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BETTER OUTCOME OF HBe Ag (-) THAN HBe Ag (+) LAMIVUDINE TREATMENT OF HBV CHRONICALLY INFECTED PATIENTS

WYŻSZA SKUTECZNOŚĆ LECZENIA PACJENTÓW Z PRZEWLEKŁYM WIRUSOWYM ZAPALENIEM WĄTROBY HBe Ag (-) NIŻ HBe Ag (+)

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STRESZCZENIE

Od maja 2006 do grudnia 2007 w Oddziale Dziennym Wojewódzkiego Szpitala Zakaźnego leczono lamiwudyną 108 pacjentów z pzw typu B. Obecność antygenu HBe potwierdzono u 46 (42.5%), a u 62 (57, 5%) antygen HBe był nieobecny. Wysokość wiremii HBV analizowano kolejno w 24, 48 i 72 tygodniu terapii stosując metodę Real Time HBV PCR firmy Abbott z limitem czułości metody 28 kopii/ml. Odpowiedź pełną na leczenie definiowano, jako obniżenie HBV DNA poniżej 10^2 kopii/ml (Grupa A). Odpowiedź niepełną definiowano, jako utrzymywanie się wiremii w granicach 10^2-10^5 kopii/ml (grupa B), a brak skuteczności leczenia, jako utrzymywanie się HBV DNA powyżej 10^5 kopii/ml (grupa C).

W świetle dotychczasowych naszych wyników pacjenci HBe Ag (-) wydają się odpowiadać lepiej na leczenie lamiwudyną niż HBe Ag (+).

Słowa kluczowe*: przewlekle zapalenie wątroby typu B, HBeAg (+), HBeAg (-), przewlekłe leczenie lamiwudyną, różne fazy choroby*

ABSTRACT

From May 2006 to December 2007 in Warsaw Hospital for Infectious Diseases one hundred and eight patients chronically infected HBV were treated with lamivudine.

Among them 46 (42.5%) were HBeAg (+) and 62 (57.5%) HBeAg (-). HBV DNA levels were analysed in weeks 24, 48 and 72 of therapy using Real Time HBV PCR (Abbott) with a limit of detection of 28 copies/ml. Complete response for treatment was defined as HBV VL of less than 10^2copies/ml (group A). Partial response was defined as HBV VL ranging from 10^2 to 10^5 copies/ml (group B), and treatment failure was determined by HBV VL above 10^5 copies/ml (group C). Presented results confirmed better response to lamivudine treatment in patients HBeAg (-) than HBeAg (+).

Key words: *chronic hepatitis, HBeAg(+), HBeAg(-), lamivudine treatment, distinct phases of diseases*

INTRODUCTION

In many countries, not only in Asia but also in Central and Eastern Europe including Poland lamivudine is still therapeutic standard for hepatitis B treatment in naive patients. The availability and low costs of therapy determined such an approach.

Long-term treatment with lamivudine is associated with drug – resistant mutants in as many as 70% of patients after 5 years of therapy (1).

The recent studies have shown better response for antiviral therapy in HBeAg negative than positive patients (2). Most of these data is coming from Asia, or from group of patients with minority of Caucasian race (3,4).The results of treatment of Polish patients are presented rarely. (5,6) .

MATERIALS AND METHODS

From May 2006 to December 2007 in Warsaw Hospital for Infectious Diseases one hundred and eight patients were treated with lamivudine. Among them 46 (42.5%) were HBeAg (+) and 62 (57.5%) HBeAg (-). The response rate was analyzed.

Patients were included to treatment, when met the criteria: chronic HBV infection, elevated ALAT, HBV level > 10^5 copies/ml for HBe Ag (+) and > 10^4 for HBe Ag (-) (7). Serum HBe antigens and antibodies was measured using immunoassays by Vitros Immunodiagnostic as a standard procedures with sensitivity < 0,35j/ml and specificity about 99,84%.

HBV DNA levels were quantified in weeks 24, 48 and 72 of therapy using Real Time HBV PCR (Abbott) with a limit of detection of 28 copies/ml.

Complete response for treatment was defined as HBV VL of less than 10^2copies/ml (group A). Partial response was defined as HBV VL ranging from 10^2 to 10^5 copies/ml (group B), and treatment failure was determined by HBV VL above 10^5 copies/ml (group C) (8,9).

RESULTS

Different response for treatment was found in HBeAg positive and negative variants. (table 1.)

Among HBeAg (+) patients: After 24 weeks of therapy in the group A there were only 3 patients (6.5 %), 13 pts were in group B (28.3 %) and 30 pts (65.2 %) in group C.

After 48 week 3 (6.5%), 12 (26%) and 31 (67.5%) patients were in groups A, B, C, respectively.

In 72 week of therapy the complete suppression was still observed among 3 pts (6.5%), the partial response only in 5 pts (10.9%), and 38 pts (82,6%) were classified as treatment failure (diagram 1)

Among HBeAg (-) patients: After 24 week of therapy complete response was observed in 34 pts (54.5%), partial in 26 pts (41.9%), and only 2 pts (3.2%) did not respond. After week 48 in group A we had already 41 pts (66.1%), group B 20 pts (32.2%), and only 1 pt remains (1.6%) non –responder.

At week 72 in the group A still remains 40 (64.5%) pts, in group B 18 (29%) pts and treatment failure occurred in 4(6.5%) of patients (diagram 2).

Differences were statistically significant in respect to HBe Ag (+) and HBeAg (-) patients.

DISCUSSION

Presented results confirmed significant differences in the effectiveness of lamivudine treatment in patients infected with different variants of the HBV virus and in consequence, necessity of different therapeutic approach in these two groups. Despite of identical etiology, HBe Ag (+) and HBeAg (-) variants remain in two distinct phases of disease, so also the response to treatment seems to be different. Lamivudine may still be reasonably chosen for naive patients with HBeAg (-). However, incomplete suppression of virus replication by inadequate drug potency provides opportunity for drug – resistant variants to be selected. Patients with HBeAg (+) should start therapy with more potent drug to avoid selection of compensatory HBV mutations. It is also known (10) that response to alternative antiviral agents is reduced in patients with lamivudine resistant HBV.

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Table 1. Total response for lamivudine treatment
Tabela 1. Zbiorcze wyniki leczenia lamiwudyną

	Week 24			Week 48			Week 72		
HBV DNA	$<10^2$	10^2-10^5	$>10^5$	$<10^2$	10^2-10^5	$>10^5$	$<10^2$	10^2-10^5	$>10^5$
HBeAg(+) N= 46	3 (6,5%)	13 (28,3%)	30 (65,2%)	3 (6,5%)	12 (26.0%)	31 (67,5%)	3 (6,5%)	5 (10,9 %)	38 (82,6%)
HBeAg(-) N= 62	34 (54,8%)	26 (41,9%)	2 (3,2 %)	41 (66,1%)	20 (32,2%)	1 (1,6%)	40 (64,5%)	18 (29,0%)	4 (6,5%)

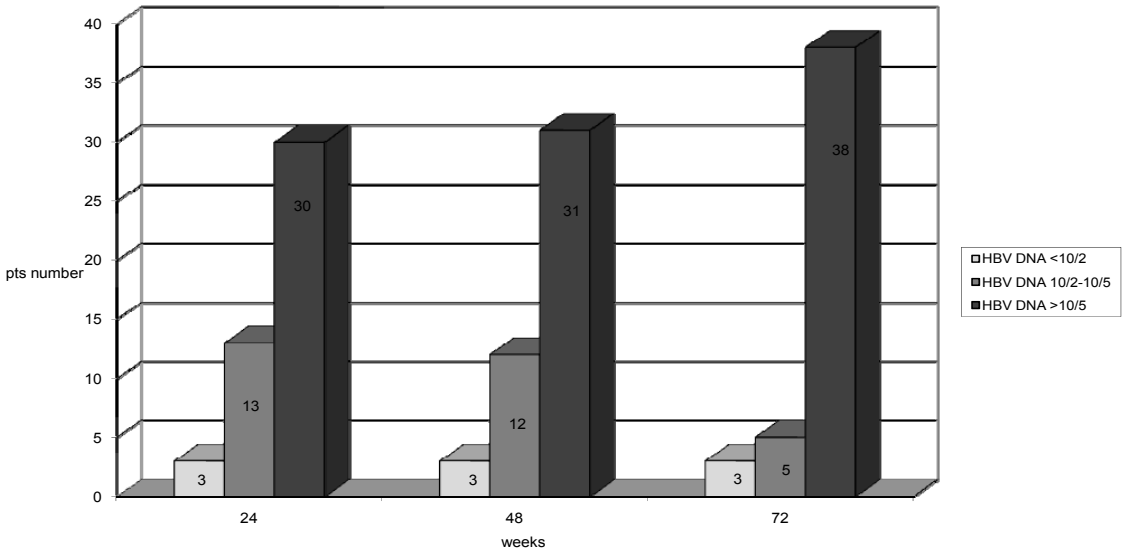

Fig. 1. Response for lamivudine treatment among HBeAg (+) patients
Ryc. 1. Wyniki leczenia lamiwudyną w grupie pacjentów HBeAg (+)

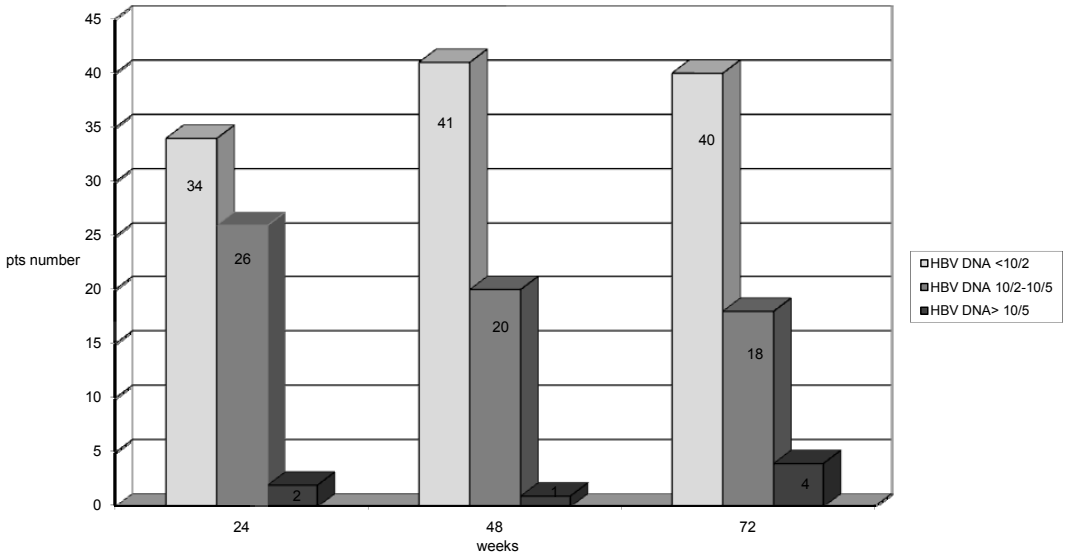

Fig. 2. Response for lamivudine treatment among HBeAg (-) patients
Ryc. 2. Wyniki leczenia lamiwudyną w grupie pacjentów HBeAg (-)

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