

Nitric oxide as regulator in preimplantation embryo development and apoptosis

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摘要

Abstract

Objective: To investigate the mechanisms of nitric oxide (NO) in the development and apoptosis of preimplantation mouse embryos.

Design: Prospective, controlled study.

Setting: Medical college laboratory.

Subject(s): Two-cell embryos from outbred ICR mice.

Intervention(s): Hyperstimulation protocol, two-cell embryos were collected, then treated with or without an NO synthase inhibitor (-NAME) or an NO donor (SNP) and combined with a cGMP analogue (8-Br-cGMP) or a selective inhibitor of NO-sensitive soluble guanylyl cyclase (ODQ).

Main Outcome Measure(s): The development of ICR mouse embryo from two cells to blastocyst stages in vitro.

Result(s): The development of blastocyst was inhibited by -NAME in a concentration-dependent manner (0.1 – 10 μ M) and 0.1 μ M SNP reversed this effect (80.5% of control). Annexin-V/propidium iodide and terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling techniques demonstrated that excessive NO (≥ 10 μ M) might induce apoptosis in the mouse embryos. 8-Br-cGMP reversed the inhibitory effect of -NAME and rescued the embryo growth. ODQ inhibited the embryo development in a dose-responsive fashion (0.1 – 100 μ M) but had no effect in the NO-induced embryo apoptosis. P53 and Bax were found to be up-regulated during the embryo fragmentation.

Conclusion(s): These results indicate that the cGMP pathway might be involved in the

NO-regulated embryonic development, but not in NO-induced apoptosis, for which P53/Bax pathway might be involved.