Introduction

Fetal growth restriction (FGR) is the most important cause of perinatal morbidity and mortality during the perinatal period. However, there is no consensus regarding the appropriate delivery time or treatment methods for fetuses with FGR. Reduced uterine arterial blood flow has been reported with FGR; however, if this is improved, then FGR may also be improved. Phosphodiesterase 5 inhibitors have vasodilating actions. When administered to the mother, they may improve FGR by improving fetal placental blood flow through improvements in uterine arterial blood flow.

Case Report

A 26-year-old woman (gravida 1, para 1) presented at 30 3/7 weeks of gestation with FGR. Her height was 153 cm, weight was 47 kg (pre-pregnancy body weight was 43 kg), and body mass index was 18.3. Her previous pregnancy was delivered via cesarean because of non-reassuring fetal status. There was no obvious cause of FGR. After achieving a spontaneous pregnancy, the patient had no abnormality during the course of her prenatal examinations. The estimated fetal weight was 1215 g (standard deviation [SD] −2.0). FGR was diagnosed because the SD was lower than -1.5 on the fetal growth curve, prepared according to the standardized ultrasonic fetal measurements (Japanese standard) recommended by the Ultrasonic Society of Japan [12]. There were no maternal infections that could have caused FGR, and fetal malformations were not observed. No abnormality was found in the placenta or umbilical cord. Oral administration of tadalafil 20 mg/day was started at 32 0/7 weeks of gestation to improve the placental blood flow. The authors measured the uterine arterial blood flow before beginning oral administration every week and plotted the median values of the uterine arterial blood flow rates according to blood flow changes that occurred over the course of gestation.
Figure 1. — Changes in uterine arterial blood flow after oral administration of tadalafil are shown. Upper graph: Standard changes in uterine arterial blood flow that occurred with each gestational week, as reported by Konje et al. Lower graph: The changes in uterine arterial blood flow of this case.

The uterine artery Doppler mode was selected when measuring the uterine arteries with a specialized machine. This ensured that settings were as standardized as possible. Pulse repetition frequency was adjusted for each examination to ensure the best fit of the waveforms.

The following preset variables were used: harmonic setting; mid, power; 100%, gain; -3, C7 M5 P3 E3, SRI II; 2, frequency; low, quality; normal, pulse Doppler wall motion filter; 60 Hz, and sample size; 2 mm. The angle correction was measured within 60 degrees.

Discussion

For singleton pregnancies involving FGR without obvious cause, the present authors started oral administration of tadalafil to improve the placental blood flow at 32 0/7 weeks of gestation. Thereafter, a marked increase in uterine arterial blood flow was observed as compared to the standard increase in uterine arterial blood flow that accompanied the increase in the number of gestation weeks. Tadalafil acts on cGMP by inhibiting PDE5 and expanding blood vessels. The authors believe that tadalafil can increase uterine blood flow and fetal growth by improving placental blood flow. This is because the increase in uteroplacental blood flow during pregnancy is due to angiogenesis and vasodilation and contributes to proper fetal growth.

The production and local release of nitric oxide, which stimulates cGMP production, lead to vasodilation in the placenta [13]. Sildenafil, a selective PDE5 inhibitor, has been used to treat pulmonary hypertension in pregnant women and has been shown to improve arterial endothelial function in the uterine muscle of pregnant women with preeclampsia and FGR pregnancies [14]. It has also been suggested to improve perfusion of the placenta and fetus when used to treat pregnancy-related hypertension. The authors administered tadalafil, which has a higher selectivity for PDE5 than sildenafil, especially in the reproductive system, and a longer half-life in cases of FGR [15]. In this case, as the blood flow increased in the uterine artery, estimated body weight also increased. This increase was remarkable compared with the body weight status before tadalafil administration (12.0 g/day; 19 weeks 5 days to 30 weeks 3 days and 223-1,125 grams; 29.0 g/day: 32 weeks 0 days to 34 weeks 5 days and 1,338-1,890 grams).

The weight of the fetus with FGR is closely associated with the long-term prognosis of pregnancy, and the authors believe that increased uterine arterial blood flow may contribute to fetal weight gain. However, it is unknown whether only increased blood flow in the uterine artery contributes to fetal weight gain. In addition, this case showed strong susceptibility to tadalafil and improved uterine arterial blood flow. Therefore, long-term measurements of uterine arterial blood flow may clarify whether the effects of increased uterine arterial blood flow are transient. More cases are needed to evaluate uterine arterial blood flow changes using similar measurement methods.
References


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