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مباحث پیشرفته یادگیری عمیق؛ شبکه های نو نه گرافی
(Graph Attention Networks)

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آموزش استفاده از وب آ پایین
Effect of selenium on immune response against hepatitis B vaccine with accelerated method in insulin-dependent diabetes mellitus patients

Abstract

Background: Poor response to various vaccines especially hepatitis B is common. The purpose of this study was to evaluate the effect of selenium on immune response against hepatitis B vaccine with accelerated method in insulin-dependent diabetes mellitus patients.

Methods: In this randomized clinical trial study, 62 insulin dependent diabetic patients were divided into case and control groups (each of 31 cases). In the control group, hepatitis B vaccine 20 µg was done by intra-deltoid injection on a 0, 10, 21 day schedule with placebo, and in case group, 200 µg of selenium as a supplement was added once daily to same vaccine schedule from the first day to the 30th day of the month. After one month, serum sample was obtained and evaluated for anti-HBs using ELISA method. Data were collected and analyzed.

Results: In the case group, 23 cases (74.2%) and in control group, 15 cases (48.4%) achieved protective level of anti-HBs irrespective to sex and age (p=0.037). The mean antibody levels were 233.75 ± 163.45U/L and 144 ± 69.29U/L in selenium and control groups, respectively.

Conclusion: Our study showed that selenium could help to increase protective rate and level of anti-HBs by accelerated vaccination method. Adding selenium by routine HBV vaccination in diabetic patients is recommended for increasing the rate and level of anti-HBs in such group.

Keywords: Selenium, IDDM, Vaccination, Hepatitis B

The immune deficiency in diabetic patients responds poorly to various vaccines. Effective vaccination against hepatitis B virus (HBV) is one of the important health strategies in this special group. It is estimated that globally up to 500 million people have been infected with HBV and more than one million die annually (1). Its prevalence in Iran is estimated to be 1.7%-5%, thus, our country is located in an intermediate prevalent area (2). Although a few reports have shown no marked difference in antibody response against HBV vaccine between the diabetic and the non-diabetic patients, some studies have represented reduced antibody response in diabetics due to impaired immune system (3-6). Hence, it may be required to inject fourth dose of vaccine to the achieved adequate antibody titer although response failure may reach up to 25% (7-9). In recent years, some investigations have shown selenium, levamisole, zinc, GM-CSF and vitamin efficacy on immune system and increase response to influenza and HBV vaccine, inversely similar effect has not been confirmed by others about vitamin A, D3, C, E, folate, zinc and selenium but levamisole induces improvement of HBV vaccine responsiveness in hemodialysis patients (10-14).
According to the different studies mentioned earlier, it seemed that stated minerals could be used to improve the efficacy of immune system special groups such as the diabetics particularly in high prevalent HBV infection communities. We conducted this study to evaluate the selenium effect in improving response to HBV vaccine by accelerated method in diabetic patients in Hepatitis and liver disease research center in Kermanshah University of Medical Sciences, western Iran.

Methods
This randomized clinical trial was carried out on insulin dependent diabetes mellitus (IDDM) patients referred to Diabetes Clinic. The information recorded was age, sex and vaccination history. In the beginning, anti-HBs was checked for all subjects and if these markers were negative, vaccination started on day 0, 10, 21 and then anti-HBs level was measured 30 days after the last dose by ELISA method (DIAPRO Kit, Italy) in Imam Reza Hospital in Kermanshah, Iran. The vaccine used in this study was Hepavax-Gen made in South Korea. All subjects were diabetic for at least one year without history of HBV vaccination and active or chronic disease.

The exclusion criteria included thalassemia, any chronic disease like chronic renal disease and immune deficiency state, cigarette smoking and age over 65. After getting the informed consent, the subjects were divided into two 31 patients as case and control groups, randomly.

The vaccine was injected in deltoid muscle with 20 mcg using dose 2 cc syringes. In the case group on the first day of vaccination, 200 mcg selenium once a day (century 21 company made) was orally added and continued for thirty days and placebo for the control group. Thirty days after the termination of vaccination, serum sample was obtained and anti-HBs level was measured. Antibody titer above 10 mIU/ml was considered as immunologic response. T-test and X² tests were used to compare the outcomes in these two groups.

Results
From 62 IDDM cases, 40 (64%) were females and 22 (36%) males. In the case group, 48.4% were females and 51.6% males and in control group 9 (29%) and 22 (71%) were males and females, respectively. Body mass index (BMI) was 25.3±1.8 in study group and 24.4±2.1 in case group (p=0.15). In selenium recipients, 23 of 31 (74.2%) had antibody response, however, 15 of 31 (48.4%) in control group had response and this difference was statistically significant (p=0.03) (table 1).

In 40 years and over, 14 of 18 (77.7%) in case group and all 3 cases in control group were responders (p=0.364). Under 40 years, 9 of 13 (69.2%) and 12 of 28 (42.1%) had appropriate response in case and control groups, respectively (p=0.116). In case group, 6 out of 15 males (67%) and in control group, 6 out of 15 (40%) showed response that was not statistically significant (p=0.206). In case group, 177 of 22 females (77.3%) and in control group 9 of 16 (56.2%) were responders that was not statistically significant (p=0.168). The mean level of antibody was 233.72±60.74 mIU/ml and 144±69.29 mIU/ml in case and control group, respectively, that this difference was statistically significant (p=0.006) (table 1).

Table 1. Comparison of Multiple variables in Selenium and Control Groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case Total</th>
<th>No (%)</th>
<th>Control Total</th>
<th>No (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody Response</td>
<td>31</td>
<td>23 (74.2)</td>
<td>31</td>
<td>15 (48.4)</td>
<td>0.037</td>
</tr>
<tr>
<td>Ab Response &lt;40 (year)</td>
<td>13</td>
<td>9 (69.2)</td>
<td>28</td>
<td>12 (42.1)</td>
<td>0.116</td>
</tr>
<tr>
<td>Ab Response&gt;40 (year)</td>
<td>18</td>
<td>14 (77.7)</td>
<td>3</td>
<td>3 (100)</td>
<td>0.364</td>
</tr>
<tr>
<td>Male</td>
<td>9</td>
<td>6 (67)</td>
<td>15</td>
<td>6 (40)</td>
<td>0.206</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>17 (77.3)</td>
<td>16</td>
<td>9 (56.2)</td>
<td>0.168</td>
</tr>
</tbody>
</table>

Discussion
Our study demonstrated that selenium as an adjuvant could result in the improvement of rate and level of antibody response against HBV vaccine in IDDM cases by accelerated vaccination method. We did not find any study about the role and effect of selenium in promoting HBV vaccine in diabetic patients, but its role has been proven in
increasing immune system function. Selenium concomitantly with vitamin E, glutathione, NAC and other agents, during H5N1 infection to decrease complications, improving vaccine effect and antiviral treatment has been shown (15).

Also, other studies showed that selenium in comparison with vitamin E and ascorbic acid and placebo for 6 months in age over 65 had no effect on delayed type hypersensitivity (DTH), while, antibody level following influenza vaccine was increased by micronutrients alone or combined with vitamins better than vitamins alone, as a result low dose selenium had increased humeral response following vaccination and decreased morbidity rate of respiratory infections (16).

There is no more available information about optimal dose and duration of selenium for this purpose. We administered 200 mcg once a day for 4 weeks although longer periods of prescription had been reported (15). More investigations about appropriate treatment duration are needed. Despite previous experience about appropriate response against HBV vaccine in adults for more than 40 years, our study do not prove the influence of age on vaccine response, therefore, we need more trials in the future.

The present study did not show marked influence of gender on vaccine response, although, some reports revealed better results in females (17). In our study, the mean antibody titer was higher in trial group; therefore it seemed that selenium might produce higher level of HBV antibody as compared to placebo. Unfortunately, we did not compare the serum level of selenium in two study groups and so eventually, the effectiveness of this agent could be related to its deficiency in serum and consequently, the correction of deficit in our patients.

Because up to now, we do not have enough information about situation of selenium serum level in Iranian population. We found one study was carried out to evaluate the role of selenium in the occurrence of esophageal cancer in several regions of Iran that reported a normal range in Golestan, Mazandaran and Kerman but with lower level (<90 mcg/dl) in 29% of Ardebil province population (18).

As a result, we think that more investigations are needed to distinguish the serum level situation in general population of our region and Iran to conclude that a probable deficiency may explain this kind of effectiveness or otherwise should be considered. In our study, the mean age of cases was higher in the study group and selenium effect was noticeable in them, consequently, it might be reasonable that selenium deficiency had increased in age and this might explain the selenium effect in the promotion of immune system. We advised vaccination by accelerated method with proven efficacy as compared to the standard method, while the antibody response in control group was 48.4% and 74.2% in the study group as compared to standard method that showed about 60% in one and more than 90% in several other studies (3-6, 9). It might be concluded that the accelerated method of HBV vaccination might not be recommended routinely in special groups such as the diabetics because of unfavorable outcome, although selenium could increase immune response in diabetics but this issue needed further studies in the future.

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Conflict of interest: Authors have no conflict of interest.

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