Effect of Vitamin D Status on Clinical Pregnancy Rate in Case of Intracytoplasmic Sperm Injection (ICSI)

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Abstract

**Background:** Vitamin D had been suggested to have a role in human reproduction. We aimed to investigate if vitamin D levels can predict implantation and clinical pregnancy rates in infertile females after Intra-cytoplasmic sperm injection (ICSI).

**Methods:** Vitamin D levels had been evaluated prospectively by levels of serum 25-hydroxy-vitamin D (25[OH]D) levels, in a cohort of one hundred and fifty couples undergoing ICSI. Serum samples had been collected one week prior to oocyte retrieval. Patients had been classified according to vitamin D serum level into sufficient (≥ 75 nmol/L) or insufficient (<75 nmol/L).

**Results:** 38.97% of included females had sufficient vitamin D levels mean while 61.03% had insufficient vitamin D levels. Females with sufficient levels of vitamin D had a higher clinical pregnancy rates per ICSI cycle (58.49%) in comparison to those with insufficient levels (36.14%; p 0.011).

Introduction

Incidence of infertility approximately more than 15% of all couples trying to conceive. Vitamin D role in human reproduction and vitamin D level in prediction of reproduction success rates after ICSI had been supported by recent studies [1,2].

Vitamin D and Infertility

Vitamin D is a pro-hormone that either synthetized in the skin endogenously or obtained from the diet exogenously. Vitamin D is metabolized primarily in the hepatocytes to (25[OH]D), the serum level of (25[OH]D) which can be used as an indicator of vitamin D status [3].

Vitamin D is recently investigating the relation between it and fertility so; there is no specific cut-off levels had been referenced in the literature [4].

While the guideline of Canada defined the Vitamin D deficiency level less than or equal 25 nmol/L. Insufficiency Vitamin D levels between 25-74 nmol/L, and sufficiency Vitamin D levels of more than or equal 75 nmol/L [5]. There is relation between lower level of vitamin D and higher incidence of different types of cancer and impaired immune response [6,7]. Lower level of vitamin is highly prevalent in females of reproductive age. There is study reported that about 25% of black and about 15% of white females of reproductive age had been insufficient vitamin D levels [8]. In previous study had been reported that a 36% of vitamin D insufficiency (50-74 nmol/L) and a 27% of deficiency (<50 nmol/L) among females of reproductive age with infertility [9]. The vitamin D insufficiency (50-75 nmol/L) or deficiency (<50 nmol/L) was 79% in a population of females undergoing ART [10].

There are vitamin D receptors found in different reproductive organs such as ovary and uterus and many studies had been investigate the relation between vitamin D level and success rate following ICSI in human [11].

A cohort prospective study that measured the level of 25-hydroxy-vitamin D in the FF of 84 females undergoing ICSI found that females with increased levels of 25-hydroxy-vitamin D in their FF were significantly increase rate of implantation and pregnancy following ICSI [12-15].

In contrast to a small prospective study that found no significant difference in biochemical or clinical pregnancy rates across the level of vitamin D in follicular fluid [11]. There is a cohort prospective study that suggested higher levels of 25-hydroxy-vitamin D, in combination with decreased levels of glucose, in follicular fluid may have a negative effect on the ICSI success rates [16,17]. In our study, we aimed to determine whether levels of vitamin D are predictive of ICSI outcomes among infertile females [13].

Subjects and Methods

This study was conducted at the International Islamic Centre for Population Studies and Research (IICPSR)-ART unit, Al-Azhar University, Cairo, Egypt. During period of six months interval. This study included 150 couples, and 136 were included in our analysis. We excluded 14 couples because they did not complete the cycle due to negative TESE result.

Informed written consent was obtained from all included couples and study was depended on the institution’s research ethics board. All included females were classified according to vitamin D serum level into two groups:

1) Group I (sufficient ≥ 75 nmol/L 25-OH vitamin D3).
Intra-Cytoplasmic Sperm Injection (ICSI)

2) Group II (insufficient <75 nmol/L 25-OH vitamin D3).

Inclusion Criteria

Age of female ranges between 20-35 years old, Follicle-stimulating hormone level 12 IU/L or lower, all patients have the same cause of infertility (male factor), all patients undergoing ovulation induction using a long protocol, all patients will be receiving the same drugs of down regulation and gonadotrophins hormones and embryo transfer will be in the third day after ICSI.

Exclusion Criteria

Patients under vitamin D therapy, renal patients, patients with parathormone gland defects and GIT disease e.g., protein enteropathy.

All included couples were subjected to the following

- Full history taking include obstetrical and gynecological history: Age, weight, height, parity, occupation, special habits and duration of infertility.
- Complete physical examination: Vital data and full general examination and pelvic assessment.
- Assessment of male partner: Ejaculated sperm evaluation or testicular Sperm evaluation.
- All females were subjected to:
  - All females' partners underwent ovulation induction using a long protocol, all patients will be receiving the same drugs of infertility (male factor), all patients undergoing ovulation induction using a long protocol, all patients will be receiving the same drugs of down regulation and gonadotrophins hormones and embryo transfer will be in the third day after ICSI.
  - Assessment of fertilization and embryo’s quality: Fertilization was assessed 15-18 h after microinjection. The injected oocytes were observed for any sign of damage and for the presence of pro-nuclei. Oocytes were classed as fertilized if two pro-nuclei (2PN) were present and the second polar body had been extruded. Abnormally fertilized oocytes (1PN or 3PN) were excluded. Normally fertilized oocytes were left in culture for a further 24 h then embryos were classified according to a simplified system based on morphological criteria [19].
- U/S done after embryo transfer by 4-5 weeks searching for gestational intrauterine sac.

Table 1: Characteristics of 136 women undergoing ICSI, by vitamin D status.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vitamin D status, mean (± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I</td>
<td>Group II</td>
</tr>
<tr>
<td>Parity</td>
<td>Yes 7.55%</td>
<td>10.84%</td>
</tr>
<tr>
<td></td>
<td>No 92.45%</td>
<td>89.16%</td>
</tr>
<tr>
<td>Abortion</td>
<td>Yes 1.89%</td>
<td>12.05%</td>
</tr>
<tr>
<td></td>
<td>No 98.11%</td>
<td>87.95%</td>
</tr>
<tr>
<td>Previous ICSI</td>
<td>Yes 18.87%</td>
<td>13.25%</td>
</tr>
<tr>
<td></td>
<td>No 81.13%</td>
<td>86.75%</td>
</tr>
</tbody>
</table>

Table 2: Characteristics of 136 women undergoing ICSI, by vitamin D status.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vitamin D status, mean (± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I</td>
<td>Group II</td>
</tr>
<tr>
<td>Basal FSH</td>
<td>5.968 ± 1.653</td>
<td>5.694 ± 1.845</td>
</tr>
<tr>
<td>No. of follicles</td>
<td>10.623 ± 5.260</td>
<td>15.545 ± 6.899</td>
</tr>
<tr>
<td>Day of HCG injection</td>
<td>14.660 ± 1.990</td>
<td>Sep-21</td>
</tr>
<tr>
<td>Basal E2 level</td>
<td>36.874 ± 8.927</td>
<td>35.496 ± 10.459</td>
</tr>
<tr>
<td>E2 level on the day of</td>
<td>2265.566 ± 932.571</td>
<td>≥ 2365.976 ± 1116.118</td>
</tr>
<tr>
<td>HCG administration</td>
<td>Clinical pregnancy</td>
<td>85.619 ± 7.524</td>
</tr>
</tbody>
</table>

Table 3: Characteristics of 136 women undergoing ICSI, by vitamin D status.

Discussion

Serum level of 25-hydroxy-vitamin D may be an ICSI predictor among females undergoing infertility treatment. Women in this cohort in group I had significantly higher of clinical pregnancy rates following ICSI compared with females in group II.

Findings are significant clinically and hold therapeutic implications as about 61% of females in our study had lower levels. These findings are agreed with those previously reported in a North American cohort of reproductive-age females who included 173 patients in analysis. All of the included females subjected to oocyte retrieval, and 162 subjected to embryo transfer. The prevalence of vitamin D deficiency, insufficiency and sufficiency was 53.8% and 45.1%, respectively. In the analyses, we grouped together females with deficient and insufficient 25-hydroxy-vitamin D levels [8].

These findings were confirmed in other study of a group of infertile Canadian women by Garbedian who subsequently underwent oocyte retrieval. Females who were 25-hydroxy-vitamin D deficient were grouped together with those who were 25-hydroxy-vitamin D insufficient. Females with sufficient 25-hydroxy-vitamin D levels had significantly higher clinical pregnancy rates per ART cycle than females with deficient and insufficient levels (52.5% versus 34.7%, p<0.001) [20].

Also Polyzos only divided women into two divisions: vitamin D deficient (<50 nmol/L) and not vitamin D deficient (≥ 50 nmol/L). Overall, 46% of patients achieved clinical pregnancy. Clinical pregnancy rates were significantly lower in vitamin D deficient women compared to their non-deficient counterparts (41% versus 54%, p=0.015) [21].

Also Anifandis and colleagues confirmed these findings in their study of a group of infertile women who subsequently underwent oocyte retrieval. Women with sufficient vitamin D levels had significantly higher rates of clinical pregnancy per ART cycle than women with insufficient/deficient levels (38.1% versus 20.8%, p<0.05) [10].

Also Ozkane were the first to report a positive correlation between vitamin D levels and IVF outcomes. In their cohort prospective study, females achieving clinical pregnancy demonstrated significantly higher FF 25-hydroxy-vitamin D levels compared to females who did not achieve clinical pregnancy (≥ 75 nmol/L ± 15.58 versus <75 nmol/L ± 10.53, p=0.013) [4].

Unlike the previously discussed studies, Aleyasin found no relationship between serum vitamin D concentration and fertilization, implantation, or pregnancy rates in their study of 82 Iranian women [11]. A study conducted by Firouzabadi supported these findings. This cohort prospective study of 180 infertile females demonstrated no significant association between serum or FF 25-hydroxy-vitamin D levels and rates of clinical pregnancy. Overall, the rate of clinical pregnancy was 33.48% (p=0.094) [21].

In current study, we measure the serum levels of 25-hydroxy-vitamin D and not measure the level of 25-hydroxy-vitamin D in FF. While, other studies have shown the levels of 25-hydroxy-vitamin D in these fluids are highly correlated, and serum levels of 25-hydroxy-vitamin D have greater clinical utility. Future studies have to focus on determining the mechanism by which 25-hydroxy-vitamin D affects rates of clinical pregnancy, and they should include investigate of embryo quality, implantation and uterine receptivity.

Citation: Gebriel AEMA, Hassan FI, Abdel Latif EM, Hassan EA, Aref MI (2017) Effect of Vitamin D Status on Clinical Pregnancy Rate in Case of Intracytoplasmic Sperm Injection (ICSI). Vitam Miner 6: 156. doi:10.4172/2376-1318.1000156
Conclusion

In our study population, we found higher prevalence of vitamin D deficiency or insufficiency. Thus, it may be beneficial to investigate vitamin D levels as part of routine infertility assessment and before ART treatment.

In current findings suggest that females with high levels of 25-hydroxy-vitamin D are significantly than those with insufficient levels to achieve clinical pregnancy following ICSI.

Recommendations

In current findings suggest that females with high levels of 25-hydroxy-vitamin D are significantly than those with insufficient levels to achieve clinical pregnancy following ICSI. Supplementation of vitamin D may be an easy and cost-effective way to improving rates of pregnancy.

Future studies should focus on determining the mechanism by which vitamin D affects clinical pregnancy, and they should include measures of embryo quality, implantation and uterine receptivity. Studies should also be performed to investigate whether vitamin D supplementation can improve the pregnancy rates following ICSI.

References


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