

Novel Protocol of Opium Tincture Oral Usage in Two Cases with Chronic Myeloid Leukemia and Hodgkin Lymphoma

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ABSTRACT

We report two cases of chronic myeloid leukemia (CML). The first patient was a 40-year-old man who presented with a prolonged history of upper abdominal discomfort, anorexia, and with fever. Examination revealed moderate hepatosplenomegaly. Examinations showed that he was found to have leucocytosis with moderate anemia. Given the leucocytosis, he was investigated for CML and found to be positive for BCR-ABL by Real-time PCR. He received imatinib 400 mg/day and achieved a complete hematological response at the end of 3 months. The second patient was a 40-year-old male diagnosed with Hodgkin lymphoma based on a Lymph node biopsy. He completed five cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) chemotherapy. Both patients were previously addicted to opium and before the cancer diagnosis, these patients were successfully treated for their addiction with a new method of using opium tincture called Dezhakam step time (DST). After the diagnosis of cancer, both patients were treated with opium tincture using a new protocol of taper up-off that took about 11 months. Both patients showed significant clinical improvement along with a dramatic reduction of pain and no craving or dependence symptoms during and after the treatment.

Keywords: Opium tincture, Chronic myeloid leukemia, Hodgkin lymphoma

ABBREVIATIONS

CML: Chronic myeloid leukemia

ODD: opioid use disorder

DST: Dezhakam step time

INTRODUCTION

Leukemia is a group of hematologic disorders that affect the blood and bone marrow and is characterized by predominant clonal proliferation, and suppression of normal cell development [1]. Leukemia has been classified as acute or chronic based on the proliferation rate of leukemic cells in blood and bone marrow, and based on the predominant cells that have been involved, such as myeloid or lymphoid [2]. Chronic myeloid leukemia (CML) is one of the four main subtypes of leukemia which

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is mostly a clonal BCR-ABL1-positive myeloproliferative neoplasm (MPN) determined by the detection of the Philadelphia (Ph) chromosome in the bone marrow cells of patients [3]. CML includes about 20 percent of all adult leukemia and more than 80 percent of CML patients are adults younger than the age of fifty [3]. Splenomegaly and anemia are the most common symptoms of CML [4]. Localized bone pain or joint pain had been reported in many CML patients [5].

Hodgkin lymphoma (HL) is a B cell-derived type of lymphoma, which is characterized by presentation of multinucleated Reed Sternberg cells (RS cells) in the patient's lymph nodes [6]. Hodgkin Reed Sternberg (HRS) cells originated from B cells but over-expression of hematopoietic cell type's markers would cause significant deregulated activation of several signaling pathways and transcription factors [7]. Up-regulation of these pathways in turn could affect the immune system and JAK/STAT pathways [8]. The prevalence of Hodgkin lymphoma is 0.98 per 100,000, and the mortality rate is 0.26 per 100,000 in 2020 [9].

Opioids are widely used as a pain reliever for management of pain in cancer patients [10]. The opioid epidemic is a worldwide concern about opioid use disorder (OUD), in patients with cancer [11]. There is a lack of information about addiction in oncology patients, and the prevalence of opioid addiction in cancer patients was estimated at 18% [12]. Several substances including alcohol and tobacco are at risk of cancer but there are no similar reports about the relationship between cancer and opium. On the other hand, opioid compounds are often used for the treatment of cancer-related pains [13].

Cancer and addiction are both multifactorial and complex health situations [14]. The case study in the present report of two patients with cancer and opium addiction is an exceptional example of the potential positive effects of successful addiction treatment and clinical usage of opium tincture with a new protocol help to advancement in the treatment of cancer.

CASE REPORT

We describe here two male cases, one diagnosed with chronic myeloid leukemia (CML) and one for Hodgkin lymphoma, both with a history of opium addiction. Before the diagnosis of cancer, patients began non-medical opioid use and were diagnosed with opium addiction. These patients were successfully treated for their addiction with a new method of taper-up-off with opium tincture called Dezhakam step time (DST) (15). The first patient was a 40-year-old man with bone pain, generalized abdominal pain, and weight loss. The blood count (CBC) and white blood cells were significantly

elevated. Lab data was WBC=210x10³/μl (Reference value: 4.0-10x10³ /μl), RBC=3.4x10⁶ /μl (Reference value:4.5-6.3x10⁶ /μl), Hemoglobin=10.5g/dl (Reference value: 14-18 g/dl), and Platelet=161x10³ /μl (Reference value: 140-440x10³ /μl). Ultrasound examination revealed no fatty liver but moderate hepatosplenomegaly, and the spleen was greater than normal (176 mm). Whole blood was collected and RNA was extracted by QIAGEN QIAamp RNA Mini kit. The cDNA was synthesized by Invitrogen kit. Qualitative probe-based real-time PCR (qRT-PCR) was done using standard primers and confirmed two times. The test result was: positive for BCR-ABL1 (t9:22) P210 mutation.

The second patient was a 40-year-old man comes to the General Practitioner's office after experiencing flu-like symptoms with swelling on the left side supraclavicular region of the neck. The patient had no report of any systemic symptoms including night sweats; weight loss or fever. The physical examination confirmed the presence of fixed lymph nodes with hard consistency in the left latero-cervical and supraclavicular area with an estimated size of 2.2 cm. There was no evidence of any lymphadenopathy or organomegaly. Patients were diagnosed for Hodgkin lymphoma based on Lymph node biopsy. He completed five cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) chemotherapy.

During the diagnosis of cancer, both patients participated in a special prescription of opium tincture using a new taper-up-off treatment method called DST for methamphetamine addiction treatment. This method was previously successfully used for the treatment of methamphetamine dependence [16].

The protocol of the DST method/ opium tincture for methamphetamine addiction treatment had been presented by an Iranian NGO called Congress 60, which has designed to preliminary replacement of the methamphetamine with opium tincture and second taper off and termination of dependence of opium tincture or other opium-based compounds after the treatment period. To achieve this goal "DST for methamphetamine" was including two phases, taper-up, and taper-off. The whole procedure would take 10 to 12 months which has been separated into three weeks steps. During the taper-up period, subjects with methamphetamine dependence would cut their methamphetamine usage at the beginning and start taking opium tincture orally. The opium tincture dosage would increase in every three weeks' step until reach the maximum dosage. After the step with maximum dosage, the taper-off phase would begin. In the taper-off phase, the oral dosage will be decreased in every 21 days' step until, the complete stoppage of opium tincture usage. Given that this method was very successful in the

treatment of methamphetamine addiction and also the rate of future opium dependence in the subject was less than one percent the method used for medical usage of opium in these cancer patients.

In CML patient the hepatosplenomegaly clinically subsided and anemia improved. The patient achieved hemoglobin of 13.7 g/dL, total leucocyte count of 8080/mm³ along with normal differential counts and platelet count of 148 000/mm³. A complete hematological response was detected in the CML patient. The patient with Hodgkin lymphoma showed a remarkable response to treatment with normalization of platelet, complete hematological response, and size reduction in the left latero-cervical lymph node to 1.6 centimeters. The patients were discharged in good condition for further follow-up and treatment and further follow-up was not applicable due to the lack of biopsies for the pathological analysis.

DISCUSSION

While the opium dependency caused by medical usage, especially in cancer patients is a health concern [17], the body of evidence had been confirmed both safety and efficacy of opium tincture gradual dose reduction regimens called DST to the treatment of opium and methamphetamine addiction [15,16]. New studies raise the potential positive effects of opium and/or opium-based components in the inhibition of oncogenesis (18). Recent studies indicated that Papaverine (a non-narcotic opium alkaloid) significantly inhibited cell proliferation and migration in cancer cells [19]. Mechanistically and in silico drug design approach determined that Papaverine could play a major role in the inhibition of HMGB1/RAGE interaction in several tumor cells, such as prostate [20, 21]; colorectal carcinoma, breast [22] and hepatocarcinoma [23].

Cell line studies reported that several opium-based products such as Noscapine, show anticancer and cell growth inhibition properties [24]. It has been determined that opium-based alkaloid, has low toxicity in humans and mice. Tubulin binding that affects microtubule assembly and arrests mammalian cells in mitosis is a potential mechanism that may explain the antitumor effects of opium-based alkaloids [25]. Previous studies revealed the apoptosis effects of opium alkaloids in lymphoid tumors, breast and bladder tumors [26].

Opium is water-soluble with a good rate of absorption by oral administration. While the chemotherapeutic potentials in different types of human cancer defiantly merit examinations, the dosage and usage protocol is essential for any treatment. The novel protocol presented in this case

report could be presented as a new safe protocol with no future dependence or abuse of opium or opioid substances.

CONCLUSION

The effects and mechanisms of opioid components in cancer cells have not been well described in the literature. We raise the potential possibility of a new method of opium medical usage that may help not only pain relief but also the inhibition of cancer advancement. These cases highlight the need for evidence-based strategies available about the molecular mechanisms and clinical symptoms induced by opium in different types of cancer survivors with and without a history of substance use.

AUTHOR CONTRIBUTIONS

Hossein Dezhakam: conceptualizing and supervision. Amin Dezhakam: writing and editing the manuscript, Ani Dezhakam: writing and editing the manuscript, Shani Dezhakam: writing and editing the manuscript, Arvin Haghighatfard: conceptualizing and supervision.

Additional Information

Conflict of interest: The authors declare no competing interests.

Ethical statement: Both human subjects participated in this study signed a written consent form regarding the publication of their information. Patients declare on their admission that their data may be used in anonymized form for scientific evaluations and for publications. The study information collection and all processes of study have been approved by the central ethical committee of Islamic Azad University. Registration of clinical in advance and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements.

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