15. Ante/Post-partum Diseases

References

Mizuno M, Sato K, Mori T, et al. Clinical evaluation of TSUMURA Tokishakuyakusan and ritodrine hydrochloride combination therapy in the management of threatened premature delivery*. *Sanka to Fujinka* (*Obstetrics and Gynecology*) 1992; 59: 469–80 (in Japanese).

1. Objectives

To objectively evaluate the usefulness of tokishakuyakusan (当帰芍薬散) combined with ritodrine hydrochloride in the management of threatened premature labor.

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

Thirty-six facilities nationwide including the Department of Obstetrics and Gynecology, University of Tokyo Hospital, Japan.

4. Participants

One hundred and forty-seven patients diagnosed with threatened premature labor (24 weeks to less than 37 weeks of pregnancy) at the above facility between June 1989 and August 1990 with a cervical dilation of <3.5 cm and effacement of <80%.

5. Intervention

Arm 1: TSUMURA Tokishakuyakusan (当帰芍薬散) Extract Granules 2.5 g t.i.d. before meals, started before or at the start of ritodrine hydrochloride (Utemerin; UT) (pretreatment group; n=78).

Arm 2: TSUMURA Tokishakuyakusan (当帰芍薬散) Extract Granules 2.5 g t.i.d. before meals, started after the occurrence of adverse reactions to UT (post-treatment group; n=69).

6. Main outcome measures

Improvement in uterine contraction and prolongation of gestation evaluated on a 5-point scale; effect on maternal heart rate, fetal heart rate, and adverse drug reactions to UT evaluated on a 5-point scale; safety evaluated on a 3-point scale based on intrapartum, neonatal, and puerperal findings and laboratory findings; and usefulness with regard to clinical efficacy and safety evaluated on a 5-point scale.

7. Main results

The pretreatment, compared with the posttreatment, allowed the UT drip rate to be significantly raised. The pretreatment significantly suppressed uterine contraction at 1 hr of UT administration. There were no significant between-arm differences in symptoms of threatened premature labor. At 2 hr of UT administration, significantly more pretreated patients (≥20%) than posttreated patients (10%) had no UT-associated palpitation (P<0.0001). Similarly, significantly fewer pretreated patients had increased heart rate, tremor, decreased blood pressure, headache, and facial flushing. Full term delivery occurred in 71.8% of the pretreatment group and 62.5% of the posttreatment group. There was no between-arm difference in style of delivery and neonatal or puerperal findings.

8. Conclusions

Tokishakuyakusan relieves the adverse reactions to ritodrine hydrochloride, thereby enabling administration of more ritodrine hydrochloride to suppress uterine contraction.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Although their incidence and severity are not mentioned, adverse drug reactions associated with UT administration were relieved in 86% and 90% of patients receiving tokihsakuyakusan pretreatment and posttreatment, respectively.

11. Abstractor's comments

This study demonstrated that tokishakuyakusan (a drug traditionally used to prevent abortion) relieves or suppresses the adverse drug reactions to ritodrine hydrochloride (a representative western medicine used for tocolysis to prevent abortion), thereby allowing maintenance therapy with ritodrine hydrochloride at higher levels. It shows that the fusion of oriental and western medicine can contribute to clinical practice. However, in principle, a tocolytic Kampo medicine should be started when pregnancy is diagnosed. Moreover, the effect of tokishakuyakusan should have been weak in patients who had already passed the stage of *mibyo* (未病, predisposition of disease) and been clinically diagnosed with threatened premature labor. Therefore, future studies should use a protocol starting in the first trimester and have an RCT design.

12. Abstractor and date

Ushiroyama N, 10 September 2008, 1 June 2010, 31 December 2013.