High implantation and pregnancy rates with transfer of human hatching day 6 blastocysts

Although improved outcomes of IVF after transfer of blastocysts has been reported (1, 2), it remains uncertain which blastocyst can develop into a viable fetus. At present, expansion of the blastocyst is the most practical selection criterion. However, if extended culture of embryos produces many expanded-stage blastocysts, it is not easy to decide which blastocysts to transfer (Fig. 1A). In addition, some blastocysts fail to hatch out of the zona, despite evidence that the blastocoelic cavity had expanded and the zona pellucida had thinned (3).

We sought to investigate the rate of blastocyst formation and hatching on day 6 after insemination and to assess the developmental potential of hatching or hatched blastocysts after transfer.

The study was approved by the institutional review board of Maria Infertility Center. One hundred thirty-nine patients were recruited between March and July 1999. Patients were ≤40 years of age (mean [±SD] age, 34.4 ± 3.7 years) and had more than seven zygotes or two good-quality embryos on day 2. The zygotes were co-cultured with cumulus cells for 120 hours in 10 μL of YS medium (Table 1) supplemented with 10% human follicular fluid. All droplets for co-culture were exchanged for a preequilibrated culture medium every morning until day 6. Embryo transfer was routinely performed on day 6.

Of 2,117 oocytes retrieved, 1,387 oocytes fertilized normally (65.5%). Of these, 757 (54.6%) developed to the early blastocyst stage, 658 (47.4%) reached the expanding blastocyst stage, and 517 (37.3%) formed expanded blastocysts. Hatching was observed in 174 blastocysts (12.5%), and 42 blastocysts (3.0%) of zygotes could hatch on day 6 (Fig. 1B). A total of 281 blastocysts were transferred to 139 patients on day 6. Fifty-six percent of the patients (78 cycles) had at least 1 hatching blastocyst for transfer, and a mean of 1.9 ± 0.2 blastocysts were transferred.

The implantation and pregnancy rates were significantly higher in patients who received one or more hatching blastocysts than in patients who received nonhatching blastocysts (P < .05). The number of multiple gestations was the same in both groups, despite replacement of fewer embryos in patients with hatching blastocysts. The overall clinical pregnancy rate per transfer of blastocyst on day 6 was 48.9%, and the implantation rate was 31.0%. The multiple gestation rate was 16.7%; no triplet pregnancy occurred.

Our results show that the chance of success in assisted reproduction can be improved if selection of the most viable embryos is based on hatching status. After day 6 of culture, 23% (757 of 1,387) of blastocysts were hatching naturally; this finding is in agreement with the data of Gardner et al. (4) (25% of blastocysts). Under our culture conditions, 54.6% of zygotes developed to the blastocyst stage by day 6, and 37.3% formed expanded blastocysts. These rates are similar to those reported with co-culture (5) and those obtained by using a simple medium (1). YS medium was designed to support development of the human zygote to the blastocyst under the cumulus cell co-culture system.

In conclusion, after 6 days of culture, at least one hatching blastocyst developed in more than 50% of patients. An increased implantation rate was observed in patients who received hatching blastocysts, and no triplet pregnancy occurred.

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Morphology of blastocysts cultured in vitro for 5 or 6 days (original magnification, ×10). (A), Expanding and expanded blastocysts formed on day 5. It was sometimes difficult to select viable embryos for transfer. (B), Blastocysts that reached the hatching (solid arrow) and hatched stage (open arrow) on day 6. These morphologic distinctions may assist in the selection of more viable embryos for transfer.


References