

拉米夫定联合阿德福韦酯治疗乙型肝炎病毒肝硬化的临床观察

袁 进*(重庆市江津区中心医院感染科,重庆 402260)

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摘要 目的:观察拉米夫定联合阿德福韦酯治疗乙型肝炎病毒(HBV)肝硬化的临床疗效和安全性。方法:将符合标准的142例HBV肝硬化患者随机均分为阿德福韦酯组、拉米夫定组和联合用药组。所有患者均给予常规治疗。在此基础上,阿德福韦酯组患者给予阿德福韦酯胶囊10 mg,口服,qd;拉米夫定组患者给予拉米夫定片100 mg,口服,qd;联合用药组患者给予阿德福韦酯+拉米夫定。各组患者疗程均为12个月。观察各组患者的临床疗效,治疗前后的肝功能指标[总胆红素(TBIL)、丙氨酸氨基转移酶(ALT)、天冬氨酸氨基转移酶(AST)],肝脏储备功能量化评分(Child-Pugh)分级,HBV脱氧核糖核酸(HBV-DNA)阴转率及转阴时间,并记录不良反应发生情况。结果:治疗后,各组患者肝功能指标均显著低于同组治疗前,且联合用药组低于阿德福韦酯组和拉米夫定组,差异均有统计学意义($P<0.05$);联合用药组患者总有效率、HBV-DNA阴转率、Child-Pugh A级患者例数均显著高于阿德福韦酯组和拉米夫定组,HBV-DNA转阴时间、Child-Pugh B、C级患者例数均显著低于阿德福韦酯组和拉米夫定组,差异均有统计学意义($P<0.05$)。各组患者不良反应发生率比较差异无统计学意义($P>0.05$)。结论:拉米夫定联合阿德福韦酯治疗HBV肝硬化较单用拉米夫定或阿德福韦酯疗效更显著,且安全性相似。

关键词 拉米夫定;阿德福韦酯;乙型肝炎病毒肝硬化;疗效;安全性

Clinical Observation of Lamivudine Combined with Adefovir Dipivoxil in the Treatment of HBV-cirrhosis

YUAN Jin (Dept. of Infection, Jiangjin District Central Hospital of Chongqing, Chongqing 402260, China)

ABSTRACT OBJECTIVE: To observe the clinical efficacy and safety of lamivudine combined with adefovir dipivoxil in the treatment of HBV-cirrhosis. METHODS: Totally 142 patients with HBV-cirrhosis were randomly divided into adefovir dipivoxil group, lamivudine group and combination group. All patients were given routine treatment. Based on it, the patients in adefovir dipivoxil group were orally given adefovir dipivoxil capsules 10 mg, qd; patients in lamivudine group were given Lamivudine tablets 100 mg, qd; and patients in combination group were given adefovir dipivoxil and lamivudine. The course of 3 groups was 12 months. The clinic data was observed, including clinical efficacy, liver function indexes (TBIL, ALT, AST), Child-Pugh grades, negative rate and negative time of HBV-DNA before and after treatment. ADR was recorded. RESULTS: After treatment, the liver function indexes in 3 groups were significantly lower than before and combination group was lower than adefovir dipivoxil group and lamivudine group, with significant differences ($P<0.05$). The total effective rate and negative rate of HBV-DNA in combination group were significantly higher than adefovir dipivoxil group and lamivudine group, patients with Child-Pugh Grade A were significantly more than adefovir dipivoxil group and lamivudine group, and negative time of HBV-DNA and patients with Child-Pugh Grade B and C were significantly less than adefovir dipivoxil group and lamivudine group ($P<0.05$). There was no significant difference in the incidence of adverse reactions in 3 groups ($P>0.05$). CONCLUSIONS: Lamivudine combined with adefovir dipivoxil has better efficacy than only lamivudine or adefovir dipivoxil in the treatment of HBV-cirrhosis with similar safety.

KEYWORDS Lamivudine; Adefovir dipivoxil; HBV-cirrhosis; Efficacy; Safety

- 的临床疗效及安全性分析[J].中国医药导刊,2013,15(10):16 601.
- [2] Stanley JS, Lars GC, Tom U, *et al.* Budesonide inhalation suspension versus montelukast in children aged 2 to 4 years with mild persistent asthma [J]. *J Allergy Clin Immunol Pract*, 2013, 1(1):58.
- [3] 中华医学会儿科分会呼吸学组.儿童支气管哮喘诊断与防治指南[J].中华儿科杂志,2008,46(10):745.
- [4] 周素香,齐红梅,李丽萍.孟鲁司特联合布地奈德治疗儿童哮喘临床疗效及对炎症因子的影响[J].临床肺科杂志,2013,18(12):2 266.
- [5] Wang L, Christopher SH, David TM, *et al.* Cost-effectiveness analysis of fluticasone versus montelukast in children with mild-to-moderate persistent asthma in the Pediatric Asthma Controller Trial [J]. *J Allergy Clin Immunol*, 2011, 127(1):161.
- [6] 李永梅,宋梅,杜昊.布地奈德联合孟鲁司特治疗小儿支气管哮喘疗效观察[J].现代中西医结合杂志,2013,22(32):3 567.
- [7] Erkka V, Maria LB, Colin FR, *et al.* Intermittent or daily montelukast versus placebo for episodic asthma in children [J]. *Annals of Allergy, Asthma & Immunology*, 2011, 106(6):518.

*副主任医师。研究方向:感染性疾病。电话:023-47520917。
E-mail:zhlyjtt@163.com

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夫定组两组间比较差异均无统计学意义($P>0.05$),详见表4。

表4 各组患者HBV-DNA阴转率及转阴时间比较[例(%)]

Tab 4 Comparison of negative rate and negative time of HBV-DNA among groups [case(%)]

组别	n	HBV-DNA阴转(率,%)	HBV-DNA转阴时间,月
阿德福韦酯组	48	34(70.83)	10.25±2.68
拉米夫定组	48	37(77.08)	9.48±3.79
联合用药组	46	42(91.30)*	6.54±4.22*

注:与阿德福韦酯组、拉米夫定组比较,* $P<0.05$

Note: vs. adefovir dipivoxil group and lamivudine group, * $P<0.05$

2.5 各组患者Child-Pugh分级例数比较

联合用药组Child-Pugh A级患者例数显著多于阿德福韦酯组和拉米夫定组,B、C级患者例数显著少于阿德福韦酯组和拉米夫定组,差异均有统计学意义($P<0.05$);但阿德福韦酯组和拉米夫定组两组间比较差异无统计学意义($P>0.05$),详见表5。

表5 各组患者Child-Pugh分级例数比较(例)

Tab 5 Comparison of Child-Pugh grades among groups (case)

组别	n	A级	B级	C级
阿德福韦酯组	48	24	19	5
拉米夫定组	48	27	16	5
联合用药组	46	39*	6*	1*

注:与阿德福韦酯组、拉米夫定组比较,* $P<0.05$

Note: vs. adefovir dipivoxil group and lamivudine group, * $P<0.05$

2.6 不良反应

阿德福韦酯组患者出现4例腹泻,不良反应发生率为8.33%;拉米夫定组患者出现2例呕吐、1例眩晕,不良反应发生率为6.25%;联合用药组患者出现2例腹泻、2例呕吐,不良反应发生率为8.33%。各组患者不良反应发生率比较差异无统计学意义($P>0.05$)。

3 讨论

阿德福韦酯是5-单磷酸脱氧阿糖腺苷的无环核苷类似物,可抑制反转录酶和DNA聚合酶的活性,与腺苷酸竞争性渗入HBV-DNA,并终止病毒DNA的合成,从而发挥强效抗HBV的作用。

拉米夫定为核苷酸类似物,在细胞内被磷酸化后以环腺苷磷酸形式经HBV多聚酶嵌入DNA,从而终止DNA合成。有研究表明,拉米夫定联合阿德福韦酯早期治疗HBV肝硬化,可有效抑制由拉米夫定引起的病毒变异,改善患者肝功能,延长寿命^[4]。

Yim HJ等^[9]研究提示阿德福韦酯治疗慢性乙型肝炎的安

全性较好,可采用定期检测肾功能来指导安全用药。代偿期肝硬化患者可长期应用核苷类药物,而对于失代偿期肝硬化患者使用核苷类药物应慎重。建议临床早期开展抗病毒治疗^[6-7]。

本研究结果显示,治疗后各组患者肝功能指标均显著低于同组治疗前,且联合用药组低于阿德福韦酯组和拉米夫定组,差异均有统计学意义;联合用药组患者总有效率、HBV-DNA阴转率显著高于阿德福韦酯组和拉米夫定组,Child-Pugh A级患者例数显著高于阿德福韦酯组和拉米夫定组,HBV-DNA转阴时间及Child-Pugh B、C级患者例数均显著低于阿德福韦酯组和拉米夫定组,差异均有统计学意义。各组患者不良反应发生率比较差异无统计学意义。

综上所述,拉米夫定联合阿德福韦酯治疗HBV肝硬化较单用拉米夫定或阿德福韦酯疗效更显著,且安全性相似。由于本研究纳入的样本量较小,此结论有待大样本、多中心研究进一步证实。

参考文献

- [1] Tseng PL, Lu SN, Tung HD, et al. Determubabts if early mortality and benefits of lamivudine therapy in patients with hepatitis B virus related decompensated liver cirrhosis[J]. *J Viral Hepa*, 2005, 12(4): 386.
- [2] 中华医学会肝病学会,中华医学会感染病学分会.慢性乙型肝炎防治指南:2010年版[J].中华肝脏病杂志, 2011, 19(1): 13.
- [3] 王恩成,唐琳,王健,等.拉米夫定治疗慢性乙型肝炎YMDD变异研究进展[J].实用医学杂志, 2013, 29(18): 2 937.
- [4] 静艳,王桂良,邱萍,等.阿德福韦酯片与阿德福韦酯胶囊治疗乙型肝炎后肝硬化失代偿期成本:效果分析[J].现代中西医结合杂志, 2013, 22(30): 3 346.
- [5] Yim HJ, Seo YS, Yoon EL, et al. Adding adefovir vs. switching to entecavir for lamivudine: resistant chronic hepatitis B (ACE study): a 2-year follow-up randomized controlled trial[J]. *Liver Int*, 2013, 33(2): 244.
- [6] 褚卫明,那丽颖,黄丽华.拉米夫定联合阿德福韦酯治疗慢性乙型肝炎的临床研究[J].实用医学杂志, 2012, 28(22): 3 815.
- [7] 熊学文.抗乙型病毒性肝炎新药:阿德福韦酯[J].中华现代中西医杂志, 2007, 5(1): 19.

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