Effect Of TNF-α Blocker (Infliximab) On Blastocyst Development Rate

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Objectives: TNF-α has gained recent attention in the pathophysiology of autoimmune disease. Numerous studies have demonstrated that TNF-α levels are elevated in serum and peritoneal fluid of patient with endometriosis. The use of immunomodulators have proven to be effective means in the management for many autoimmune diseases. Perhaps a similar therapy may prove useful in treating endometriosis. As such, targeting TNF-α would be a logical starting point in the development of novel treatments for the endometriosis. Infliximab (Remicade) is currently approved for the treatment of rheumatoid arthritis and Chron’s disease. It is a chimeric monoclonal antibody that binds both soluble and membrane forms of TNF-α and neutralizes its biological effects. There is no data available on its effects on early embryonic development. During controlled clinical trials, maximum iflximab plasma levels do not exceed 10 µg/ml, even at maximum doses. The objective of this study was to evaluate the effects of variable doses of infliximab on early embryo development using two-cell stage mouse embryo model.

Design: Experimental study in a research laboratory in a tertiary care facility.

Materials and methods: Thawed mouse embryos were pooled and randomly distributed between 7 groups: (A) composed of HTF supplemented with infliximab 1 µg/ml, (B) HTF supplemented with infliximab 10 µg/ml, (C)HTF supplemented with infliximab 50 µg/ml, (D) HTF supplemented with infliximab 100 µg/ml, (E) HTF supplemented with infliximab 200 µg/ml, (F) HTF supplemented with infliximab 400 µg/ml and a control group composed of plain HTF media (G). The numbers of embryos were from 30 to 50 embryos per group. Blastocyst development rates (BDR) were checked after 72 hours of incubation.

Results: Blastocyst development rates were 96.3%, 86.7%, 77.3%, 86.7%, 80%, 10% and 96% for the 7 groups respectively (Figure). BDR rates of all groups but F were comparable with the control group. On the other hand, Group F had significantly lower BDR compared to the control group (P<0.0001).

Conclusions: At concentrations similar to the maximum in vivo levels, infliximab does not affect BDR. Embryotoxic effects of infliximab appear only at a concentration 40 fold its maximum in vivo level. Infliximab does not have any toxic effects on early cleaving embryos. Infliximab can be used safely either before or during ovulation induction for patients with endometriosis.

Figure: Effect of different concentrations of infliximab on the blastocyst development rate of mouse embryos.
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- **I Agree:** True

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