DOI:10.31557/APJCB.2019.4.4.69

EDITORIAL

Cancer and Opium Addiction

Hossein Ghahremani[1], Alireza Mosavi Jarrahi[2,3], Siamak Salami[1]

[1]Department of Clinical Biochemistry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [2]Department of Social Medicine, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [3]Cancer Research Center, Cancer Institute of Iran.

Asian Pac J Cancer Biol, **4 (4)**, 69-70

Submission Date: 08/28/2019 Acceptance Date: 11/08/2019

Introduction

Drug abuse remains a serious health and social threat in the world. According to the United Nations Office of Drugs and Crime (UNODC) 1n 2010, an estimated 16.5 million people use opium or its derivatives illicitly [1]. Meanwhile, Iran has the first rank in the prevalence of opium consumption [2], and Opium is the most commonly abused drug in Iran. Opium is the air-dried extract obtained from the seed capsules of the opium poppy, which is used for recreational or medical purposes in different parts of the world [3]. Approximately 8 to 14 percent of opium is made up of morphine, which is processed chemically to produce heroin and other synthetic opioids for medicinal use and also for drug abuse [4].

Epidemiological studies indicated that there is a positive association between opium addiction and higher risk of cancers of the pancreas [5], oral cavity [6-7] esophagus [8-9], stomach [10-11], lung [12-13] larynx [14], and bladder [15-17].

Several mechanisms have been suggested for the opium-induced development of different cancers. In addition to its addictive properties, several mutagenic compounds in opium and its pyrolyzed derivatives have been identified, all containing a hydroxy-phenanthrene moiety [18], hence opium possesses genotoxic or carcinogenic properties [19]. Mutagenicity of pyrolysis-derived nitrogen containing heterocyclic components of opium has been proved by observation of the sister chromatid exchanges in CHO cells and human peripheral blood lymphocytes [20]. Also, opium dross displayed mutagenic activity in Ames test using Salmonella typhimurium strains TA98 and TA100 in the presence of rat liver microsomes [21] and caused frameshift mutations in Salmonella typhimurium strains TA1538 and TA98 after metabolic activation [22]. Morphine, as the most prevalent and important alkaloid in opium, has also been associated with carcinogenesis via increasing the methylation of DNA through the reduction of N-nitrosamines and N-nitrosodimethylamine through liver clearance [15-23].

In addition to the genotoxic effects, the opium derivatives have inhibitory effects on different aspects of tumorigenesis, including angiogenesis, proliferation, migration and Epithelial-Mesenchymal Transition (EMT)[5]. For example, it has been shown that morphine stimulates angiogenesis by activating proangiogenic and survival-promoting signaling and promotes breast tumor growth in mouse models [24]. Besides, the Mu opioid receptor promotes opioid induced proliferation, migration and EMT in human lung cancer [25]. Similarly, downregulation of the opioid receptor can inhibit both in vivo and in vitro human liver cancer progress via an increase of the apoptotic rate and stimulate JNK activation [26].

Another mechanism proposed for the opium-induced cancer development is the contamination of opium with toxic heavy metals due to adulteration during the opium preparation. Presence of heavy and toxic metals such as lead and arsenic in opium and thallium in heroin samples as impurities and adulteration has been reported from some countries. Specifically, lead poisoning in opium addicts has been reported from Iran [27]. Indeed, opium consumers had higher blood lead levels [28].

There are some limitations to those mechanistic studies which could be summarised as: First, the reports have been mainly segregated to middle esat, particularly Iran. Although it stem from geographical proximity to cultivation area of opium, but results from other countries could fortify the current findings. Second, controversies in some fininding motivates further studies to clarify the direct relationship between opium consumption and cancer. Third, the dose of usage, the administration route, and also the duration of opium addiction might be critical factors that need to be taken into attention. Finally, although some studies have been done on the

Corresponding Author:
Dr. Siamak Salami
Department of Clinical Biochemistry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Email: salami.si@gmail.com

morphine-induced carcinogenesis, most of the mechanistic studies have used pyrolyzed opium, isolation of opium derivatives and elucidation of their association with cancer have been remained for further research.

References

1. Drugs UNOo, Crime. World drug report 2010: United Nations Publications; 2010.
2. Afarinesh MR, Haghpanah T, Divsalar K, Dehyadegary E, Shaikh-Aleslami A, Mahmoodi M. Changes in serum biochemical factors associated with opium addiction after addiction desertion. Addiction & health. 2014;6(3-4):138.
3. Alzaidi MA, Arab HA, Amanpour S, Shirkoohi R, Muhammadnejad S, Sasani F. Opium Consumption and the Incidence of Cancer: Does Opium Account as an Emerging Risk Factor for Gastrointestinal Cancer? Journal of gastrointestinal cancer. 2018;49(2):172-80.
4. Kapoor L. Opium poppy: botany, chemistry, and pharmacology: CRC Press; 1995.
5. Moossavi S, Mohamadnejad M, Pourshams A, Poustchi H, Islami F, Sharafkhah M, et al. Opium use and risk of pancreatic cancer: a prospective cohort study. Cancer Epidemiology and Prevention Biomarkers. 2018;27(3):268-73.
6. Lyons D, Yazdi I. The carcinogenic potentials of'opium smoker's tongue'. Journal of oral medicine. 1969;24(3):67-72.
7. Fahmy MS, Sadeghi A, Behmard S. Epidemiologic study of oral cancer in Fars Province, Iran. Community dentistry and oral epidemiology. 1983;11(1):50-8.
8. Nasrollahzadeh D, Kamangar F, Aghcheli K, Sotoudeh M, Islami F, Abnet C, et al. Opium, tobacco, and alcohol use in relation to oesophageal squamous cell carcinoma in a high-risk area of Iran. British journal of cancer. 2008;98(11):1857-63.
9. Malekzadeh MM, Khademi H, Pourshams A, Etemadi A, Poustchi H, Bagheri M, et al. Opium Use and Risk of Mortality from Digestive Diseases--A Prospective Cohort Study. The American journal of gastroenterology. 2013;108(11):1757.
10. Shakeri R, Malekzadeh R, Etemadi A, Nasrollahzadeh D, Aghcheli K, Sotoudeh M, et al. Opium: an emerging risk factor for gastric adenocarcinoma. International journal of cancer. 2013;133(2):455-61.
11. Sadjadi A, Derakhshan MH, Yazdanbod A, Boreiri M, Parsaeian M, Babaei M, et al. Neglected role of hookah and opium in gastric carcinogenesis: a cohort study on risk factors and attributable fractions. International journal of cancer. 2014;134(1):181-8.
12. Masjedi MR, Naghan PA, Taslimi S, Yousefifard M, Ebrahimi SM, Khosravi A, et al. Opium could be considered an independent risk factor for lung cancer: a case-control study. Respiration. 2013;85(2):112-8.
13. MacLennan R, Da Costa J, Day N, Law CH, Ng Y, Shanmugaratnam K. Risk factors for lung cancer in Singapore Chinese, a population with high female incidence rates. International journal of cancer. 1977;20(6):854-60.
14. Mousavi MRA, Damghani MA, Haghdoust AA, Khamesipour A. Opium and risk of laryngeal cancer. The Laryngoscope. 2003;113(11):1939-43.
15. Hosseini SY, Safarinejad MR, Amini E, Hooshyar H, editors. Opium consumption and risk of bladder cancer: a case-control analysis. Urologic Oncology: Seminars and Original Investigations; 2010: Elsevier.
16. Karbakhsh M, Dabbagh N, Shabani A, Tabibi A, Akhavizadegan H. Age at diagnosis in bladder cancer: does opium addiction play a role? Asian Pacific Journal of Cancer Prevention. 2013;14(8):4723-5.
17. Aliasgari M, Kaviani A, Gachkar L, Hosseini-Nassab S. Is bladder cancer more common among opium addicts? Urology journal. 2009;1(4):253-5.
18. Friesen M, O'neill I, Malaveille C, Garren L, Hautefeuille A, Cabral J, et al. Characterization and identification of 6 mutagens in opium pyrolysates implicated in oesophagel cancer in Iran. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis. 1985;150(1-2):177-91.
19. Li J-H, Lin L-F. Genetic toxicology of abused drugs: a brief review. Mutagenesis. 1998;13(6):557-65.
20. Perry P, Thomson E, Day N, Bartsch H. Induction of SCE by opium pyrolysates in CHO cells and human peripheral blood lymphocytes. Carcinogenesis. 1983;4(2):227-30.
21. Hewer T, Rose E, Ghadirian P, Castegnaro M, Malaveille C, Bartsch H, et al. Ingested mutagens from opium and tobacco pyrolysis products and cancer of the oesophagus. The Lancet. 1978;312(8088):494-6.
22. Malaveille C, Friesen M, Camus A-M, Garren L, Hautefeuille A, Bereziat J-C, et al. Mutagens produced by the pyrolysis of opium and its alkaloids as possible risk factors in cancer of the bladder and oesophagus. Carcinogenesis. 1982;3(5):577-85.
23. Ribeiro Pinto LF SP. Opium and oesophageal cancer: effect of morphine and opium on the metabolism of N-nitrosodimethylamine and N-nitrosodiethylamine in the rat. Carcinogenesis 1997;18:365–9.
24. Gupta K, Kshirsagar S, Chang L, Schwartz R, Law P-Y, Yee D, et al. Morphine stimulates angiogenesis by activating proangiogenic and survival-promoting signaling and promotes breast tumor growth. Cancer research. 2002;62(15):4491-8.
25. Lennon FE, Mirzapoiazova T, Mambetsariev B, Poroyko VA, Salgia R, Moss J, et al. The Mu opioid receptor promotes opioid and growth factor-induced proliferation, migration and Epithelial Mesenchymal Transition (EMT) in human lung cancer. PloS one. 2014;9(3).
26. Lu J, Liu Z, Zhao L, Tian H, Liu X, Yuan C. In vivo and in vitro inhibition of human liver cancer progress by downregulation of the μ-opioid receptor and relevant mechanisms. Oncology reports. 2013;30(4):1731-8.
27. Soltaninejad K, Shadnia S. Lead poisoning in opium abuser in Iran: A systematic review. International journal of preventive medicine. 2018;9.
28. Salehi H, SAYADI AAR, Tashakori M, YAZDAN DR, Soltanpour N, Sadeghi H, et al. Comparison of serum lead level in oral opium addicts with healthy control group. 2009.