C 肝合併 B 肝療法研究登國際期刊，健亞利甘平合併 C 肝口服藥顯優勢

2021 年 12 月 10 日 上午 9:34

【財訊快報／記者何美如報導】由肝病權威陳培哲院士指導，集全台 7 家教學醫院參與抗 B 肝與 C 肝的口服藥物的臨床試驗，由**健亞生技(4130)提供抗 B 肝病毒藥物利甘平(Livepro)**，實驗結果，無搭配服用抗 B 肝藥物有 50%B 肝復發(HBV virologic reactivation)，搭配服用則為 0，結果發表於 CGH 期刊(Clinical Gastroenterology and Hepatology)。 肝病號稱是我國的「國病」，慢性肝病與肝硬化及肝癌是國人健康大敵，盤據國人十大死因數十年，B、C 肝炎的高罹患率更是背後的隱形推手。在台灣，大多數的人是先得到 B 型肝炎之後再感染 C 型肝炎，C 型肝炎病毒活性較強，常常需要先治療 C 型肝炎，但是 C 肝口服藥治療對 B 肝病毒的消滅控制沒有幫助，反而有 B 肝再活化的風險，根據台大內科部劉俊人教授於 2018 年發表的臨床試驗研究報告顯示，約有 8%病人治療 C 肝時，因 ALT 指數升高到超過正常值兩倍，而需治療 B 肝；因此，對於合併 B 肝與 C 肝的治療最適策略，一直是待解決的問題。

一項由肝病權威陳培哲院士指導，臺大內科部暨肝炎研究中心主任劉俊人醫師與成大消化系內科鄭斌男醫師共同主持；在衛福部支持的台灣肝臟疾病臨床試驗合作聯盟下執行，集全台 7 家教學醫院參與，對合併 B 肝、C 肝病人的治療新策略，同時給予抗 B 肝與 C 肝的口服藥物，完成的臨床試驗，其結果剛發表於 CGH 期刊(Clinical Gastroenterology and Hepatology)。該試驗總共收治 56 名合併 B 肝與 C 肝的患者，隨機分為 3 組，在給予 C 肝口服藥 12 周的同時，第一組沒有搭配服用抗 B 肝藥物，第二組及第三組搭配服用 12 周或 24 周的抗 B 肝病毒藥物(利甘平，Livepro；由健亞生技提供)，試驗全程為 72 周。

試驗結果在 C 肝口服藥期間，第一組有 50% B 肝復發(HBV virologic reactivation)，而第二組與第三組為 0。第二、三組則在抗 B 肝藥物停藥 12

周後，可能發生 B 肝復發。該試驗報告結論建議，對於合併 B 型與 C 型肝炎患者，使用 C 肝口服藥時，應搭配抗 B 肝藥物(如利甘平)使用 12 周，可以有效預防 C 肝口服藥治療期間的 B 肝復發，但用藥結束後仍應追蹤注意後續 B 肝復發的風險。此結論亦呼應並證實歐洲肝臟醫學會(EASL)對 B、C 肝合併感染者之治療指引，在治療 C 肝時，要同時服用抗 B 肝藥物預防復發。

陳培哲院士表示，台灣在肝病的創新研究與對患者治療，早已享譽國際，此次結合台灣產官學研資源所完成，針對合併 B 肝與 C 肝病人所設計的療效試驗，再次登上國際期刊，希望在 2025 消除 C 肝的目標與健保署近日取消開立 C 肝口服藥處方科別限制的當下，特別是針對由「國家消除 C 肝辦公室」定義為高風險及中高風險的鄉鎮，如雲林縣、嘉義縣、台南市、高雄市及屏東縣鄉鎮區的執業醫師們，能提供一項實證醫學證據，對 B、C 肝合併感染者做為臨床治療指引。

Clin Gastroenterol Hepatol
2021 Dec 2;S1542-3565(21)01270-2.
doi: 10.1016/j.cgh.2021.11.032. Online ahead of print.

Entecavir prevents HBV reactivation during direct acting antivirals for HCV/HBV dual infection: a randomized trial

Pin-Nan Cheng[1]成大鄭斌男醫師, Chun-Jen Liu[2]臺大劉俊人醫師, Chi-Yi Chen[3]嘉基陳啟益醫師, Kuo-Chih Tseng[4]大林慈濟曾國枝醫師, Ching-Chu Lo[5]聖馬爾定羅清池醫師, Cheng-Yuan Peng[6]中國醫藥彭成元醫師, Chih-Lin Lin[7]北市立聯合林志陵醫師, Hung-Chih Chiu[8]成大邱宏智醫師, Yen-Cheng Chiu[8]成大邱彥程醫師, Pei-Jer Chen[9]陳培哲院士

Affiliations

- [1]Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan. Electronic address: cjliu@ntu.edu.tw.
- [2]Department of Internal Medicine, National Taiwan University Hospital; Hepatitis Research Center, National Taiwan University Hospital; Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine Taipei, Taiwan. Electronic address: pncheng@mail.ncku.edu.tw.
- [3]Department of Internal Medicine, Ditmanson Medical Foundation Chiayi Christian Hospital, Chiayi, Taiwan.
- [4]Division of Gastroenterology, Department of Medicine, Dalin Tzu Chi Hospital, Buddhist Tzu. Chi Medical Foundation, Chia-Yi; School of Medicine, Tzu Chi University, Hualien, Taiwan.
- [5]Department of Internal Medicine, St. Martin de Porres Hospital, Chia-Yi, Taiwan.
- [6]Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan.
- [7]Department of Gastroenterology, Taipei City Hospital, Renai Branch, Taipei, Taiwan.
- [8]Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan.
- [9]Department of Internal Medicine, National Taiwan University Hospital; Hepatitis Research Center, National Taiwan University Hospital; Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine Taipei, Taiwan; Department of Medical Research, National Taiwan University Hospital, Taipei, Taiwan.

Abstract

Background & aims: A strategy to prevent hepatitis B virus (HBV) virologic reactivation (HBVr) and clinical reactivation (CR) during direct acting antiviral (DAA) treatment of hepatitis C virus (HCV)/HBV dual infection remains an unresolved issue.

Methods: Non-cirrhotic patients with dual HCV/HBV infection were enrolled and randomly allocated to one of three groups as 12-week DAA alone (Group 1), 12-week DAA plus 12-week entecavir (Group 2) or 12-week DAA plus 24-week entecavir (Group 3). The entire study duration was 72 weeks. Primary endpoint was the occurrence of HBVr (defined by an increase of HBV DNA level > 10 folds with quantifiable HBV DNA at baseline or presence of HBV DNA with prior unquantifiable HBV DNA) and CR (defined by serum ALT >2 folds upper limit of normal in addition to HBVr).

Results: Fifty-six patients were randomly allocated as 20 patients in Group 1, 16 patients in Group 2, and 20 patients in Group 3. In Group 1, HBV DNA levels rose significantly as early as 4 weeks after initiation of DAA and persisted until end of study. During DAA treatment, HBVr occurred in 50% of Group 1 vs. 0% of Group 2 and 0% of Group 3 ($p<0.001$), whereas the majority of HBVr in Group 2 and Group 3 occurred since 12 weeks following cessation of entecavir (cumulative incidence: 93.8% in Group 2 and 94.7% in Group 3). Three patients (5.4%; one in each group) exhibited CR at week 48 and did not receive entecavir treatment.

Conclusions: A 12-week entecavir is suggested to co-administer with DAA for HCV/HBV dually infected patients.