



不同丙氨酸氨基转移酶状态下乙型肝炎病毒对女性乙肝患者性激素水平及生活质量的影响*

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【摘要】目的 探讨在不同丙氨酸氨基转移酶(alanine aminotransferase, ALT)状态下乙型肝炎病毒对女性乙型肝炎(简称乙肝)患者性激素水平、绝经、睡眠、抑郁、焦虑及生活质量的影响。**方法** 分层随机选取不同ALT状态下不同病毒载量的女性慢性乙肝患者306例,分别比较分析在不同ALT状态下,乙型肝炎病毒对性激素水平、绝经、睡眠、抑郁、焦虑及生活质量的影响。并对ALT ≥ 2 倍正常上限的110例女性慢性乙肝患者进行抗病毒治疗,随访24周,对比分析抗病毒治疗前后患者上述指标的变化。**结果** 在ALT正常组及正常上限 $\leq$ ALT < 2 倍正常上限组中不同病毒载量的乙型肝炎病毒对女性慢性乙肝患者性激素水平、绝经、睡眠、抑郁、焦虑及生活质量的影响无明显差异,而在ALT ≥ 2 倍正常上限组中,随病毒载量升高(低复制组 $\rightarrow$ 高复制组):雌二醇质量浓度从(84.20 $\pm$ 7.78) pg/mL降至(64.60 $\pm$ 9.18) pg/mL,睾酮质量浓度从(0.33 $\pm$ 0.02) ng/mL升至(0.45 $\pm$ 0.04) ng/mL,卵泡生成激素浓度从(47.82 $\pm$ 7.62) mIU/mL升至(59.68 $\pm$ 7.19) mIU/mL,绝经率从55.56%升至86.11%,匹兹堡睡眠质量指数从11.02 $\pm$ 0.52升至15.93 $\pm$ 0.71,焦虑自评量表评分从46.06 $\pm$ 4.92升至64.66 $\pm$ 6.18,抑郁自评量表评分从44.14 $\pm$ 5.47升至67.08 $\pm$ 4.57,生活质量各维度均显著下降,差异均有统计学意义($P < 0.05$)。对ALT ≥ 2 倍正常上限的110例女性患者行抗病毒治疗后,雌二醇明显增高,睾酮及卵泡生成激素明显下降,各项睡眠指标和抑郁、焦虑评分明显下降,而各项生活质量指标明显升高(均 $P < 0.05$)。**结论** 在不同ALT状态下乙型肝炎病毒对女性乙肝患者的影响机制不同,对于ALT ≥ 2 倍正常上限的患者积极进行抗病毒治疗可明显改善女性患者性激素水平及各项生理心理指标,从而提高生活质量。

【关键词】 乙型肝炎 病毒载量 性激素 生活质量 丙氨酸氨基转移酶

The Influence of Hepatitis B Virus on Sex Hormone Levels and Quality of Life in Female Hepatitis B Patients With Different Alanine Aminotransferase States

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[Abstract] Objective This study examines the effects of hepatitis B virus on sex hormone levels, menopause, sleep, depression, anxiety, and quality of life in female hepatitis B patients under different alanine aminotransferase (ALT) conditions. **Methods** A total of 306 female patients with chronic hepatitis B, exhibiting different viral loads and varying ALT statuses, were randomly selected for stratified sampling. The effects of hepatitis B virus on sex hormone levels, menopause, sleep, depression, anxiety, and quality of life were compared and analyzed across different ALT statuses. Among these, 110 female patients with chronic hepatitis B and ALT levels ≥ 2 times the upper limit of normal received antiviral treatment and were followed for 24 weeks. Changes in the above indicators before and after antiviral treatment were compared and analyzed. **Results** In the ALT-normal group and the group with ALT levels ≤ 2 times the upper limit of normal, there was no significant difference in the effects of different hepatitis B virus viral loads on sex hormone levels, menopause, sleep, depression, anxiety, or quality of life in female patients with chronic hepatitis B. However, in the group with ALT ≥ 2 times the upper limit of normal, as the viral load increased (from the low replication group to the high replication group), the estradiol concentration decreased from (84.20 $\pm$ 7.78) pg/mL to (64.60 $\pm$ 9.18) pg/mL, testosterone increased from (0.33 $\pm$ 0.02) ng/mL to (0.45 $\pm$ 0.04) ng/mL, follicle-stimulating hormone increased from (47.82 $\pm$ 7.62) mIU/mL to (59.68 $\pm$ 7.19) mIU/mL, the menopause rate increased from 55.56% to 86.11%, the Pittsburgh Sleep Quality Index increased from 11.02 $\pm$ 0.52 to 15.93 $\pm$ 0.71, the Self-Rating Anxiety Scale score increased from 46.06 $\pm$ 4.92 to 64.66 $\pm$ 6.18, the Self-Rating Depression Scale score increased from 44.14 $\pm$ 5.47 to 67.08 $\pm$ 4.57, and all

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dimensions of quality of life significantly decreased, with all differences being statistically significant ($P < 0.05$). After antiviral treatment in 110 female patients with ALT ≥ 2 times the upper limit of normal, estradiol significantly increased, testosterone and follicle-stimulating hormone significantly decreased, sleep indicators and depression and anxiety scores significantly decreased, and all quality of life indicators significantly increased (all $P < 0.05$). **Conclusion** The impact of hepatitis B virus on female patients varies under different ALT conditions. For patients with ALT levels at or above twice the upper limit of normal, actively initiating antiviral treatment can significantly improve sex hormone levels and various physiological and psychological indicators in female patients, thereby enhancing their quality of life.

[Key words] Hepatitis B Viral load Sex hormones Quality of life Alanine aminotransferase

人体感染乙型肝炎病毒(hepatitis B virus, HBV)后可分为HBV携带者和乙型肝炎(简称乙肝)患者^[1]。对于HBV携带者,机体大多无明显症状和体征,而丙氨酸氨基转移酶(alanine aminotransferase, ALT)也大多处于正常状态或轻微增高^[2]。而对于乙肝患者,可出现腹部不适、巩膜黄染、乏力、恶心等症状和体征,而ALT也大多异常,甚至出现2倍以上增高^[3]。性激素是人体重要的一类激素,在人体的生长发育、成熟与衰老中均有重要作用,而对于成年女性性激素紊乱可明显影响到睡眠、心理状态以及生活质量^[4-5],但是目前鲜见有文献探讨在不同ALT状态下HBV对女性乙肝患者性激素水平、绝经、睡眠、抑郁、焦虑以及生活质量的影响,鉴于此,本研究就此进行探讨。

1 资料与方法

1.1 研究对象

本研究经兰州大学第一医院伦理委员会批准(批准文号LDYYLL2025-359)。分层随机选取2021年1月-2023年12月在兰州大学第一医院门诊和住院确诊为慢性乙肝及病毒携带者的女性患者306例,年龄35~60岁。按照ALT水平进行分层:ALT正常的患者97例(ALT<40 U/L),ALT大于等于正常上限(upper limit of normal, ULN)且小于2倍增高的患者99例(40 U/L $\leq$ ALT<80 U/L,即ULN $\leq$ ALT<2 ULN),ALT大于等于正常上限2倍增高的患者110例(80 U/L $\leq$ ALT,即2 ULN $\leq$ ALT)。各ALT分层又按HBV病毒载量分为低复制组(HBV DNA<4.0 lg copies/mL)、中复制组(4.0 lg copies/mL $\leq$ HBV DNA<6.0 lg copies/mL)和高复制组(HBV DNA $\geq$ 6.0 lg copies/mL)。并随机选取兰州大学第一医院体检中心健康体检女性30例作为对照组。分别观察在不同组别中不同载量的HBV对女性慢性乙肝患者性激素水平、绝经、睡眠、抑郁、焦虑及生活质量的影响。同时对ALT大于等于正常上限2倍增高的慢性乙肝患者给予恩替卡韦(0.5 mg/d)治疗,随访24周,对比分析抗病毒治疗前后患者上述指标的变化。同时排除妊娠期妇女,中度、重度脂肪肝患者,酒精肝患者,药物性肝损伤患者,有心、肺、肾等重大系统

疾患及内分泌疾病患者,应用激素治疗的患者,以及未能完成本研究全部项目的患者。

1.2 研究方法

1.2.1 标本的采集与保存

采集患者早晨空腹静脉血5 mL。绝经患者可在任何一天采集,未绝经患者在月经周期的第2~4天采集。所采集的血液以3 500 r/min离心10 min后分离血清,置于-20℃冰箱保存待测。

1.2.2 标本的测定

采用电化学发光法测定性激素:雌二醇(estradiol, E2)、总睾酮(testosterone, T)、孕酮(progesterone, P)、卵泡生成激素(follicle stimulating hormone, FSH)、黄体生成激素(luteinizing hormone, LH)、催乳激素(prolactin, PRL),采用瑞士罗氏Cobas e 801电化学发光仪器测定;乙型肝炎病毒载量HBV DNA采用德国Lightcycler ROCH公司荧光定量PCR扩增仪测定;肝功能指标采用日本OLYMPUS公司全自动生化分析仪测定。所有测定均严格按照标准化操作程序进行,并严格做好质控工作,均采用相应配套试剂进行测定。

1.2.3 检测患者睡眠质量、心理状况和生活质量

①采用匹兹堡睡眠质量量表(PSQI)评价患者的睡眠质量,PSQI评分总分为21分,分值越低表明睡眠质量越好。②采用焦虑自评量表(SAS)、抑郁自评量表(SDS)评价患者的心理状况,SAS评分及SDS评分总分均为100分,分值越低分别表明焦虑和抑郁程度越轻。③采用SF-36健康量表评价患者的生活质量,SF-36健康量表总分共100分,分数越高表明生活质量越好。

为减少主观偏差等影响,所有自评量表均采用双盲法进行实施。

1.3 统计学方法

采用SPSS 26.0软件进行统计分析。对所有定量资料进行正态分布检验,符合正态分布的数据用 $\bar{x} \pm s$ 表示,本研究中多组资料中定量资料的组间比较采用Dunnett T3方差分析,定性资料采用R $\times$ C表卡方检验,抗病毒治疗前后的配对样本之间的比较采用配对样本 t 检验, $\alpha=0.05$ 。

2 结果

2.1 HBV对女性患者性激素水平的影响

结果显示(表1),在ALT正常组及ULN≤ALT<2 ULN组中不同病毒载量的HBV对女性患者性激素水平的影响

无明显差异($P>0.05$),而在2 ULN≤ALT组中,随着病毒载量的增加,E2明显下降,T和FSH均明显增高($P<0.05$),而P、LH和PRL均无明显变化($P>0.05$)。

表 1 乙型肝炎病毒对女性患者性激素水平的影响

Table 1 The influence of hepatitis B virus on sex hormone levels in female patients							
Group	<i>n</i>	E2/(pg/mL)	T/(ng/mL)	P/(ng/mL)	FSH/(mIU/mL)	LH/(mIU/mL)	PRL/(ng/mL)
Control	30	118.98 ± 5.98	0.25 ± 0.04	0.55 ± 0.08	30.15 ± 3.89	18.96 ± 5.98	16.25 ± 5.12
ALT normal							
Low replication	33	111.75 ± 6.37	0.26 ± 0.03	0.56 ± 0.07	29.20 ± 4.09	19.64 ± 6.68	16.00 ± 4.58
Medium replication	34	110.95 ± 5.50	0.25 ± 0.03	0.57 ± 0.09	29.30 ± 4.76	19.29 ± 4.47	14.23 ± 4.55
High replication	30	110.42 ± 6.41	0.25 ± 0.02	0.57 ± 0.06	28.61 ± 4.61	21.06 ± 5.22	15.47 ± 3.61
<i>F</i>		0.385	0.581	0.300	0.212	0.904	0.897
<i>P</i>		0.681	0.561	0.742	0.809	0.409	0.411
ULN ≤ ALT < 2 ULN							
Low replication	31	89.77 ± 9.36	0.30 ± 0.04	0.55 ± 0.06	33.22 ± 2.97	20.53 ± 4.11	14.13 ± 3.69
Medium replication	34	88.01 ± 5.20	0.29 ± 0.04	0.56 ± 0.06	32.82 ± 2.62	20.83 ± 4.42	13.77 ± 3.21
High replication	34	88.72 ± 6.21	0.30 ± 0.03	0.54 ± 0.07	32.15 ± 3.25	20.61 ± 2.97	13.17 ± 3.38
<i>F</i>		0.508	0.335	0.656	1.089	0.052	0.650
<i>P</i>		0.603	0.716	0.521	0.341	0.950	0.524
2 ULN ≤ ALT							
Low replication	36	84.20 ± 7.78	0.33 ± 0.02	0.55 ± 0.07	47.82 ± 7.62	20.42 ± 5.26	13.33 ± 3.30
Medium replication	38	74.32 ± 7.61 [*]	0.38 ± 0.04 [*]	0.54 ± 0.09	50.50 ± 5.54 [*]	21.86 ± 6.60	13.97 ± 3.02
High replication	36	64.60 ± 9.18 ^{*,#}	0.45 ± 0.04 ^{*,#}	0.55 ± 0.08	59.68 ± 7.19 ^{*,#}	20.63 ± 4.40	13.86 ± 2.66
<i>F</i>		51.278	108.926	0.446	30.04	0.738	0.474
<i>P</i>		< 0.001	< 0.001	0.641	< 0.001	0.480	0.624

ULN: upper limit of normal; E2: estradiol; T: testosterone; P: progesterone; FSH: follicle stimulating hormone; LH: luteinizing hormone; PRL: prolactin. ^{*} $P<0.05$, vs. low replication group; [#] $P<0.05$, vs. medium replication group.

2.2 HBV对女性患者绝经情况的影响

结果显示(表2),在ALT正常组及ULN≤ALT<2 ULN组中不同病毒载量的HBV对女性患者绝经情况的影响无明显差异($P>0.05$),而在2 ULN≤ALT组中,随着病毒载量的增加,绝经率明显增加($P<0.05$)。

2.3 HBV对女性患者睡眠情况的影响

结果显示(表3),在ALT正常组及ULN≤ALT<2 ULN组中不同病毒载量的HBV对女性患者睡眠的影响无明显差异($P>0.05$),而在2 ULN≤ALT组中,随着病毒载量的增加,各项睡眠指标均明显增加($P<0.05$)。

2.4 HBV对女性患者抑郁、焦虑及生活质量的影响

结果显示(表4),在ALT正常组及ULN≤ALT<2 ULN组中不同病毒载量的HBV对女性患者抑郁、焦虑及生活质量的影响无明显差异($P>0.05$),而在2 ULN≤ALT组中,随着病毒载量的增加,抑郁、焦虑评分明显升高,而各

表 2 乙型肝炎病毒对女性患者绝经情况的影响

Table 2 The influence of hepatitis B virus on the menopausal status in female patients

Group	<i>n</i>	Menopause/case (%)	χ^2	<i>P</i>
Control	30	15 (50.00)		
ALT normal	97	49 (50.51)	0.020	0.990
Low replication	33	17 (51.51)		
Medium replication	34	17 (50.00)		
High replication	30	15 (50.00)		
ULN ≤ ALT < 2 ULN	99	49 (49.49)	0.140	0.932
Low replication	31	16 (51.61)		
Medium replication	34	17 (50.00)		
High replication	34	16 (47.06)		
2 ULN ≤ ALT	110	78 (70.91)	8.148	0.017
Low replication	36	20 (55.56)		
Medium replication	38	27 (71.05)		
High replication	36	31 (86.11)		

ULN: upper limit of normal.

表 3 乙型肝炎病毒对女性患者睡眠情况的影响

Table 3 The influence of hepatitis B virus on the sleep patterns in female patients

Group	<i>n</i>	Subjective sleep quality	Sleep onset latency	Actual sleep duration	Sleep efficiency	Sleep disorders	Daytime dysfunction	Hypnotic drug use	PSQI score
Control	30	0.99 ± 0.09	1.04 ± 0.12	0.95 ± 0.11	0.83 ± 0.09	1.01 ± 0.09	0.95 ± 0.08	0.73 0.11	6.51 ± 0.23
ALT normal									
Low replication	33	1.02 ± 0.13	1.03 ± 0.13	0.93 ± 0.10	0.86 ± 0.10	1.00 ± 0.08	0.97 ± 0.10	0.74 ± 0.13	6.56 ± 0.25
Medium replication	34	1.00 ± 0.13	1.04 ± 0.10	0.96 ± 0.09	0.87 ± 0.10	1.02 ± 0.09	0.97 ± 0.09	0.75 ± 0.13	6.62 ± 0.22
High replication	30	1.01 ± 0.13	1.02 ± 0.11	0.93 ± 0.11	0.88 ± 0.13	1.00 ± 0.09	0.96 ± 0.10	0.73 ± 0.16	6.49 ± 0.25
<i>F</i>		0.264	0.944	0.927	0.104	0.744	0.266	0.216	2.019
<i>P</i>		0.768	0.393	0.399	0.901	0.478	0.767	0.806	0.138
ULN ≤ ALT < 2 ULN									
Low replication	31	1.23 ± 0.10	1.29 ± 0.13	1.36 ± 0.15	1.18 ± 0.17	1.37 ± 0.18	1.23 ± 0.18	1.02 ± 0.26	8.68 ± 0.47
Medium replication	34	1.19 ± 0.11	1.29 ± 0.12	1.34 ± 0.13	1.15 ± 0.16	1.40 ± 0.17	1.21 ± 0.18	1.02 ± 0.24	8.69 ± 0.47
High replication	34	1.21 ± 0.12	1.29 ± 0.12	1.34 ± 0.11	1.17 ± 0.14	1.36 ± 0.17	1.21 ± 0.15	1.03 ± 0.13	8.62 ± 0.39
<i>F</i>		0.816	0.034	0.180	0.261	0.494	0.119	0.063	0.290
<i>P</i>		0.445	0.967	0.836	0.771	0.612	0.888	0.939	0.749
2 ULN ≤ ALT									
Low replication	36	1.52 ± 0.17	1.72 ± 0.24	1.56 ± 0.22	1.59 ± 0.23	1.89 ± 0.19	1.58 ± 0.18	1.19 ± 0.23	11.02 ± 0.52
Medium replication	38	1.85 ± 0.23 [*]	1.92 ± 0.22 [*]	1.86 ± 0.19 [*]	1.96 ± 0.18 [*]	2.11 ± 0.19 [*]	1.94 ± 0.21 [*]	1.50 ± 0.23 [*]	13.15 ± 0.48 [*]
High replication	36	2.26 ± 0.34 ^{*,#}	2.28 ± 0.30 ^{*,#}	2.23 ± 0.22 ^{*,#}	2.28 ± 0.26 ^{*,#}	2.53 ± 0.31 ^{*,#}	2.33 ± 0.25 ^{*,#}	2.04 ± 0.28 ^{*,#}	15.93 ± 0.71 ^{*,#}
<i>F</i>		77.134	42.870	94.813	84.358	66.774	114.584	108.254	656.544
<i>P</i>		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

ULN: upper limit of normal; PSQI score: Pittsburgh Sleep Quality Index score. ^{*} *P* < 0.05, vs. low replication group; [#] *P* < 0.05, vs. medium replication group.

表 4 乙型肝炎病毒对女性患者抑郁、焦虑及生活质量的影响

Table 4 The influence of hepatitis B virus on depression, anxiety, and quality of life in female patients

Group	<i>n</i>	SAS	SDS	Physiological function	Social function	Vitality	Mental health	Physiological function	Emotional function	Somatic pain	Overall health
Control	30	26.35 ± 4.92	31.28 ± 5.51	90.15 ± 5.19	91.12 ± 5.98	91.12 ± 5.53	90.02 ± 5.01	89.92 ± 5.03	90.13 ± 4.03	91.26 ± 3.99	89.69 ± 5.09
ALT normal											
Low replication	33	27.98 ± 4.63	30.43 ± 5.89	89.36 ± 5.50	90.03 ± 6.26	90.94 ± 5.90	86.67 ± 4.97	88.31 ± 4.67	90.54 ± 3.82	93.03 ± 3.69	85.65 ± 5.23
Medium replication	34	29.32 ± 6.08	28.97 ± 4.15	89.59 ± 5.15	89.37 ± 4.09	90.04 ± 3.78	87.64 ± 5.09	86.68 ± 5.03	90.04 ± 3.09	93.17 ± 3.65	85.57 ± 5.03
High replication	30	29.28 ± 5.42	30.78 ± 4.93	90.98 ± 4.56	88.60 ± 4.34	91.95 ± 2.15	85.34 ± 4.55	88.61 ± 3.85	90.39 ± 5.45	91.82 ± 2.08	86.24 ± 3.84
<i>F</i>		0.653	1.189	0.915	0.759	1.588	1.775	1.692	0.127	1.603	0.183
<i>P</i>		0.523	0.309	0.404	0.471	0.210	0.175	0.190	0.881	0.207	0.833
ULN ≤ ALT < 2 ULN											
Low replication	31	38.05 ± 6.25	40.42 ± 9.55	85.15 ± 5.13	78.31 ± 8.36	85.20 ± 5.38	80.00 ± 6.82	79.56 ± 7.78	85.11 ± 6.89	81.29 ± 4.82	80.61 ± 7.43
Medium replication	34	39.22 ± 5.80	41.21 ± 9.87	84.59 ± 5.27	78.88 ± 7.29	85.45 ± 5.19	79.84 ± 6.68	78.48 ± 6.49	85.23 ± 4.61	79.32 ± 4.60	79.35 ± 6.89
High replication	34	39.92 ± 6.56	41.70 ± 8.54	86.26 ± 4.38	77.63 ± 8.25	85.12 ± 4.00	81.22 ± 6.40	77.61 ± 5.55	86.04 ± 5.20	79.14 ± 6.11	80.01 ± 6.96
<i>F</i>		0.748	0.153	1.000	0.210	0.015	0.435	0.701	0.272	1.663	0.258
<i>P</i>		0.476	0.858	0.372	0.811	0.985	0.649	0.499	0.763	0.195	0.773
2 ULN ≤ ALT											
Low replication	36	46.06 ± 4.92	44.14 ± 5.47	76.59 ± 6.21	70.69 ± 6.76	73.35 ± 6.25	71.97 ± 6.12	67.87 ± 6.81	70.37 ± 6.42	77.33 ± 6.31	78.71 ± 4.88
Medium replication	38	56.42 ± 6.51 [*]	54.92 ± 4.51 [*]	67.18 ± 6.54 [*]	59.88 ± 5.11 [*]	64.12 ± 6.16 [*]	62.36 ± 6.67 [*]	52.87 ± 5.07 [*]	62.96 ± 6.00 [*]	69.25 ± 5.65 [*]	68.75 ± 3.70 [*]
High replication	36	64.66 ± 6.18 ^{*,#}	67.08 ± 4.57 ^{*,#}	56.34 ± 7.60 ^{*,#}	50.58 ± 8.28 ^{*,#}	52.79 ± 7.93 ^{*,#}	51.30 ± 5.62 ^{*,#}	46.93 ± 7.74 ^{*,#}	50.64 ± 6.61 ^{*,#}	58.48 ± 4.77 ^{*,#}	54.75 ± 5.67 ^{*,#}
<i>F</i>		89.231	200.602	79.849	78.676	82.112	101.096	96.257	88.939	116.193	226.569
<i>P</i>		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

ULN: upper limit of normal; SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale. ^{*} *P* < 0.05, vs. low replication group; [#] *P* < 0.05, vs. medium replication group.

项生活质量指标明显下降($P<0.05$)。

2.5 抗病毒治疗前后女性患者性激素水平的变化

对ALT ≥ 2 ULN的110例患者给予恩替卡韦(0.5 mg/d)治疗,随访24周,对比分析抗病毒治疗前后患者性激素水平的变化。结果显示(表5),抗病毒治疗后,E2明显增高,T及FSH均明显下降,差异有统计学意义($P<0.05$),而P、LH及PRL均无明显变化($P>0.05$)。

2.6 抗病毒治疗前后女性患者睡眠情况的变化

结果显示(表6),抗病毒治疗后各项睡眠指标均明显下降,差异有统计学意义($P<0.05$)。

2.7 抗病毒治疗前后女性患者抑郁、焦虑及生活质量的变化

结果显示(表7),抗病毒治疗后抑郁、焦虑指数明显下降,而各项生活质量指标均明显升高,差异有统计学意义($P<0.05$)。

表 5 抗病毒前后女性患者性激素水平的变化 ($n=110$)

Table 5 Changes in sex hormone levels in female patients before and after antiviral treatment ($n = 110$)						
Treatment	E2/(pg/mL)	T/(ng/mL)	P/(ng/mL)	FSH/(mIU/mL)	LH/(mIU/mL)	PRL/(ng/mL)
Before	74.37 $\pm$ 11.38	0.39 $\pm$ 0.06	0.55 $\pm$ 0.08	52.63 $\pm$ 8.44	20.99 $\pm$ 5.51	13.72 $\pm$ 2.99
After	100.94 $\pm$ 8.15	0.30 $\pm$ 0.08	0.55 $\pm$ 0.08	33.20 $\pm$ 3.07	20.77 $\pm$ 5.46	13.77 $\pm$ 3.29
<i>t</i>	−19.854	18.032	0.058	27.529	1.142	−0.287
<i>P</i>	< 0.001	< 0.001	0.954	< 0.001	0.256	0.775

E2: estradiol; T: testosterone; P: progesterone; FSH: follicle stimulating hormone; LH: luteinizing hormone; PRL: prolactin.

表 6 抗病毒治疗前后女性患者睡眠情况的变化 ($n=110$)

Table 6 Changes in sleep patterns in female patients before and after antiviral treatment ($n = 110$)								
Treatment	Subjective sleep quality	Sleep onset latency	Actual sleep duration	Sleep efficiency	Sleep disorders	Daytime dysfunction	Hypnotic drug use	PSQI score
Before	1.87 $\pm$ 0.40	1.97 $\pm$ 0.34	1.88 $\pm$ 0.34	1.94 $\pm$ 0.36	2.18 $\pm$ 0.36	1.94 $\pm$ 0.38	1.57 $\pm$ 0.43	13.36 $\pm$ 2.08
After	1.36 $\pm$ 0.11	1.42 $\pm$ 0.20	1.26 $\pm$ 0.271	1.19 $\pm$ 0.27	1.47 $\pm$ 0.25	1.41 $\pm$ 0.23	1.11 $\pm$ 0.26	9.22 $\pm$ 1.25
<i>t</i>	18.350	35.603	44.336	57.200	36.650	31.655	23.29	48.793
<i>P</i>	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

PSQI score: Pittsburgh Sleep Quality Index score.

表 7 抗病毒治疗前后女性患者抑郁、焦虑及生活质量的变化 ($n=110$)

Table 7 Changes in depression, anxiety, and quality of life in female patients before and after antiviral treatment ($n = 110$)										
Treatment	SAS	SDS	Physiological function	Social function	Vitality	Mental health	Physiological function	Emotional function	Somatic pain	Overall health
Before	55.73 $\pm$ 9.58	55.37 $\pm$ 10.50	66.71 $\pm$ 10.65	60.37 $\pm$ 10.60	63.43 $\pm$ 10.76	61.88 $\pm$ 10.39	56.02 $\pm$ 10.38	61.36 $\pm$ 10.26	68.37 $\pm$ 9.29	67.54 $\pm$ 10.81
After	35.59 $\pm$ 9.40	38.94 $\pm$ 7.30	77.36 $\pm$ 8.62	79.90 $\pm$ 10.05	84.14 $\pm$ 11.24	78.51 $\pm$ 9.36	81.43 $\pm$ 8.97	77.86 $\pm$ 8.84	79.00 $\pm$ 9.89	82.59 $\pm$ 12.00
<i>t</i>	47.461	26.809	−17.746	−28.418	−39040.701	−18.127	−43.707	−38.286	−24.746	−17.563
<i>P</i>	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale.

3 讨论

HBV作为嗜肝性DNA病毒,由包膜与核壳体构成,传染性强,严重威胁人类身心健康^[6-7]。已有文献报道,女性HBV感染者的性激素水平、睡眠质量、身心状态及生活质量均会受到显著损害^[8-9],但目前关于HBV载量高低及抗病毒治疗对该损害的影响,相关研究鲜见。HBV感染人体后会呈现病毒携带、乙肝发病等不同阶段,不同阶段中ALT的表达存在明显差异^[10-11],因此本研究依据ALT水平分层,探讨不同载量HBV对女性患者性激素水平、

睡眠质量及身心状态的影响,并分析抗病毒治疗前后上述指标的变化规律。

本研究证实,不同ALT状态下HBV对女性性激素水平的影响存在显著差异:ALT正常及轻度增高时,HBV载量高低对性激素水平无明显影响;而ALT ≥ 2 倍正常上限时,随病毒载量升高,E2呈显著下降趋势,T与FSH则明显增高,P、LH及PRL均无明显变化。究其原因,ALT正常及轻度增高时,机体多处于免疫耐受阶段,免疫系统与HBV相互耐受,肝细胞损伤轻微,ALT释放量少,肝功能基本正常,对全身脏器损伤较小,免疫防御机制未被激活,故

无论病毒载量高低,均不会引发女性性激素水平紊乱^[12-14]。而ALT ≥ 2 倍正常上限时,机体进入免疫激活状态,免疫系统与HBV相互攻击,病毒载量越高,肝细胞破坏越严重,ALT释放越多,肝功能损伤越显著,机体会释放大量的内毒素、补体及免疫炎症介质等^[15-16],并通过多途径损伤女性性激素分泌:①上述物质直接作用于卵巢,造成卵巢颗粒细胞坏死,引发卵巢功能下降,导致性激素释放紊乱^[17];②肝细胞大量破坏致肝功能下降,使雌激素受体数量或活性增强,负反馈作用增强,降低血清雌激素水平^[18];③HBV感染引发的炎症及免疫激活释放的干扰素 α 、白细胞介素6、肿瘤坏死因子 α 等细胞因子,可抑制下丘脑-垂体-性腺轴,减少促性腺激素释放,抑制卵巢芳香化酶活性及雌激素合成,同时影响性激素结合球蛋白合成、性激素灭活及肾上腺雄激素合成,最终导致性激素水平失衡^[19]。而T增高的原因主要为:①肝功能受损致使T代谢减慢,其向E2的转化减少^[20];②肝细胞破坏致血浆白蛋白降低,结合态T减少,游离态有生物活性的T相对增高^[21];③E2降低通过负反馈抑制T代谢、促进T合成^[22]。本研究同时发现,不同ALT状态下HBV对女性绝经的影响存在差异,机制与性激素紊乱相仿,即HBV诱导的炎症物质直接损伤卵巢,且性激素紊乱加速卵巢损伤与衰老。

本研究进一步分析发现,HBV对女性睡眠质量、心理状况及生活质量的影响规律与性激素一致:ALT正常或轻度增高时,HBV对上述指标影响甚微;而ALT异常组尤其是ALT ≥ 2 倍正常上限时,随病毒载量增加,患者睡眠质量显著下降,抑郁、焦虑评分明显升高,生活质量评分显著降低。该机制与性激素紊乱密切相关,性激素对女性睡眠及身心状态有重要调控作用^[23],多导睡眠图证实,E2水平下降与睡眠效率降低、睡眠呼吸障碍及运动觉醒频率升高相关^[24],围绝经期和绝经后失眠女性的血浆FSH水平显著高于无失眠症女性,且FSH水平与睡眠效率、深度睡眠呈负相关,与睡眠后觉醒次数等呈正相关^[25]。同时,性激素紊乱引发的卵巢功能退化会导致下丘脑-垂体-卵巢轴功能失调,雌激素水平降低,使女性成为焦虑性失眠高发群体,进而引发记忆力衰退、注意力不集中等问题,严重影响正常生活^[26-27],这也是ALT异常患者抑郁、焦虑评分上升且生活质量下降的核心原因。

本研究对ALT ≥ 2 倍正常上限的女性慢性乙肝患者实施抗病毒治疗后疗效良好,患者性激素水平趋于正常,睡眠质量、心理状况及生活质量均明显改善。ALT ≥ 2 倍正常上限是目前公认的抗病毒治疗适应证之一,本研究结果亦为此提供了临床佐证。其核心机制为,该阶段机体免疫系统处于激活状态,病毒载量越高,病理性免疫损

伤越严重,抗病毒治疗可有效抑制病毒复制,减轻免疫损伤,保护肝细胞并改善肝功能,进而稳定性激素水平,缓解睡眠及身心障碍。本研究从不同病毒载量组别、抗病毒治疗前后的性激素水平变化,阐明了肝损伤对女性性激素水平的影响,具有一定临床参考意义;但性激素紊乱是否会反向加重肝脏损伤,仍需更多研究论证。此外,本研究数据较多,指标间可能存在相关性,存在假阳性风险,研究结果仅作探索性分析。

综上所述,不同ALT状态下,HBV对女性慢性乙肝患者的性激素水平、睡眠质量、身心状态及生活质量的影响存在显著差异,该差异与HBV感染后机体的免疫反应状态密切相关。深入理解这一关联规律,可为女性慢性乙肝患者的个体化诊疗提供理论依据,有助于提升临床治疗的针对性与有效性。

* * *

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Author Contribution GAO Peng is responsible for conceptualization, data curation, formal analysis, funding acquisition, project administration, writing--original draft, and writing--review and editing. ZHOU Wei is responsible for investigation and visualization. LI Junfeng is responsible for resources, software, and supervision. YAO Liqiong is responsible for conceptualization, methodology, supervision, validation, and writing--review and editing. All authors consented to the submission of the article to the Journal. All authors approved the final version to be published and agreed to take responsibility for all aspects of the work.

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