14. Genitourinary Tract Disorders (including Climacteric Disorders)

References

Ogita Y, Fujimoto S, Ushiroyama T, et al. Efficacy of formulation TK-061 for various climacteric symptoms – comparison with Teikoku Keishibukuryogan Extract Granules*. *Rinsho Fujinka Sanka* (*Clinical Gynecology and Obstetrics*) 2002; 56: 799-810 (in Japanese). Ichushi Web ID: 2003004448

Ogita Y, Fujimoto S, Ushiroyama T, et al. Keishibukuryogan formulation TK-061 prepared with crude drug – verification of efficacy for various climacteric symptoms*. *Sanka to Fujinka* (*Obstetrics and Gynecology*) 2002; 69: 953-62 (in Japanese). Ichushi Web ID: 2003004359 MOL, MOL-Lib

1. Objectives

To investigate the equivalence between non-extracted keishibukuryogan (桂枝茯苓丸) and keishibukuryogan (桂枝茯苓丸) extract.

2. Design

Randomized controlled trial (RCT).

3. Setting

Twenty facilities (the Department of Obstetrics and Gynecology, Osaka City University School of Medicine, the Department of Obstetrics and Gynecology, Hokkaido University School of Medicine, the Department of Obstetrics and Gynecology, Osaka Medical College School of Medicine, et al.), Japan.

4. Participants

One-hundred and ninety-three patients who were diagnosed with climacteric disorders during a 1 year and 5 month period from November 1999 to March 2001, untreated with hormone replacement therapy within 4 weeks before the start of the study, and having body mass index (BMI) ≥20 and body fat <35%. (The per-protocol population included 158 out of these 193 patients).

5. Intervention

Arm 1: oral administration of 6 keishibukuryogan (桂枝茯苓丸) pills containing 5 ingredients (TK-061) t.i.d. (18 tablets/day), n=75.

Arm 2: oral administration of 2.5 g of TEIKOKU Keishibukuryogan (桂枝茯苓丸) Extract Granules (TKK-25) t.i.d. (7.5 g/day), n=83.

6. Main outcome measures

Simple Menopause Index (SMI) improvement rated on a 5-point scale; improvement in blood stasis score; changes in blood hormone concentrations; adverse events.

7. Main results

Response rate to TK-061 and TKK-25 were similar (55.8% *vs* 51.0%, respectively). Blood stasis score was decreased with time after the start of treatment to similarly reduced levels for both arms at week 8. Blood concentrations of estradiole (E2), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) remained unchanged from baseline. The incidences of adverse drug reactions were similar: 22.4% with TK-061 and 23.2% with TKK-25. These adverse drug reactions disappeared naturally or were relieved by symptomatic therapy, suggesting that a causal relationship with treatment cannot be ruled out.

8. Conclusions

TK-061 is equivalent or superior to TKK-255 in increasing the SMI improvement rating, the primary endpoint. Both increase blood stasis score to a similar extent. In addition, neither affects the endocrine system.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Adverse events occurred in 22 patients receiving keishibukuryogan pills (22.4%) and 23 patients receiving keishibukuryogan extract granules (23.2%). No serious adverse events occurred. Adverse drug reactions occurred in 12 patients (12.2%) and 9 patients (9.1%), respectively. The global safety was “satisfactory” in 79 patients (80.6%) and 88 patients (88.9%), respectively.

11. Abstractor’s comments

This paper describes a clinical trial comparing keishibukuryogan pills to its extracted formulation, and demonstrates the efficacy of both for climacteric symptoms. Regrettably, however, *ganzai* (丸剤, pills), which proved more effective than the extract in the per-protocol population, is not on the NHI Drug Price list. For the moment, keishibukuryogan pill is only available as an OTC drug.

12. Abstractor and date

Nakata H, 1 April 2008, 1 June 2010, 31 December 2013.