

Effect of Insulin Like Growth Factors on the Development of Hypoplastic Lungs in Connexin 43 Knockout Mice

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Abstract

Aim: The prognosis of patients with hypoplastic lungs is very severe. Since the postnatal treatment is not effective for improving the hypoplastic lungs, prenatal treatment is thought to be required. Insulin-like-growth factors (IGFs) are known to accelerate the maturation of the fetal lungs. Therefore, we investigate whether the administration of IGFs can improve fetal hypoplastic lungs in Cx43 knockout mice.

Method: Male and female heterozygous Cx43 mice (Cx43^{+/-}) were mated overnight and the day that the vaginal plug was confirmed was designated as embryonic day 0. Fetuses were obtained by cesarean section on the embryonic day 17, and the fetal lungs were dissected out and divided into the following three groups: IGF-I group, IGF-II group, and Control group. These fetal lungs were incubated for 48 or 72 hours in three types of mediums supplemented with IGF-I, IGF-II, or in the absence of IGFs. The lungs from homozygous Cx43 fetuses (Cx43^{-/-}) were investigated by immunohistochemistry and for the mRNA expression of T1 alpha protein, surfactant protein-C, and alpha smooth muscle actin.

Result: Both the number of positive cells and the mRNA expression of all markers were observed to increase in the IGF-I group compared to control group, although there was no significance between the IGF-II and control group. In addition, there were no significant differences between the IGF-I and IGF-II groups.

Conclusions: Based on our result, the administration of IGF-I to the fetus during the late gestational period might be effective for improving the severe hypoplastic lungs.

Key words: Connexin43, IGFs, lung development, CDH