

## 中医药防治原发性肝癌的困境与出路

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### Traditional Chinese medicine in prevention and treatment of primary liver cancer: Research dilemmas and possible ways out

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### Abstract

Primary liver cancer is one of the most common malignant tumors worldwide. The two leading types of treatment based on Western medicine are local and systemic therapies, which still cannot meet the needs of good effect. Traditional Chinese medicine (TCM) has unique advantages in the prevention and treatment of primary liver cancer and has achieved good clinical efficacy, but the scientific research is still far from satisfaction. This article will discuss the problems faced by TCM in the prevention and treatment of primary liver cancer and the possible solutions, with regard to the role of TCM in different stages of liver cancer, the preventive and therapeutic mechanisms of TCM, and the dosage form and administration route, with an aim to improve TCM research and therapy in primary liver cancer.

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**Key Words:** Liver cancer; Traditional Chinese medicine; Prevention; Treatment

### 背景资料

中医药在我国原发性肝癌的防治中发挥着不可替代的作用,可延长患者的生存期、提高患者生存质量,但在临床治疗中存在一些问题。为进一步提高中医药的疗效,迫切需要了解中医药防治原发性肝癌的困难以及解决的方案。

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## ■ 研发前沿

中医药防治原发性肝癌存在许多问题,如治疗原发性肝癌的作用机制不明、中医药的给药方式致患者依从性差,如何解决这些问题成为中医药防治原发性肝癌的瓶颈,有待于进一步探索其解决方案。

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## 摘要

原发性肝癌是世界上最常见恶性肿瘤之一,西医学目前以局部治疗和全身治疗为主,但疗效仍存在局限性。中医药在临床防治原发性肝癌方面具有独特优势,但在科学研究方面仍有诸多不足。本文从中医药在防治原发性肝癌不同阶段中的作用、防治原发性肝癌的作用机制、中药剂型和给药途径等3个方面阐述了中医药在原发性肝癌防治研究中存在的问题和解决方案,以期对原发性肝癌的科学研究及临床疗效改善提供一定参考。

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关键词: 原发性肝癌; 中医药; 预防; 治疗

**核心提要:** 根据原发性肝癌不同阶段特点采取不同的中医药治则、研究中医药防治原发性肝癌的作用机制和中医药剂型及给药途径的改革等3个方面阐述中医药防治原发性肝癌的困境和出路。

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## 0 引言

原发性肝癌是我国癌症死亡的第三大原因,其5年生存率不超过50%,目前西医治疗方法以局部治疗和全身治疗为主<sup>[1]</sup>。由于肝癌起病隐匿,症状、体征出现较晚,就诊时往往已属中晚期,错失局部治疗机会。全身治疗主要包括放疗、化疗及靶向治疗,但肝癌对放化疗不敏感,靶向药物价格昂贵,且治疗后期会产生耐药性,仅能延长患者数月存活期<sup>[2]</sup>。中医学自《黄帝内经》就有关于包括肝癌的各种肿瘤认识,至宋代《卫济宝书》首先出现“癌”字,宋代《圣济总录》将积聚、癥瘕统称为“瘤”,形成了以扶正祛邪为主线的治法。大量的临床实践表明,中医药治疗肝癌可取得延

长生存期、提高生存质量等较好疗效<sup>[3-5]</sup>。但中医药在参与肝癌防治研究过程中还有许多问题值得引起重视。

## 1 明确中医药在肝癌防治不同阶段中的作用

目前中医药防治肝癌,虽然强调基于中医基础理论,辨证施治,但没有明确可行的诊疗规范。随着现代医学的发展,中医不能无视西医疗疗肝癌的理念及有效方法,仍故步自封,沉浸在自己所谓的“辨证不辨病”中。西医学根据巴塞罗那临床肝癌(Basel Clinic Liver Cancer, BCLC)标准不同分期,治疗原则、方法和目的是不同的。实际上在肝癌防治的不同阶段中医药能发挥的作用也是不一样的,这方面具体规范化十分必要。比如在BCLC 0期(极早期)时,肝癌治疗首选手术切除,在BCLC A期(早期)时,肝移植或消融术为首选<sup>[6]</sup>,手术和消融均属于根治疗法。在此两期,中医药可以起辅助作用,在术后促进患者康复以及防止肝癌复发转移是主要目的,治疗以“扶正为主,祛邪为辅”为原则。扶正可辨证运用滋阴补肾、养血柔肝、健脾益气等治法,祛邪以清热解毒为用。在BCLC B期(中期)时,西医治疗以经导管动脉化疗栓塞(transcatheter arterial chemoembolization, TACE)为主,有门脉侵犯的C期(晚期)则推荐目前唯一靶向药索拉非尼,此两期的治疗为姑息疗法<sup>[6]</sup>。中医药在此阶段,应以控制肿瘤进展为目的。治疗以“驱邪为重,扶正为辅”为原则。祛邪以软坚散结、解毒通络为主,扶正以健脾和胃、扶助胃气为要。在BCLC D期(终末期),此时西医治疗原则为对症治疗,并无具体针对肿瘤的治疗措施<sup>[6]</sup>。而中医药对此期的治疗价值尤为凸显。被划分为终末期的患者其实可分成两大类:一类为肝内病灶较小或相对局限,且无远处转移,但因为肝功能较差,Child-Pugh分级为C级,因其他慢性疾病或年迈体弱等因素,体力状况(performance status, PS)评分>2分,对此类患者,中医药治疗目的为改善肝脏功能及全身情况,重新分期后争取有效的局部治疗以更好控制肿瘤进展。治疗还是以“扶正为主,祛邪为辅”;另一类患者肝内病灶体积巨大或者多发,有其他器官转移等情况,加之肝功能及PS差,已属不治阶段,对此类患者,治疗目标是减轻或缓解病痛,维持患者的生命。多数患者已难以耐受口服中药

## ■ 创新盘点

本文从3个方面阐述了中医药防治原发性肝癌的困境和出路,可以更深入的了解中医药因人因时制宜的特点、进一步探索中医药防治原发性肝癌的作用机制及方法、通过纳米技术等先进工艺进一步改进中医药的剂型和途径以提高中医药的疗效并减少不良反应。

汤剂, 可适当试用外治法以减轻患者痛苦, 如针灸、中药穴位敷贴等方法。

## 2 加强中医药防治肝癌的作用机制研究

临床上, 我们确实发现中医药能够提高肝癌综合治疗的效果<sup>[7-16]</sup>, 比如, 有些中药有抗肿瘤作用, 有些中药能在不同程度上减轻化疗药物的不良反应, 有些则能提高和调整机体免疫机能。中医药的具体作用机制尚不明晰, 在哪些环节有效, 为什么有效, 有效的作用成分是什么, 有效的作用剂量是多少? 这些问题并不能阐释清楚, 这严重阻碍了国际同行对中医药的认识、理解和接受。因此, 这种局面亟需中医学界探索抗肝癌中医药的具体作用靶点及机制, 以期广泛运用和发展。结合现代研究方法, 我们可以从以下几个方面入手开展中医药研究。第一, 从肝癌的经典信号通路入手, 借助药物筛选平台, 针对通路中的重要靶点分子, 可以筛选出一系列对某条信号通路有作用的中药, 再围绕这些中药开展进一步抗肿瘤机制及功能研究; 第二, 针对某些临床上发现的有较好抗肿瘤疗效的药物, 可首先在一系列肝肿瘤细胞系中证实功能, 分别提取蛋白或RNA做分子高通量筛选, 比如蛋白质谱检测或信号通路芯片, 来发现差异分子靶点, 再作具体信号通路分析。在此基础上, 还可以具体分析药物中有作用的单体, 深入探究抗肿瘤机制; 第三, 肿瘤免疫目前越来越受到重视<sup>[17,18]</sup>, 中医药对改善机体内环境, 尤其重塑肿瘤相关的微环境有着一定优势。研究中药干预肿瘤免疫微环境, 从整体多维的角度观察分析肿瘤微环境与中医药调控免疫的关系具有重要的临床意义。研究可以从中药对肿瘤微环境中炎性信号通路的干预, 调节改善M1/M2表型巨噬细胞、Fas/FasL、细胞毒性T淋巴细胞/调节性T细胞、树突状细胞/DCreg等双向免疫功能细胞的作用入手<sup>[13,19-22]</sup>。

## 3 促进中药剂型及给药途径改革

目前, 有关中药治疗肝癌有效的报道多数仍停留在方药的水平上, 随着时代发展及生活节奏的改变, 传统汤剂有使用不便的缺点, 且给临床疗效的重复验证也带来了不确定性。虽然目前有一些抗肿瘤中成药的静脉制剂, 但还存在疗效有限, 易致敏等临床问题。因此, 为促进中医药在肝癌防治研究中的作用及地位得到进一步提高, 应将药物靶向新技术应用于中药的

研究和开发。肝癌因其特有的生物学特性, 对局部治疗(如射频、微波、TACE等)效果优于全身治疗(化疗、放疗等)<sup>[6]</sup>, 因此通过提高药物在瘤体局部浓度, 延长其作用时间, 减少不良反应, 有效杀灭肿瘤细胞的靶向治疗, 已成为目前肝癌治疗的重要研究方向<sup>[23-25]</sup>。在明确中药药效物质的基础上, 通过对中药进行修饰, 如制成不同粒径大小的微粒, 表面连接配体或受体等, 使其具有主动或被动靶向肝癌病灶作用, 可以解决抗癌中药难以在肝癌组织中达到有效浓度的难题<sup>[26-29]</sup>。以纳米微粒或微球作为中药载体, 可以达到药物缓释目的<sup>[30]</sup>; 还可以将中药进一步加工制成针剂、片剂、贴剂等, 使中药以微粒的形式进入体内, 提高体内抗癌药物血药浓度, 从而提高中药抗肝癌效果; 且靶向制剂能在肝肿瘤组织周围很快达到所需药物浓度, 从而降低药物剂量, 减少不良反应, 提高生物利用度<sup>[29]</sup>。因此中药靶向治疗是肝癌治疗值得研究的方向之一。

## 4 结论

中医药在预防肝癌发生、减少复发、减轻痛苦、提高生存质量、延长生存期等方面有着独特的作用, 但尚缺乏完善的诊治体系及研究方法, 许多潜在的优势未能发挥, 且不能得到国际认可及推广。我们需要走中西医结合道路, 抓住肝癌现代研究的前沿, 紧密结合中医基本理论, 大胆摸索, 反复实践, 使中医药防治肝癌的潜在优势得到充分发挥, 从而对人类防治肝癌整体水平的提高起到积极的推动作用。

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## 应用要点

本文旨在通过总结中医药防治原发性肝癌所存在的问题, 探讨其解决方案。



## ■ 名词解释

纳米中药: 指运用纳米技术, 将中药的有效成分或部位负载到用高分子材料制造的直径 $<100\text{ nm}$ 的纳米微球上或微囊内, 有效控制药物以最适合的速度和给药量在特定部位释放。

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#### 同行评价

本文结合中医药防治原发性肝癌的临床研究实践, 阐述了中医药在防治原发性肝癌过程中的一些问题, 提出了一些解决方法, 值得临床进一步研究证实。

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• 消息 •

## 《世界华人消化杂志》栏目设置

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