Cancer and Opium Addiction

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Introduction

Drug abuse remains a serious health and social threat in the world. According to the United Nations Office of Drugs and Crime (UNODC) in 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 east, 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
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.

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