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# Relationship between activity of nitric oxide synthase and pathogenesis of essential hypertension in local vascular tissue

Chen Yu, Liu Guangyao (Department of Cardiology, Daping Hospital, Third Military Medical University, Chongqing, 400042)

**Abstract** Objective: To explore the role of the activity of nitric oxide synthase (NOS) in pathogenesis of essential hypertension (EH) in the regulative process of local vascular tension. Methods: 18 patients undergoing abdominal operation were selected. Of the patients, 9 were hypertensive and 9 normotensive (NT). Specimen of the mesenteric artery in all the patients was extracted to determine NOS activity in local vascular wall in vitro. After digestion, the culture of vascular smooth muscle cells (VSMCs) of the isolated mesenteric artery was conducted with the induction of interleukin-1 (IL-1) and intervention of NG-monomethy-L-arginine (L-NMMA) to determine the levels of NO and endothelin-1 (ET-1) in the supernatant. Results: NOS activity in local vascular tissue was lower in hypertensive patients than in NT ones. $NO_2$ level in supernatant of cultured VSMCs was lower in hypertensive patients than in NT ones. After the induction with IL-1, the $NO_2$ level was increased in both kinds of patients but still lower in hypertensive patients than in NT ones. After intervention with L-NMMA, the level of ET-1 was increased in both kinds of patients. Conclusion: The increased vascular tension resistance in patients with EH might be related to the decrease of NOS activity and increase of ET level in local vascular tissue.

**Key words** essential hypertension; nitric oxide synthase

# 肝硬变大鼠肝部分切除术后肝细胞再生机理的实验研究

# An experimental study on the mechanism of liver regeneration after partial hepatectomy in cirrhotic rats

陈 平* 韩本立 (第三军医大学附属西南医院肝胆外科中心) 重庆, 400038

弥漫性肝损害如在肝硬变情况下,广泛肝切除术常常引起手术后肝功能衰竭。病人肝脏基础的好坏,决定病人的预后,随着肝脏基础病变的加重,其手术死亡率增高。肝硬变状态下,肝细胞再生功能会发生变,影响细胞的增殖。因此了解肝细胞再生机制对于有效地防治术后肝功能衰竭,更大程度地发挥肝部分切除术的作用,有非常重要的意义,同时可以通过过对肝细胞再生机理的研究,为更好地防治术后肝功能衰竭寻找新的治疗方法和手段。

用健康雄性 Wistar大鼠,体重220~250 g用于本实验,大鼠肝硬变模型参照吴孟超的方法,即皮下注射 $CCl_4$+口服乙醇的方法;肝部分切除术参照 Higgin的方法,即切除大鼠左肝和中肝,观察时相为大鼠术后6、24、48、72 h和1周。

本实验的主要结果和结论如下:① 采用在 $CCl_4$诱导肝硬变的大鼠模型,切除大鼠左肝和中肝叶,能很好的诱导肝细胞再生。模型制作所需时间短,死亡率低,手术耐受性好。② 肝硬变大鼠肝部分切除术后肝再生过程出现明显变化,肝细胞再生启动时间和再生周期明显延长,增殖速度减慢,这可能是术后肝功能衰竭的重要原因,提示肝切除术后肝功能衰竭与残肝细胞再生能力之间有密切的关系。③ KC在肝细胞再生过程中发挥重要作用,KC再生的启动为肝细胞增殖创造了条件。KC能被 LPS活化,但活化后对肝细胞再生产生不同的效应。④ HGF、TGF-α、EGF和 TNF等细胞因子是肝细胞再生启动的信号,通过与相应的受体结合,引起 NORs相关蛋白的变化,改变 rRNA基因活性,从而诱导肝细胞再生,这些细胞因子可作为肝细胞再生状况的标志。TGF-α、EGF等在再生过程中含量的变化,可能与再生的能力有关。⑤ HGF和 TGF-α mRNA表达与肝硬变大鼠的肝细胞再生密切相关,而 TGF-α是肝细胞再生中最重要的物质。IGFBP-1s mRNA表达降低反应了肝硬变大鼠术后肝细胞代谢明显受损,而 PCNA mRNA表达可提示肝细胞增多殖能力。在肝细胞再生过程中,细胞因子相互作用,共同推动肝细胞再生,细胞因子作为诱导细胞 DNA合成的基本刺激信号。⑥ 肝细胞增殖不仅受细胞因子的影响,更受细胞周期蛋白的调控。肝细胞在生长因子的刺激之下,使 Cyclin D和 Cyclin A在 $G_1$期适量的表达,从而启动肝细胞再生。Cyclin和 RB等癌基因产物共同作用,调节细胞周期的进程。⑦ 肝细胞可通过 RB蛋白影响 Cyclin功能的活性,从而调节肝细胞再生;而肝细胞再生过程中,TGF-β的高表达将促使肝细胞 p27的活化,从而抑制肝细胞再生。

关键词 肝再生;肝硬变;细胞周期;细胞因子;肝部分切除术;大鼠

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(编辑 王红)

* 陈 平 男,33岁,主治医师,讲师,博士研究生

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