Neurodevelopmental Status of Infants Conceived Assisted Reproductive Techniques in Royan Institute

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Received July 2011; Revised and accepted September 2011

Abstract

Objective: There is a large amount of information published about ART infants worldwide but apparently the similar data did not published by Iranian ART centers till now. This study is a comparative study for developmental assessment of these infants.

Materials and methods: In one case- control study 400 ART ' infants have been compared with 420 NC ' infants. Their developments have been assessed two times with test of Denver II until 9 months old. All of them were citizen of Tehran and assessed in one center. They have been adjusted for duration of pregnancy and delivery result. Chi- Square test and Wilcoxon Singned Ranks test were used for analysis of data.

Results: From 400 infants of ART, 31/3% was preterm and 42/8% were multi fetal pregnancy, which were higher than NC. There was not significant difference in development of infants of ART and NC in different methods of ART in two times assessment (without concerning premature and multi fetal pregnancy) (P>0/05). There was not significant difference between development of term and single fetal pregnancy of ART and NC in first and second time of assessment of development (p values were 0/7 and 0/4 respectively).

Conclusion: We concluded that there is not any difference in development of term and single fetal pregnancy in infants of ART and NC until 9 months old.

Keywords: Assisted Reproductive Techniques, neurodevelopmental state, Infants, Denver II

Introduction

Today Assisted Reproductive Techniques (ART) are used for treatment of human infertility all over the world by producing embryos through mixing of egg and sperm in laboratory with assisted device. More than one million children are born by means of these techniques (1,2). These children may differ from children of normal conception (NC) (3). They are mostly multi fetal pregnancy which increase prematurity and low birth weight and caused complication in these infants (4-6). Mean age of women who received these techniques of fertilization is 5 years more than women of normal conception. (7). The main cause of infertility and intervention for
treatment of infertility are effective factors of health of these children (8-10). Development is all abilities which achieved by a child at each age. Assessment of neurodevelopmental status is one of the aspects of health of these infants. It reflects growth and function of brain of infants.

Birth weight, sex, prematurity, education of mother, socioeconomic level of family, congenital defect (Like hearing loss) and disease are important factors which affect neurodevelopment of child (11).

Many studies have been done about development of infants conceived by ART in other countries. Most of them show normal pattern of development in comparison with children of NC. In studies which have been done in Finland (12), Denmark (13), Sweden (14), England (15-18) and Germany (19), they have not seen any significant difference in neurodevelopment and psychomotor development of these two groups of children.

In three systematic review, which compared neurodevelopment and motor development of ART’ children with normal conception, development of ART’ children did not have difference with control group (20-22).

There are other studies which show developmental delay in ART children in comparison to NC children. In one study in Japanese children of ART have shown delay in communication and cognitive skills in comparison to control group (23). In another study in Australia, receptive language development of children of In Vitro Fertilization (IVF) have delay in comparison with control group and expressive language, motor and social development were similar in both groups (24).

In two studies, infants of Intra cytoplasmic Sperm Injection (ICSI) have shown developmental delay in cognition and communication (25,26), specially they have more motor developmental delay in comparison to control group (26). Another study which compared development of one year old ICSI ’infant with infants of IVF and NC showed that, developmental delay were 17%, 2% and 1% respectively and more in ICSI’ infants (27).

Apparently there is no study about development of ART’ infants have been done yet in Iran and this study assessed neurodevelopmental status of these infants and comparing infants of different methods of ART, (ICSI and IVF) with NC.

**Materials and Methods**

In one case-control and cross sectional study, development of 400 infants of IVF or ICSI method of Royan Institute and 400 infants of NC who came to child Health Development Research Center of Tehran within 22 months have been assessed. child Health Development Research Center of Tehran within 22 months have been assessed.

The Research Ethics committee of Iran Medical Sciences branch of Academic Center for Education, Culture and Research (ACECR) and Royan Institute approved the study. After signing of informed consents by parents, infants’ development have been assessed two times, first time between birth and 6 months old and second time between 6 and 9 months old (interval between two assessment was 3 months) by test of Denver II in four fields of communication, fine motor, and gross motor and personal-social.

Samples were selected by the non-incidental consecutive method in both groups (ART and NC) from infants who came to our center in the period of study. Infants were born between September 2007 and June 2009 in Tehran. The ART’ infants refer by Royan institute and NC’ infants came from all parts of Tehran to our center. Data were gathered by interview, and developmental of infants by assessed by pediatrician by test of Denver II. The pediatrician did not know the method of conception. Test has been done after adjustment of age. Infants who were suspicious of developmental delay were assessed one month later.

Data were analyzed by SPSS-version 10 using Wilcoxon Signed Ranks and Chi-square tests. Confidence interval 95% was concerned.

**Results**

In this study development of 400 ART’ infants have been compared with 420 NC ’ infants by two times test of Denver II in four fields of communication, fine motor, gross motor and personal social.

In table 1, duration and result of pregnancy in different methods of fertility have been compared. Multi fetal pregnancy and prematurity were higher in ART’ infants. There were not significant differences in duration and result of pregnancy in IVF and ICSI’ infants (p=0/08 & p=0/05 respectively).

Table 2, shows developmental delay in four fields in two times assessment of infants of different methods of fertility. There were not significant difference (P>0/05). Number of infants with developmental delay did not increase by increasing age of infants.
Neurodevelopmental status of ART infants

Table 1: Prevalence of variable in different methods of fertility

<table>
<thead>
<tr>
<th>Fertility Method</th>
<th>Art</th>
<th>IVF</th>
<th>ICSI</th>
<th>ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of infants</td>
<td>420</td>
<td>87</td>
<td>313</td>
<td>400</td>
</tr>
<tr>
<td>Pregnancy Duration</td>
<td>Preterm</td>
<td>15</td>
<td>7</td>
<td>125</td>
</tr>
<tr>
<td></td>
<td>Term</td>
<td>403</td>
<td>14/5</td>
<td>272</td>
</tr>
<tr>
<td></td>
<td>Post term</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Delivery</td>
<td>Single</td>
<td>411</td>
<td>14/7</td>
<td>229</td>
</tr>
<tr>
<td>Result</td>
<td>Multiple</td>
<td>9</td>
<td>7</td>
<td>171</td>
</tr>
</tbody>
</table>

Table 2: Prevalence of four Fields of developmental delay in two tests in different methods of fertility

<table>
<thead>
<tr>
<th>Fertility Method</th>
<th>First</th>
<th>Second</th>
<th>First</th>
<th>Second</th>
<th>First</th>
<th>Second</th>
<th>First</th>
<th>Second</th>
</tr>
</thead>
<tbody>
<tr>
<td>Art</td>
<td>1/5</td>
<td>1/2</td>
<td>5</td>
<td>1/2</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td>1/2</td>
</tr>
<tr>
<td>IVF</td>
<td>0/9</td>
<td>0/5</td>
<td>2</td>
<td>0/5</td>
<td>7</td>
<td>1/7</td>
<td>11</td>
<td>2/7</td>
</tr>
<tr>
<td>ICSI</td>
<td>1/5</td>
<td>1/2</td>
<td>2</td>
<td>0/5</td>
<td>10</td>
<td>2/5</td>
<td>15</td>
<td>3/75</td>
</tr>
<tr>
<td>NC</td>
<td>2/4</td>
<td>1/9</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>1/2</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

There were not significant difference between development of infants of ART and NC in two times assessment, in chi - square test (p>0.05) 31% of ART infants were preterm and 42/8% were multi fetal pregnancy. After excluding these infants, 212 single and term ART infants were assessed. Also we excluded 3/5% preterm and 2/2% multi fetal pregnancy of NC infants and 400 single and term infants were assessed. We did not compare preterm and multi fetal pregnancy of ART and NC, because they were not similar number of infants in two groups.

In table 3 four fields of development of single and term infants of ART and NC have been compared. Wilcoxon signed Ranks test has not been show significant difference between first and second time assessment of infants of ART and NC (p=0/12 & p=1 respectively). Chi-square test has not been shown difference between single and term infants of ART and NC either (first assessment p=0/7 & second assessment p=0/4 respectively).

Discussion

The major problem in assessment of development of ART' infants is that they can not be compared with NC' infants. The basic problem of infertile parent, drugs and treatments which need for survival of fetus, psychological stress of these parents, and request of parents to transfer of more than one embryo to increase probability of pregnancy which causes multi fetal pregnancy and prematurity, are the important risk factors (28-30).

In this article we match the control group with ART' infants from the points of number of delivery, their age, birth year, birth place and pediatrician who assessed them.

Many studies have been done about development of infants conceived by ART in other countries and compared them with NC' infants. Most studies about development of ART' infants and children have not been shown difference with NC' infants. In one study in Greek (2004) in one years old children (31) and in
other study in England (1999) in 12-24 months old (16) there were not significant difference between development of ART' infants and NC' infants.

Also, developmental pattern of ART' infants in three years old (12), four years old (13) and five years old (15, 32) in comparison with control group did not show difference and in one of these studies 1.5% of IVF' infants and the same percent of NC' infants had developmental delay (13).

Some of these studies have shown developmental delay in these infants. In one study in Tiland (2001), development of ICSI' infants without control group have been assessed with test of Denver II, 14.7% of infants had developmental delay (33).

In other study in Australia (1998), 17% of ICSI' infants have been assessed with Bayley Scales of Infant Development and they had developmental delay in one years old (27).

In two other studies, development of ICSI' infants have been compared with NC' infants in age of one and five years old, developmental delay of ICSI' infants were reported too (25, 26).

In two studies, developmental delay of communication and language in one years old (23), and three years old (23) in ART' infants have been seen in comparison with control group.

We assessed development of infants of ART and NC by test of Denver II in four fields of communication, fine motor, and gross motor and personal – social two times (from birth to 6 months old and 6-9 months old) and we did not find significant difference.

In our study, percent of prematurity (31.3% and 3.5% in ART' and NC' infants respectively) and multi fetal pregnancy (42.8% and 2.2% in ART' and NC' infants respectively) in ART' infants were higher than NC' infants. In study of Bergh and his colleges , the prevalence of premature infants in IVF method and control group were 30.3% and 6.3% respectively and also multi fetal pregnancy were 27% and 1% respectively (5). In one study which has done by Koivurova and his colleges the prevalence of prematurity in IVF’ infants was 6 times more than normal neonatal population (6). Both prematurity and multi fetal pregnancy affect development of these infants (11). So we excluded these infants from our analysis and we analyzed the remain 212 term and single infants of ART and 400 infants of NC again.

we did not see any significant difference in first and second times assessment of term and single infants of ART and NC either.4.5% of infants of ART and 4.6% of infants of NC had developmental delay in 9 months old, so we can conclude that their developmental delay pattern are similar until this age.

In general, in this study and other similar studies, neurodevelopment of term and single ART' infants did not show difference with NC' infants and we can be hopeful of normal development of these children.

Conclusion

In this study, we assess development of infants conceived by ART and NC have been compared two times until 9 months old. It did not show any difference. After excluding preterm and multi fetal pregnancy, we did not see any difference either.

This study assess infants development until 9 months old, for complete assessment, prospective study with more infants must be designed and also assessed their development in older age.

Acknowledgements

This study was supported by Iran Medical Sciences Branch of Academic Center for Education, Culture and Research (ACECR) and the authors express their gratitude to Mrs. Afsane Azari and Miss Sharareh Dadashloo for their cooperation .There is no conflict of interest in this article.

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