma 厚朴: Magnoliae Cortex 枳實: Aurantii Fructus Immaturus 芍藥: Paeoniae Radix	HSP is safe and effective for alleviating functional constipation. According to the study in reference 31, those in the HSP group benefited in terms of increased complete spontaneous bowel movement, relief in the severity of constipation and straining, and an effective reduction in the use of rescue therapy when compared with placebo. HSP is safe and effective for alleviating functional constipation.	HSP is a very safe purgative. No adverse events were reported.	QoE: moderate RS: strong

Table 1.
Screening tool to alert doctors to right treatment (START).

7. Conclusion

As mentioned above, evidences of traditional medicine for geriatrics accumulated little by little, and a part of it is accepted modern medical doctors. Systematic education for traditional medicine and medical care needed.

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