Effect of opium smoking cessation on the nasopharyngeal microbial flora

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ABSTRACT

الأهداف: تحديد أثر الإنقطاع أو الامتناع عن تدخين الأفيون على تكرار ونوع الأحياء الدقيقة في الأنف البلعومي لمدخني الأفيون.

الطريقة: أجريت هذه الدراسة – قسم الطب النفسي والأنف والأذن والحنجرة – مستشفى موارادي – جامعة رفسنجاني للعلوم الطبية – جمهورية إيران خلال الفترة ما بين يونيو إلى نوفمبر 2008م. تم أخذ مسحة من مزرعة البكتريا في منطقة الأنف البلعومي لعدد 50 مدخن أفيون قبل وبعد 2 شهر و3 شهر من الامتناع عن تدخين الأفيون. تم تحديد الجينات المرضية الكامنة.

النتائج: تم عزل 8 جينات مرضية من مزرعة البكتريا بمنطقة الأنف البلعومي التي تم الحصول عليها من 43 فرد قبل توقفهم عن تدخين الأفيون. و عدد 4 أفراد شفيوا من 33 فرد بعد الامتناع عن التدخين (p=0.03). المكورات العنقودية لذات الرئة والمكورات العنقودية الحقيقية و المكورات العنقودية الدموية لم يتم رؤيتها في فحص مزرعة البكتريا الثانية. أكثر المضادات للحساسية هو عقار سيفترياكسون (84%)، عقار سيبروفلوكساسين (74%) وعقار كلوكساسيلين (72%) وأكثرهما مقاومة للأموكسيسيلين (26%) وأقلها مقاومة للكلورامفينيسول.

خاتمة: وفقاً لدراستنا، انخفضت بعض الجينات المرضية الكامنة أو حتى غابت بعد التوقف عن تدخين الأفيون. يبدو أن تدخين الأفيون له تأثيرات على منطقة الأنفي البلعومي.

Objectives: To determine the effect of opium smoking cessation on the frequency and type of microorganisms in the nasopharynx of opium smokers.

Method: This cross-sectional study was performed in the Psychiatry, and Ear, Nose, and Throat Departments, Moradi Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran from June to November 2008. Nasopharyngeal cultures were taken from 50 opium smokers before, and 2-3 months after cessation of opium smoking. Potential pathogens were identified. Patients were not advised to change their number of cigarettes, and we used methadone for the substitution of opium.

Results: Eight potential pathogens were isolated from nasopharyngeal cultures obtained from 43 individuals before opium smoking cessation, and 4 were recovered from 33 individuals after cessation (p=0.03). *Streptococcus pneumoniae*, *Staphylococcus saprophyticus*, *Streptococcus alpha hemolytic*, and *Staphylococcus aureus* were not found in the second culture. The most sensitivity to antibiotics was for ceftriaxone (84%), ciprofloxacin (74%), and cloxacillin (72%), and the most resistance for amoxicillin (26%) and the least resistance for chloramphenicol.

Conclusion: Some potential pathogens decrease or are even absent after opium cessation. Opium smoking affects the nasopharyngeal flora.

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Addiction is a threat to society and family and destroy the nations. Abuse of opium and its derivatives is one of the most important problems of many countries.[1] Opioids derive their name from the Greek ottiou for poppy sap. Various preparations of the opium poppy, *Papaver somniferum*, have been used for pain relief for centuries.[2-4] Opium emerged as the first widely used narcotic analgesic by the time of the Renaissance, generally in the form of a powder or sticky gum. It was often combined with alcohol to form laudanum. The Prussian pharmacist Friedrich Sertürner isolated

morphine from opium in the 19th century.[5] These drugs have led to many medical complications because of their abuse potential and frequent parenteral route of administration. The major cardiac complication of opioid abuse is bacterial endocarditis caused by injection drug use. *Staphylococcus aureus* is the most frequently reported bacterial isolate, and the tricuspid valve is the most commonly involved. Left-sided valvar infection is associated with a poor prognosis, as are the uncommon gram-negative and fungal infections. Opioid abusers normally have acute rather than subacute endocarditis. The initial clinical finding can be fever alone in half the cases, or fever may be associated with pulmonary infiltrates from right-sided emboli or systemic embolic phenomena, such as arthritis, abscess, and osteomyelitis. Other cardiac complications associated with opioid abuse include toxic cardiomyopathy, perivalvar abscess, abnormalities of the conduction system such as QT prolongation and ST-T wave changes, and cor pulmonale.[6] The nasopharyngeal flora of smokers contains fewer aerobic and anaerobic organisms with interfering capability, and more potential pathogens compared with those of nonsmokers, and smoking is associated with an increased risk of respiratory tract infection in adults, and also with oral colonization by some potentially pathogenic microorganisms.[7] The purpose of this study was to determine the effect of opium smoking cessation on the frequency of potential pathogens in the nasopharynx of opium smokers.

Methods. This cross-sectional study was performed in the Psychiatry, and Ear, Nose, and Throat Departments, Moradi Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran from June to November 2008. Fifty healthy adults who had smoked at least 5 grams of opium a day for the past one year, and had completely ceased opium smoking were included in the study. None were immune deficient or had otitis, sinusitis, or tonsillitis; had received antimicrobial therapy 3 months before study; or had a respiratory tract infection in the past 2 months prior to the time when the first and second culture samples were taken. All the opium smokers were men. We used the methadone pill as a substitution for opium. Two culture samples were obtained from each individual: one sample before cessation of opium smoking, and the other 2-3 months after they stopped opium smoking. The culture specimens were taken using sterile calcium alginate swabs and were collected from the nasopharynx (through the mouth), and were immediately plated into media supportive of the growth of aerobic bacteria. The Institutional Review Board and Ethical Committee of Rafsanjan University of Medical Sciences, related to the Iran Ministry of Health, approved the protocol and informed consent was obtained.

Microbiologic findings. Sheep's blood (5%), chocolate, and MacConkey agar plates (Base: Merck, Darmstadt, Germany) were inoculated for the isolation of aerobic organisms. The culture plates were incubated aerobically at 37°C (MacConkey agar) and under 5% carbon dioxide (blood and chocolate agars), and they were examined at 24 until 48 hours. All types of colonies on each plate were isolated. Aerobic bacteria were identified by previously described methods.[7,8] Antibiogram disks were used for antibiograms as per the recommendation of the National Committee for Clinical Laboratory Standards.[34,35]

Statistical analysis was carried out using the Fisher exact test and t-test. Statistical software was SPSS version 16. The level of significant was $p<0.05$.

Results. Eight potential pathogens were isolated from nasopharyngeal cultures obtained from 43 individuals before opium smoking cessation, and 4 were recovered from 33 individuals after cessation ($p=0.03$) (**Table 1**). The mean ± standard deviation, number of nasopharyngeal microorganisms found in samples before cessation was 1.1±0.647 (95% confidence interval: 0.92-1.28), and after cessation was 0.66±0.479 (95% confidence interval: 0.53-0.79), with a significant difference ($p<0.0001$). The frequency of positive/negative culture results before and after cessation is shown in **Table 2**. *Streptococcus pneumoniae*, *Staphylococcus saprophyticus, Streptococcus alpha hemolytic* and *Staphylococcus aureus* were not found in the second culture. The greatest sensitivity to antibiotics was found for ceftriaxone, followed by ciprofloxacin, and cloxacillin, and the greatest resistance was found to amoxicillin, and the least resistance to chloramphenicol (**Table 3**).

Discussion. This study compares the rate of potential pathogens from the nasopharynges of opium smokers before cessation of smoking and 2-3 months

Table 1 - Number and type of microorganisms before and after cessation.

Type of microorganism	Number of before cessation	Number of after cessation
Enterococcus	3	2
Streptococcus aureus	5	Not Seen
Streptococcus epidermis	26	17
Stafilococos saprofiticus	7	Not Seen
Streptococos alpha hemolytic	1	Not Seen
Streptococos beta hemolytic	3	2
Streptococcus pneumoniae	4	Not Seen
Viridans Streptococcus	6	4
Negative what???	7	17

Table 2 - Frequency of samples at result of nasopharyngial culture before and after cessation

Culture result	Before of cessation		After of cessation		Total	
	n	(%)	n	(%)	n	(%)
Positive	43	(86)	33	(66)	76	(76)
Negative	7	(14)	17	(34)	24	(24)
Sum	50	(100)	50	(100)	100	(100)

Fisher's exact test, p=0.03 difference is significance.

Table 3 - Pattern on antibiogram in samples.

Type of antibiotic	Sensitivity		Inter-mediate		Resistance		Total	
Amoxicillin	5	(12)	27	(62)	11	(26)	**43**	**(100)**
Ciprofloxacin	32	(74)	8	(19)	3	(7)	**43**	**(100)**
Chloramphenicol	14	(32)	28	(66)	1		**43**	**(100)**
Ceftriaxone	36	(84)	5	(12)	2	(4)	**43**	**(100)**
Tetracycline	26	(60)	13	(30)	4	(10)	**43**	**(100)**
Cephalothin	26	(60)	11	(25)	6	(15)	**43**	**(100)**
Erythromycin	10	(10)	28	(65)	6	(12)	**43**	**(100)**
Vancomycin	13	(30)	27	(62)	3	(8)	**43**	**(100)**
Cloxacilin	31	(31)	10	(23)	2	(5)	**43**	**(100)**

Data are express as number and percentage (%)

after cessation of smoking, and we observed that a high number of microorganisms revert to normal levels after complete cessation of opium smoking. In western countries, heroine has the most use among drug abusers (a derivative of the opium poppy).[9] Therefore, most of the research on addiction is focused on the effects of this agent on body systems. However, in Iran and some Asian countries, the use of opium in smoking form is the most popular drug among addicted subjects.[10] This variation in nasopharyngeal microbial flora in addicts depends on several factors. The effects of opium and other opioids on the immune system (immunosuppressive effects) have been extensively reviewed. Experimental evidence, both in vivo and in vitro, has shown that opiates modulate the functions of immune cells both directly through interaction with their surface receptors, and indirectly through the central nervous system and neuroendocrine circuits.[11] Opioids are known to modulate the induction and production of several cytokines; nevertheless, the details of mechanism remain largely evasive. Opioids and cigarette are factors of quantity and quality disorder in cell fagositos and immune of addicts that this is a reason for increase of pathogens in nasopharynx.[12] The enhanced binding of pathogenic bacteria to epithelial cells of smokers may account for their predominance.[7] Some studies have shown that opium cessation is associated with an increase of immunoglobulin (Ig)M and a decrease of IgE.[13] Opium smokers have higher numbers of circulating T helper (TH)2 and TH3 lymphocytes, and lower numbers of TH1 than non-dependent opium smokers. However, due to lower activity of TH2 and higher activity of TH1 lymphocytes, dependent individuals may be at higher risk during infections.[14] Some organisms with interfering potential can play a role in the prevention of upper respiratory tract infections. Lack of these organisms in smokers may contribute to their increased risk of acquiring respiratory pathogens and their greater susceptibility to respiratory infections.[15,16] Saliva is the first biological fluid that encounters the inhaled opium smokers.[17] Several studies indicate that exposure to both, gas and particulate phase of cigarette smokers caused a statistically significant decrease in salivary uric acid, lactate dehydrogenase (LDH), and amylase activity (important factors of the antioxidant salivary system).[17-19] These changes in saliva are associated with mutation of microflora in oral ecosystems, and can lead to an increase of respiratory tract infections and supragingival plaque associated with the development of caries or cancer.[20] Thus, it is recommended that patients who are under treatment with radiotherapy or some medications or smokers attend more to dental care.[21] The role of gastro-esophageal reflux disease in the pathogenesis of miscellaneous respiratory disorders has been discussed for decades and established in asthma and cough.[22] Opium smoking associated with gastroesophageal reflux that this is a factor for inflammation of nasopharynx and incline increase of pathogens. Thus, cessation of opium smoking decreases gastroesophageal reflux and nasopharyngeal pathogens.[23-26] The poor oral and dental care in opiate addicts leads to an increase of some pathogens and periodontal diseases. Likewise, abnormal and poor nutrition in these people leads to infirmity of the immune system and more infectious diseases.[27,28] In laboratories animals, studies have shown that after injection of morphine, reproduction of lymphocytes decreased by 85%,[29-31] with suppression of lymphocytes activity.[32,33]

In conclusion, our study demonstrates the beneficial effects of opium smoking cessation in restoring the number of bacteria to normal levels. These are potentially beneficial bacteria that can interfere with the growth of potential pathogens. Further studies are warranted to investigate whether colonization of the nasopharynx with interfering organisms and/or cessation of smoking would be beneficial, allowing for the return of the normal inhibitory flora and the reduction in the number of pathogens.

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