

二甲双胍与肿瘤相关性的新观点与挑战

《现代肿瘤医学》[ISSN:1672-4992/CN:61-1415/R] 期数: 2020年03期 页码: 486-489 栏目: 综述 出版日期: 2019-12-26

Title: New ideas and challenges on the correlation between metformin and tumor

作者: 李璞; 乔虹

哈尔滨医科大学第二附属医院内分泌科, 黑龙江 哈尔滨 150086

Author(s): Li Pu; Qiao Hong

Department of Endocrinology, the Second Affiliated Hospital of Harbin Medical University, Heilongjiang Harbin 150086, China.

关键词: 二甲双胍; 糖尿病; 癌症; 肿瘤; 化疗; 防治; 预后

Keywords: metformin; diabetes mellitus; cancer; tumour; chemotherapeutic; prevention and treatment; prognosis

分类号: R730.5

DOI: 10.3969/j.issn.1672-4992.2020.03.032

文献标识码: A

摘要: 2型糖尿病 (T2DM) 是一种慢性疾病, 在全球范围内迅速增长, 它是各类癌症的重要风险因素。而二甲双胍是治疗 T2DM最常用的处方药。通过流行病学和临床研究表明, 使用二甲双胍可以降低T2DM患者的癌症风险, 改善癌症患者的预后和生存率。此外, 二甲双胍在癌症治疗中的临床试验正在扩大到非糖尿病人群。越来越多的研究者认为二甲双胍将会成为癌症预防和治疗的有吸引力的候选药物。在这里, 我们总结了近年来二甲双胍在肿瘤预防与治疗中的流行病学证据与相关研究进展、二甲双胍的抗肿瘤机制, 并探讨了提高二甲双胍对肿瘤的敏感性和预防肿瘤转移的可能性。

Abstract: Type 2 diabetes mellitus (T2DM) is a chronic disease, and it is rapidly growing in worldwide and is an important risk factor for various types of cancer. Metformin is the most commonly prescribed drug for type 2 diabetes mellitus. Epidemiological and clinical observation studies have shown that metformin use reduces risk of cancer in patients with type 2 diabetes mellitus and improves prognosis and survival rate of the cancer patients. Furthermore, ongoing clinical trials of metformin in cancer therapy are extending to nondiabetic population. A growing number of researchers believe that metformin will become an attractive candidate for cancer prevention and treatment. This review summarizes recent epidemiological evidence and progress in studies of metformin use in cancer, mechanism of metformin's anticancer effect and discusses the possibility to enhance its sensitivity to tumors and to prevent cancer metastasis.

参考文献/REFERENCES

- [1] Pernicova I, Korbonits M. Metformin-mode of action and clinical implications for diabetes and cancer [J]. *Nat Rev Endocrinol*, 2014, 10(3): 143-156.
- [2] Evans JM, Donnelly LA, Emslie-Smith AM, et al. Metformin and reduced risk of cancer in diabetic patients [J]. *BMJ*, 2005, 330(7503): 1304-1305.
- [3] Lu MZ, Li DY, Wang XF. Effect of metformin use on the risk and prognosis of ovarian cancer: An updated systematic review and meta-analysis [J]. *Panminerva Med*, 2019, 18(1): 364-367.
- [4] Morales DR, Morris AD. Metformin in cancer treatment and prevention [J]. *Annual Review of Medicine*, 2015, 66(1): 17-29.
- [5] Chu D, Wu J, Wang K, et al. Effect of metformin use on the risk and prognosis of endometrial cancer: A systematic review and meta-analysis [J]. *BMC Cancer*, 2018, 18(1). doi:10.1186/s12885-018-4334-5.
- [6] Gandini S, Puntoni M, Heckman-Stoddard BM, et al. Metformin and cancer risk and mortality: A systematic review and meta-analysis taking into account biases and confounders [J]. *Cancer Prev Res (Phila)*, 2014, 7(9): 867-885.
- [7] Parikh AB, Kozuch P, Rohs N, et al. Metformin as a repurposed therapy in advanced non-small cell lung cancer (NSCLC): Results of a phase II trial [J]. *Invest New Drugs*, 2017(35): 813-819.
- [8] Miranda VC, Braghieri MI, Faria LD, et al. Phase 2 trial of metformin combined with 5-Fluorouracil in patients with refractory metastatic colorectal cancer [J]. *Clin Colorectal Cancer*, 2016, 15(4): 321-328.
- [9] Sivalingam VN, Kitson S, McVey R, et al. Measuring the biological effect of presurgical metformin treatment in endometrial cancer [J]. *Br J Cancer*, 2016, 114(3): 281-289.

- [10] Martinez JA, Chalasani P, Thomson CA, et al. Phase II study of metformin for reduction of obesity-associated breast cancer risk: A randomized controlled trial protocol [J]. *BMC Cancer*, 2016(16): 500.
- [11] Cai D, Sun H, Qi Y, et al. Insulin-like growth factor 1/mammalian target of rapamycin and AMP-activated protein kinase signaling involved in the effects of metformin in the human endometrial cancer [J]. *Gynecol Cancer*, 2016, 26(9): 1667-1672.
- [12] Qian W, Li J, Chen K, et al. Metformin suppresses tumor angiogenesis and enhances the chemosensitivity of gemcitabine in a genetically engineered mouse model of pancreatic cancer [J]. *Life Sci*, 2018, S0024-3205(18): 30432-30436.
- [13] Li L, Jiang L. Combination of metformin and gefitinib as first-line therapy for non-diabetic advanced NSCLC patients with EGFR mutations: A randomized, double-blind phase 2 trial [J]. *Clin Cancer Res*, 2019(19): 0437-0439.
- [14] Wenxiu X, Xiaowei Z, Haiying D, et al. Impact of metformin use on survival outcomes in non-small cell lung cancer treated with platinum [J]. *Medicine*, 2018, 97(51).doi:10.1097/MD.00000000000013652.
- [15] Zhang J, Wu J. The prognostic value of metformin for advanced non-small cell lung cancer: A systematic review and meta-analysis [J]. *Transl Lung Cancer*, 2018, 7(3): 389-396.
- [16] Hirsch HA, Iliopoulos D, Tsihchlis PN, et al. Metformin selectively targets cancer stem cells, and acts together with chemotherapy to block tumor growth and prolong remission [J]. *Cancer Research*, 2009, 69(19): 7507-7511.
- [17] Zhao Z, Cheng X, Wang Y, et al. Metformin inhibits the IL-6-induced epithelial-mesenchymal transition and lung adenocarcinoma growth and metastasis [J]. *PLOS ONE*, 2014:9.
- [18] Zhang J, Shen C, Wang L, et al. Metformin inhibits epithelial-mesenchymal transition in prostate cancer cells: Involvement of the tumor suppressor miR30a and its target gene SOX4 [J]. *Biochemical and Biophysical Research Communications*, 2014, 452(3): 746-752.
- [19] Duque JE, Cruz N, Samudio I, et al. Antitumor mechanisms of metformin: Signaling, metabolism, immunity and beyond [J]. *Universitas Scientiarum*, 2010, 15(2): 122-129.
- [20] Lei Y, Yi Y, Liu Y, et al. Metformin targets multiple signaling pathways in cancer [J]. *Chin J Cancer*, 2017, 36(1): 17.
- [21] Abo-Elmatty DM, Ahmed EA, Tawfk MK, et al. Increased soluble CD155 in the serum of cancer patients [J]. *Plos One*, 2016, 11(4): e0152982.
- [22] Luengo A, Sullivan LB, Heiden MG. Understanding the complexity of metformin action: limiting mitochondrial respiration to improve cancer therapy [J]. *BMC Biology*, 2014, 12(1): 82.
- [23] Levy A, Doyen J. Metformin for non-small cell lung cancer patients: Opportunities and pitfalls [J]. *Crit Rev Oncol Hematol*, 2018(125): 41-47.
- [24] Eikawa S, Nishida M, Mizukami S, et al. Immune-mediated antitumor effect by type 2 diabetes drug, metformin [J]. *Proc Natl Acad Sci USA*, 2015, 112(6): 1809-1814.
- [25] Dagan M, Dufay Wojcicki A, d'Hayer B, et al. Metformin: An anti-diabetic drug to fight cancer [J]. *Pharmacol Res*, 2016, 113(Pt A): 675-685.
- [26] Shackelford D, Abt E, Gerken L, et al. LKB1 inactivation dictates therapeutic response of non-small cell lung cancer to the metabolism drug phenformin [J]. *Cancer Cell*, 2013, 23(2): 143-158.
- [27] Birsoy K, Possemato R, Lorbeer FK, et al. Metabolic determinants of cancer cell sensitivity to glucose limitation and biguanides [J]. *Nature*, 2014, 508(7494): 108-112.
- [28] Kuo CL, Hsieh Li SM. The antitumor properties of metformin and phenformin reflect their ability to inhibit the actions of differentiated embryo chondrocyte [J]. *Cancer Manag*, 2019, 15(11): 6567-6579.
- [29] Liu C, Wang F, Fan QX, et al. Advances of clinical trials of metformin in antitumor therapy [J]. *Chin J Clin Oncol*, 2018, 45(20): 189-193.
- [30] Yang C, Zhao N. Metformin improves the sensitivity of ovarian cancer cells to chemotherapeutic agents [J]. *Oncol Lett*, 2019, 18(3): 2404-2411.
- [31] Meireles CG, Pereira SA, Valadares LP, et al. Effects of metformin on endometrial cancer: Systematic review and meta-analysis [J]. *Gynecol Oncol*, 2017, 147(1): 167-180.

备注/Memo: National Natural Science Foundation of China(No.81673108, 81872560);国家自然科学基金资助项目(编号: 81673108, 81872560)

更新日期/Last Update: 1900-01-01