Research Article

Efficacy of Nucleotide/Nucleoside Analogues and Hepatitis B Immunoglobulin Therapy in Blocking Mother-to-Child Transmission of Hepatitis B in an Eastern Chinese Group

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Received 15 May 2020; Revised 19 October 2020; Accepted 24 November 2020; Published 17 December 2020

Academic Editor: Susan Cu-Uvin

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The objective of this study was to investigate the efficacy and potential side-effects of nucleotide/nucleoside analogues and hepatitis B immunoglobulin injection of newborns in blocking mother-to-child transmission of hepatitis B virus in the middle and late pregnancy period. 238 cases of enrolled pregnant women were divided into the Telbivudine group, the Tenofovir group, the Lamivudine group, and the hepatitis B immunoglobulin (HBIG) group. Enrolled patients received corresponding therapies. Clinical and laboratory data were collected. Results showed that the levels of HBV DNA of the enrolled pregnant women in the Telbivudine, Tenofovir, and Lamivudine groups decreased rapidly after 12 weeks of drug intervention compared with those in the control. HBsAg positive rate in newborns and in children 24 weeks after birth was 0/60, 0/60, 0/60, 3/30, and 11/28 in the Telbivudine, Tenofovir, Lamivudine, HBIG, and control groups, respectively. No significant side-effects were identified after following up to 12 months after birth. Our results show that routine HBV vaccine plus HBIG injections is insufficient in blocking mother-to-child HBV transmission. Administration of nucleotide/nucleoside analogues or HBIG at pregnancy is suggested to maximize the blocking of vertical HBV transmission.

1. Introduction

The hepatitis B virus (HBV) infection remains a major health problem in China and worldwide. Infant infection from pregnant women as hepatitis B carriers is still a major concern [1–3]. For mothers with HBV infection in China, newborns are injected with HBIG and hepatitis B vaccine to interrupt mother-to-child transmission of HBV. However, mother-to-child transmission of HBV still accounts for about 30% to 50% new HBV infection [4]. Researches had shown that mother-to-child transmission of HBV mainly occurred in late pregnancy and lactation [3, 5, 6]. nucleotide/nucleoside analogues (NA) have been used in addition to HBIG and HBV vaccine to interrupt vertical transmission of HBV [7]. To search for more effective approaches in blocking the vertical transmission, we treated pregnant women in middle and late pregnancy period with nucleotide/nucleoside analogues and treated newborns with HBIG to interrupt mother-to-child transmission of HBV, and our results added more thoughts to the prevention strategies of mother-to-child transmission.

2. Materials and Methods

2.1. Subjects, Grouping, and Treatment. With the approval of the Ethics Committee of Taizhou People’s Hospital, all the enrolled pregnant women signed the informed consent form. All 238 pregnant women were chronic HBV carriers who received obstetric examination in Taizhou People’s Hospital from September 2010 to April 2018. Diagnosis was made according to the diagnostic criteria established in 2010 in
3. Results

The levels of HBV DNA of the enrolled pregnant women in the Telbivudine, Tenofovir, and Lamivudine groups decreased rapidly after 12 weeks of NA treatment, compared with those in the control group, $P < 0.05$ (Table 2). The decrease in HBV levels in the HBIG group was limited (Table 2). There were 2/60, 1/60, 1/60, 4/30, and 12/28 HBsAg-positive newborn cases in the Telbivudine, Tenofovir, Lamivudine, HBIG, and control groups, respectively, at birth. Reexamined at 24 weeks after birth, there were 0/60, 0/60, 0/60, 3/30, and 11/28 newborn cases of HBsAg positivity in the Telbivudine, Tenofovir, Lamivudine, HBIG, and control groups, respectively, $P < 0.05$ (Table 3).

There was no severe adverse reaction during the treatment period in the treatment groups. Transient mild increase in serum creatine kinase was found in 1 case in the Telbivudine group and 1 case in the Lamivudine group; the level returned to normal after two weeks. There was no significant difference in gestational age, mean weight, and Apgar score among all groups (Table S1). There were no complications such as fetal distress, neonatal asphyxia, amniotic fluid contamination, abnormal development, or malformations in each group. When the infants in each group were followed up to the age of 12 months, no deformity or other abnormalities were found.

All the patients enrolled in this study carried HBV genotype B or C. Our results showed that HBsAg, HBeAg, genotyping, HBV drug resistance, or the number of NK cells was not significantly correlated with treatment outcomes in patients (Table S2).

4. Discussion

Mother-to-child transmission is still a main transmission route of HBV infection in China. Over 90% of the newborns who get infected HBV develop into chronic hepatitis B carrier status [9, 10]. Infants infected by mother-to-child transmission could carry HBV for dozens of years [4]. High HBV DNA level and abnormal liver function lead to high mother-to-child transmission rates and adverse pregnancy events [11]. At present, active and passive immune intervention still could not completely interrupt the transmission from mother to child, with about 9% newborns from HBV carrier mothers still getting infected [12]; the infection rate could be around 40% if no intervention is provided [13].

High HBV DNA level can easily lead to placental dysplasia which makes the trophoblast cells of the placenta lose the protective barrier function, resulting in transplacental...
Table 2: The blood HBV DNA levels in study subjects.

<table>
<thead>
<tr>
<th>Group</th>
<th>Before treatment</th>
<th>12 weeks after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Telbivudine group</td>
<td>6.69 ± 1.72</td>
<td>2.18 ± 1.35*</td>
</tr>
<tr>
<td>Tenofovir group</td>
<td>6.72 ± 1.56</td>
<td>2.26 ± 1.40*</td>
</tr>
<tr>
<td>Lamivudine group</td>
<td>6.80 ± 1.59</td>
<td>2.34 ± 1.44*</td>
</tr>
<tr>
<td>HBIG group</td>
<td>6.77 ± 1.51</td>
<td>5.17 ± 1.83</td>
</tr>
<tr>
<td>Control group</td>
<td>6.72 ± 1.64</td>
<td>6.80 ± 1.56</td>
</tr>
</tbody>
</table>

Numbers were M ± SD of the group at log scale. *Statistical significance compared with the control group, P < 0.05.

Table 3: HBsAg status in newborns.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cases</th>
<th>HBsAg+ cases at birth</th>
<th>HBsAg+ cases 24 weeks after birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Telbivudine group</td>
<td>60</td>
<td>2</td>
<td>0*</td>
</tr>
<tr>
<td>Tenofovir group</td>
<td>60</td>
<td>1</td>
<td>0*</td>
</tr>
<tr>
<td>Lamivudine group</td>
<td>60</td>
<td>1</td>
<td>0*</td>
</tr>
<tr>
<td>HBIG group</td>
<td>30</td>
<td>4</td>
<td>3*</td>
</tr>
<tr>
<td>Control group</td>
<td>28</td>
<td>12</td>
<td>11</td>
</tr>
</tbody>
</table>

*Statistical significance compared with the control group, P < 0.05. *Statistical significance compared with the HBIG group, P < 0.05.

In summary, our results showed that administration of nucleotide/nucleoside analogues Telbivudine, Tenofovir, and Lamivudine and, to a lesser extent, the sequential hepatitis B immunoglobulin injections in pregnant women were effective in blocking mother-to-child transmission of hepatitis virus. Routine HBV vaccine plus HBIG injections was insufficient in blocking mother-to-child HBV transmission. Administration of nucleotide/nucleoside analogues or HBIG at pregnancy is suggested to maximize the blocking of vertical HBV transmission.

Data Availability

All data generated or analyzed in this study are included in the article and its supplementary information files.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors’ Contributions

Xiaojun Sun and Chengwei Wang contributed equally to the work.

Acknowledgments

The work was supported in part by NSF of Jiangsu Province for basic research (BK2011538, SML).

Supplementary Materials

Table S1: characteristics of newborns. Table S2: other characteristics of subjects in each group. (Supplementary Materials)

References


