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EFFICACY OF LAMIVUDINE VS TENOFOVIR IN HBSAG POSITIVE PREGNANT WOMEN TO REDUCE VERTICAL TRANSMISSION OF HEPATITIS B VIRUS

Gastroenterology

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ABSTRACT

Chronic hepatitis B virus (HBV) infection can cause chronic liver disease and hepatocellular carcinoma. Perinatal infection is the main route of transmission in Asian countries which leads to high rates of chronic infection. Therefore, it is important to prevent mother-to child transmission (MTCT) of HBV. The current study aims at comparing the use of antivirals (lamivudine vs tenofovir) in decreasing MTCT. **Materials and Methods:** A total of 72 HbsAg-positive pregnant women were enrolled in the prospective study to test the efficacy of antivirals to reduce MTCT and monitor hepatitis B viral status in infant. HbsAg-positive pregnant women aged 18–40 years at gestational age between 28 and 32 weeks were followed up. They were tested for HBsAg, liver function test and HBeAg. In whom HbeAg was positive, HBV viral load was tested. 72 patients with high viral load ([6 log copies/ml) were recruited and randomized into Group 1 and Group 2 which had 36 subjects each treated with lamivudine and tenofovir respectively starting from 28 to 32 weeks of gestation (third trimester) and continued to 1 month after delivery.The newborn babies were given HBIG within 24 h after delivery and HBV vaccines at 0, 1 and 6 months. HBsAg infectivity was tested in the infant at 1 year after birth. **Results:** Antivirals, lamivudine/tenofovir treatment in HBV carrier mothers from 28 weeks of gestation along with active and passive immunization of new born may interrupt MTCT of HBV efficiently. Tenofovir, category B drug, is more effective in preventing transmission of HBV infection to infants.

KEYWORDS

HBV Viral load, Lamivudine, Tenofovir

INTRODUCTION

Screening of the mothers during routine antenatal checkup helps to find out hepatitis B infection. Those who have hepatitis B infection can be treated accordingly with respect to their hepatitis and HBV viral load. Active and passive immunoprophylaxis have reduced the perinatal transmission of hepatitis B virus (HBV) dramatically. Without immunoprophylaxis, chronic HBV infection occurs in up to 90% of children by age of 6–18 months if the mother is positive for both hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg). There is a failure rate of 10–15% even with immunoprophylaxis because of which neonates develop hepatitis infection due to intrauterine infection transmission. According to European Association for the study of liver(EASL) and American Association for the study of Liver Diseases (AASLD) , all pregnant women should be screened for HbsAg during the Ist trimester, even if previously vaccinated or tested [1]. If patient is HbeAg positive, HBV DNA levels need to be estimated. Wang et al. used 6 log copies/ml as cut-off, and if HBV DNA levels were < = 6 log copies/ml, the failure rate of prevention of MTCT was 1.9%, and if levels were >= 6 log copies/ml, the failure rare was as high as 23.4% [1]. Antiviral therapy during the third trimester of pregnancy in high-risk women with chronic HBV infection reduces viral load in the mother and may decrease the risk of perinatal transmission [2].

METHODOLOGY

This prospective study was conducted at King George Hospital, Andhra Medical College,Visakhapatnam, India from July 2015 to June 2019. Institutional ethics committee approval was taken. Informed consent was taken from the patients. HbsAg-positive pregnant women aged 18–40 years at gestational age between 28 and 32 weeks were followed up. They were tested for HBsAg, liver function test and HBeAg. In whom HbeAg was positive, HBV viral load was tested. 72 patients with high viral load (>= 6 log copies/ ml) were recruited in the study. Alternate patients were randomized into two groups. Group 1 comprised 36 subjects treated with lamivudine 100 mg daily starting from 28 to 32 weeks of gestation (third trimester) and continued to 1 month after delivery. Group 2 comprised 36 pregnant women who were treated with tenofovir 300 mg daily from 28 to 32 weeks of gestation and continued to 1 month post-partum.

The newborn babies were given HBIG within 24 h after delivery and HBV vaccines at 0, 1 and 6 months. HBsAg status was tested in the infant at 1 year after birth.

Statistical Analysis

Data were entered into Microsoft Excel sheet and analysed using IBM SPSS Statistics (2017) version 25.0 . Data presented as mean and percentage. Unpaired t test was used to test the difference between the two groups. Paired data were analysed using paired t test. Chisquare test was used to analyse the difference in proportion, and p value was calculated. The primary outcome was considered significant if p value was < 0.05.

RESULTS

A total of 72 women were enrolled in the study with 36 patients in Group 1, receiving lamivudine 100 mg daily and 36 patients in Group 2 receiving 300 mg daily tenofovir from 28 to 32 weeks till one month post-partum. There was no significant difference with respect to age and parity between the two groups (Table 1). Age was ranged between 20 and >30 years and parity from 1 to >3. Table 2 shows that 66% of partners were HbsAg positive and 34% were HbsAg negative. 58% of patients were diagnosed as HbsAg positive in their first pregnancy, 38% in their second pregnancy and 4% in their third pregnancy. 40 patients delivered vaginally, and 32 patients underwent caesarean section according to obstetric indications. Liver function test was normal in 74% of patients, and mild elevation of liver enzymes abnormality was seen in 26% of patients for which no active medical intervention was required. Antiviral therapy was initiated before 30 weeks of gestation in 44% of patients, between 31 and 34 weeks in 42% and beyond 34 weeks in 14% of patients in both the groups. 88% had no side effects with both the drugs but 12% had minor side effects like headache, dizziness or nausea, which was not significant in both the groups. Mean maternal viral load was 6.4 log copies in Group A patients and 6.6 log copies in Group B patients. Antiviral therapy was initiated at mean 30.2 weeks of gestation in Group 1 and 28.4 weeks in Group 2 patients. Those mothers who received antiviral therapy for < 5–6 weeks had HbsAg-positive babies than those mothers who had antiviral therapy for > 9 weeks (p = 0.001), mothers with antiviral started before 30 weeks had nil infectivity to their babies while those who were started on antiviral between 31 and 34 weeks of gestation had 22.6% babies infected and those who started beyond 34 weeks had 74.6% infectivity , which is statistically significant (p = 0.001). In total, 13.8% of infants delivered vaginally were HbsAg positive compared to 9.8% who delivered by caesarean section although not statistically significant (p = 0.07). Table 3 shows a comparative analysis of the two drugs. Only minor side effects were seen with the usage of lamivudine and tenofovir which was not significant. There was no significant

difference between the pre-treatment HBV viral load between the two groups (p = 0.11). There was no significant difference in the duration of antiviral treatment in the two groups, 9.6 weeks in Group 1 versus 9.2 weeks in Group 2. However, the difference in HbsAg status of babies at 1 year of age was statistically significant (p = 0.005), with 23.5% of babies having infection with maternal lamivudine (Group 1) use and 4.8% with mothers on tenofovir (Group 2).

Table 1 : Demography

Age group (years) n=72	Number	%
< 20	5	7
20-30	54	75
>30	13	18
Parity		
Para 1	26	36
Para 2	24	34
Para 3 and above	22	30

Table 2 : Comparison between HbsAg Positive and HbsAg negative cases

Husband HbsAg status		%
Positive	48	66
Negative	24	34
Diagnosis of HBV infection		
1st pregnancy	42	58
2nd pregnancy	27	38
3rd pregnancy	3	4
Mode of delivery		
Vaginal	40	55
Caesarean	32	45
Liver function test		
Normal	53	74
Abnormal	19	26
Initiation of antiviral therapy (weeks)		
<30	31	44
31-34	30	42
>34	11	14
Side effects of anti viral therapy		
Nil	63	88
Minor	9	12
Initiation of treatment (mean in weeks)		
Group 1 (lamivudine)	30.2	P = 0.89
Group 2 (tenofovir)	28.4	
	Positive (%)	Negative(%)
Mean duration of treatment (weeks) and baby status		P = 0.001
< 30	0	100
31-34	22.6	77.4
>34	74.6	25.4
Mode of delivery and baby status		P= 0.07
Normal labour	13.8	86.2
Caesarean section	9.8	90.2

Table 3 : Comparative analysis between Lamivudine and Tenofovir

	Group 1 (Lamivudine)	Group 2 (Tenofovir)	P
HBV DNA load	6.4 log copies	6.6 log copies	0.11
Duration of treatment (weeks)	9.6	9.2	0.92
Baby status			
HbsAg positive	23.5%	4.8%	0.004

DISCUSSION

According to various studies, there is a linear co-relation between vertical transmission and maternal log10 viral load, although mother to-child transmission is less likely when HBV DNA levels are less than 5.3 log copies at the time of delivery [3,4]. In current study, the mean level of HBV DNA at which antiviral therapy was initiated was 6.4 and 6.6 log copies, respectively, in Group 1 and Group 2. The infection transmission to the newborn was seen in 23.5% in Group 1 (Lamivudine) and 4.8% in Group 2 (Tenofovir), in spite of receiving immunoglobulin and active immunization at birth. In the current study even though the treatment duration was same between both groups, the Group 2 receiving tenofovir was more effective in reducing maternal-to child transmission [3]. The analysis also shows that if the antiviral was started before 28 weeks, there was no perinatal transmission of hepatitis infection, but if the treatment was started beyond 34 weeks the viral transmission was as high as 74.6% [5]. With regard to MTCT of HBV during delivery, it is still controversial whether the mode of delivery (vaginal vs caesarean section) affects the vertical transmission rate of HBV [4]. The most likely route for intrapartum HBV transmission could be transplacental leakage of HBVpositive maternal blood during uterine contractions during delivery. With high viral load, an elective caesarean section before the onset of labour may reduce the risk of intrapartum transmission of HBV infection. In current study, 13.8% of patients with normal delivery had infants positive with HbsAg and 9.8% of those who underwent caesarean section (p = 0.07).The indication of caesarean section in the current study was according to obstetric indications.

CONCLUSIONS

Antiviral therapy in HBV carrier mothers who have high viral load effectively reduces MTCT. Both lamivudine and tenofovir
are safe for HBV carrier mothers in late pregnancy but tenofovir has better efficacy in prevention of vertical transmission in addition to immunoglobulins and hepatitis vaccination. The role HBV DNA viral load to determine Caesarean against normal vaginal delivery has to be determined in future studies.

REFERENCES

1. Terrault NA, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, Brown RS Jr, Bzowej NH, Wong JB. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology. 2018 Apr;67(4):1560-1599. doi: 10.1002/hep.29800. PMID: 29405329; PMCID: PMC5975958..
2. Zhang Z, Chen C, Li Z, et al. Individualized management of pregnant women with high hepatitis B virus DNA levels. WJG 20th anniversary special issue (9): hepatitis B virus. World J Gastroenterol. 2014;20(34):12056–61.
3. Papadakis MA, Elefsiniotis IS, Vlahos G, et al. Intrauterinetransplacental transmission of hepatitis B virus (HBV) from hepatitis B e antigen negative (precore mutant, G1896A) chronic HBV infected mothers to their infants. Preliminary results of prospective study. J Clin Virol. 2007;38(2):181–3 Epub 2006 Dec
4. Umar M, Hamama-Tul-Bushra, Umar S, Khan HA. HBV perinatal transmission. Int J Hepatol. 2013;2013:875791. doi: 10.1155/2013/875791. Epub 2013 Apr 22. PMID: 23738081; PMCID: PMC3659463.
5. Calvin Q, Pan MD, Zhongping Duan MD, et al. Tenofovir to prevent hepatitis B transmission in mothers with high viral load. N Engl J Med. 2016;374:2324–33.