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The effect of Prosopis Farcta extract on teratogenic effects of valproic acid and expression of BMP4 and Runx2 in skeletal system of rat embryo

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Abstract

Sodium valproate (SV), as a common anti-epileptic drug, causes teratogenic effects on skeletal system by reactive oxygen species (ROS) generation. Herbal extract of Prosopis Farcta (PF), as a natural antioxidant necessary for many physiological activities, can probably ameliorate the teratogenic effects of SV during pregnancy. This study aimed to investigate the possible anti-teratogenic role of PF and Vitamin E (VE) on skeletal anomalies caused by SV in rat fetuses. Adult female rats (n=30) were categorized into 6 groups including control, SV (400 mg/kg), SV+VE (100mg/kg), and three doses of PF (50, 100, and 150 mg/kg) + SV. Each male rat mated with three adult female rats. The rats received SV, PF and VE at the 8th and 9th days of pregnancy by intraperitoneal injection. The animals were anesthetized and the laparotomy was applied at the 20th day of pregnancy. Skeletal abnormalities were analyzed using Alizarin red and Alcian blue staining. The expression of Runx2 and BMP2 genes was assessed using qPCRTM analysis in limbs bones. SV showed significant teratogenic effects including decrease in the rate of animal weight, Crown-rump length (CRL), various skeletal anomalies. The mRNA expression of Runx2 and BMP2 was also reduced in SV exposed animals. Administration of PF (especially 100mg/kg) in SV-exposed animals increased the weight of animals, CRL index, expression of Runx2 and BMP2, and reduced skeletal anomalies. The body weight, CRL index, Runx2 and BMP2 mRNA expression significantly increased, and skeletal anomalies decreased in VE group compared to the SV group. The results showed that PF could ameliorate the skeletal abnormalities and thus decreased osteogenic associated genes induced by SV in rat offsprings.

Key words: Sodium valproate, Skeletal anomaly, Prosopis Farcta, Teratogenicity, Runx2, BMP2

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