



THE EFFECT OF OPIUM ON THE CARDIOVASCULAR SYSTEM

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ABSTRACT

Opioids have the best price of illicit drug intake after hashish worldwide. Opium, after tobacco, continues to be the maximum generally abused substance within the Middle East. In addition to the convenience of availability, one cause for the excessive intake of opium in Asian international locations is probably a conventional notion amongst Eastern human beings or even scientific team of workers that opium may also have ameliorating consequences on cardiovascular diseases (CVDs) in addition to diabetes mellitus, hypertension, and dyslipidemia. Over the final decade, many studies were achieved on human beings and animals to assess the interaction among opium intake and solid coronary artery disease, acute coronary syndromes, and atherosclerosis. In this review, we finish that opium intake must be taken into consideration a chance thing for CVDs. Healthy individuals, as nicely as cardiac and diabetic patients, must be knowledgeable and knowledgeable approximately the dangerous consequences of opium intake on cardiovascular and different persistent diseases.

1. Introduction

Papaversomniferum L. is among the oldest medicinal plants, and the dried latex of its poppy, opium, has been used for medicinal or leisure functions conventionally.1 Opioids have the highest fee of illicit drug intake after hashish worldwide. In 2017, the United Nations Office on Drugs and Crime suggested that 29 million persons, 50% better than estimates, had used opiates within the previous yr globally.2 Notably, opium, after tobacco, continues to be the maximum usually abused substance within the Middle East.three One of the motives for the excessive use of opium on this location is probably the convenience of get entry to and additionally the area within the predominant pathway of the opium transit as the principle opium-generating nations which includes Afghanistan, and to a lesser extent, Myanmar, and Laos are positioned on this region. In addition to the benefit of availability, any other motive is probably a conventional perception amongst Eastern humans or even scientific team of workers that opium may also have ameliorating outcomes on cardiovascular diseases (CVDs) in addition to diabetes mellitus, hypertension, and dyslipidemia.4e9 Over the remaining decade, many research were executed on people and animals to assess the impact of opium consumption on blood lipid and glucose profiles, and additionally on CVDs. In 2013, we posted the primary assessment article at the cardio-metabolic outcomes of opium consumption.1 In this assessment, we aimed to acquire and combine the latest proof with our preceding expertise to make clear the outcomes of opium on CVDs and its underlying mechanisms.

2. Pharmacotoxicology

The phrase opium (lachrymapapaveris, Teriak) is derived from the Greek call for juice; a milky juice extracted with the aid of using incising the unripe capsules (poppy) of Papaversomniferum L. 10 After being uncovered to air, it turns into a brown, sticky, or crumbly substance. It is a complex Cocktail of materials that, similarly to water, includes extra than forty alkaloids11 and over 70 components.12 Only 5 of those alkaloids account for certainly all the quantitative alkaloid content material of opium (Fig. 1), inclusive of morphine (8e17% through weight), noscapine (1e10%), papaverine (0.5e1.5%), codeine (0.7e5%), and thebaine (approximately 0.2%). eleven Morphine and codeine are powerful ache relievers thru the activation of the m (mu) opioid receptor. However, they also are abused for leisure functions due to the fact the activation of the m receptor reasons euphoria and drowsiness. thirteen Noscapine (previously referred to as narcotine) is an antitussive agent.14 Papaverine has no morphine-like actions, however because it relaxes clean muscles, it is usually used for the prevention and remedy of vasospastic illnesses along with the spasm of coronary artery skip grafts.eleven,14 Opium is used thru special routes.

It may be ingested orally or smoked after direct heating with burning charcoal in specialized gadgets along with an opium pipe (Vafour). In every other route (SikhSang), a stick is heated and the opium is placed on the heated stick with a hairpin, after which the smoke is inhaled.15 When opium is ingested, the onset of motion is delayed.1 This is while, within the case of opium smoking, morphine reaches the mind inside seconds due to the fast absorption of its vapor throughout the pulmonary capillaries into the bloodstream. Therefore, the onset of motion is an awful lot extra fast and extreme after smoking, however the period of motion is longer after oral consumption due to the fact the absorption from the intestine, despite the fact that slower, keeps over a extended period.

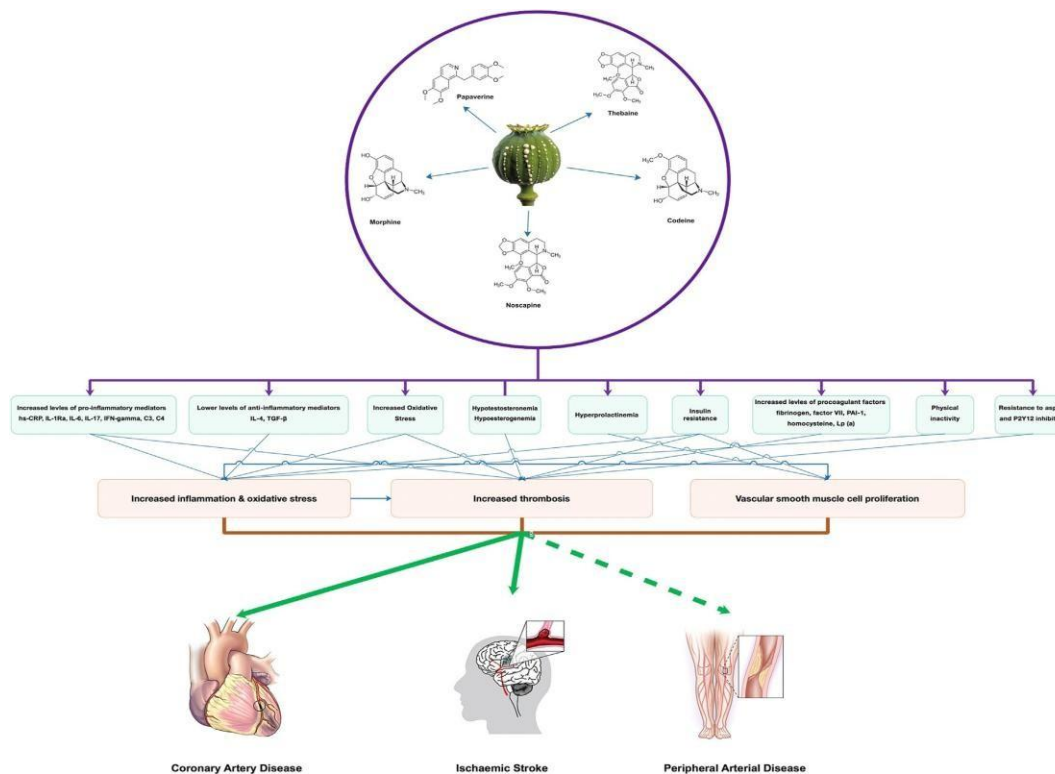


Fig. Central illustration: Chemical structure of five main alkaloids of opium (*Papaversomniferum L.*) and the potential mechanisms of the harmful effects of opium consumption on coronary artery disease, ischemic stroke, and peripheral arterial disease. hs-CRP, high sensitivity C-reactive protein; IL, interleukin; IL-1Ra, interleukin-1 receptor antagonist; IFN- g, interferon-g; Lp (a), lipoprotein (a); PAI-1, plasminogen activator inhibitor-1; TGF- b, transforming growth factor-b.

3. Stable coronary artery disease

Clinical research

In the first actual look at the affiliation among opiates and coronary artery disease (CAD), investigators as compared ninety eight decedents with methadone or opiate (M/O) of their blood on the time of post-mortem and ninety seven decedents with out M/O, and located a decreased severity of CAD many of the former sixteen Although they concluded that long-time period opiate publicity would possibly mitigate CAD severity and its fatal consequences, they referred to as for warning at the same time as decoding their outcomes primarily based totally on numerous limitations, which includes a loss of information at the decedents` smoking histories, lipid profiles, and lifestyles. sixteen Subsequently, majority of research besides few located that opium intake is related to greater excessive and extensive involvements of coronary arteries, even after modifications for viable confounders (Table 1).^{10,17e22} A cross-sectional take a look at determined no affiliation among opium intake with the aid of using any route and ischemic coronary heart diseases.²³ However, the authors referred to as for warning at the same time as decoding their outcomes because the opium dosage, the suggest period of opium intake, and the purity of opium had been now no longer assessed of their take a look at (Table 1).²³ A latest meta-analysis confirmed that opium intake turned into related to a extensively more threat of CAD (odds ratio [OR]: 2.77, 95% confidence interval [CI]: 2.04 to 3.75).²⁴ Besides research comparing the affiliation among opium intake and the presence, severity, and extension of stable CAD, opium abuse has been validated to be associated to coronary microvascular dysfunction.

Opium abuse turned into an unbiased predictor of coronary microvascular dysfunction (OR: 3.575, 95% CI: 1.418 to 9.016; $p \frac{1}{4}$ 0.0069) in a cross-sectional take a look at on sufferers with documented microvascular dysfunction.²⁵ Further, every other latest take a look at found out that opium intake turned into an unbiased threat thing for CAD and coronary artery ectasia.

Animal studies

It has been verified that opium dependancy has aggravating results at the development of atherosclerosis withinside the aorta of hypercholesterolemic rabbits.^{four} However, this atherogenic impact was confined to hypercholesterolemic as opposed to normocholesterolemic conditions.^{four} Concordantly, 4 weeks of opium smoking increased the atherogenic index in hypercholesterolemic rabbits and now no longer in normocholesterolemic ones.²⁷ Another look at confirmed that despite the attenuation of myocardial necrosis in rabbits with myocardial ischemia, opium publicity annoyed ischemia susceptibility, myocardial congestion, and hemorrhage.²⁸ In summary, there's steady proof helping the affiliation among opium intake and solid CAD.

4. Acute coronary syndromes

Although there's an settlement amongst contemporary research that opium intake is undoubtedly related to the presence and severity of CAD, there's controversy approximately the affiliation between opium intake and acute myocardial infarction (MI).²⁹ Some investigations have suggested unfavorable effects,^{30,31} whilst others have proven impartial effects (Table 2).³² Despite the talk concerning the affiliation between opium intake and the occurrence of acute MI, there's an settlement concerning the effect of opium intake at the inhospital and mid-time period effects of acute MI. Research has proven that opium use isn't correlated with multiplied rates of posteMI mortality, morbidity, and readmission.^{6,31,33e35} Nevertheless, some investigators have suggested remarkably longer health facility lengths of stay,³⁵ better readmission rates,³⁶ and borderline extensively better in-health facility mortality rates (11.5% vs. 5.9%; $p \frac{1}{4} 0.072$)³⁶ in opium-established sufferers with acute MI in preference to non-opium users (Table 2). Altogether, now no longer handiest is there no proof for assisting a reduced hazard of acute MI or a good posteMI final results in opium-established sufferers however additionally it can be related to more posteMI complications. Summary of studies evaluating the association of opium consumption with acute coronary syndrome and its outcomes.

Study	Method	Sample	Incidence	Results
Klockgether et al. (1997)	Case report Gluteal compartment syndrome	30-year-old male IV heroin user	Symptoms: painful swelling of right leg, complete sciatic nerve palsy following IV injection of heroin Elevated serum CK, rhabdomyolysis	Neurological recovery after 4 weeks; rhabdomyolysis suspected as cause
Melantri et al. (1996)	Case report	Opioid user with hypoxic coma	Myocardial biopsy showed damage: focal lesions formed by small mononuclear inflammatory cells with a few neutrophils, associated with degenerated and necrotic myocardial fibers, interstitial edema and congestion of intrinsic blood vessels	Suggested that hypoxic coma following opioid overdose led to rhabdomyolysis and myocardial damage
Yang et al. (1996)	Case report	29-year-old male 1 day after heroin overdose	Symptoms: paralysis of lower extremities, swelling and tenderness of the four extremities, absent lower extremity deep tendon reflexes and positional sense Elevated plasma CK; transient acute renal failure	Resolution of most neurological signs and symptoms in 4 weeks
Study	Method	Sample	Incidence	Results
Binder & Vavrinikova (2008)	Prospective randomized comparative study Opioid replacement therapy in pregnancy and infant outcomes	117 women, randomized to 3 groups: 47 no replacement (on heroin), 32 methadone substitution, 38 buprenorphine substitution Infants: no premature delivery prior to 34 weeks	Heroin-exposed infants: highest incidence of LBW, IUGR, placental changes ($p < 0.05$); NAS most severe in methadone-exposed infants ($p < 0.001$)	Confounding variables may account for some findings; buprenorphine substitution therapy recommended rather than methadone
Kuczowski (2007)	Literature review Risks associated with drugs of abuse and pregnancy	All drugs of abuse and management of patients in perinatal period	Maternal medical complications opioid use: cellulitis, skin abscesses, thrombophlebitis, hepatitis, AIDS, endocarditis, malnutrition Infant outcomes: IUGR, fetal distress	Methadone recommended for replacement therapy; anesthesia can precipitate hypotension, and larger doses of pain medication are needed because of cross-tolerance
Jansson et al. (2007)	Descriptive study Severity of NAS in infants ECG	50 methadone-maintained pregnant women	Vagal tone response to methadone during times of trough or peak (effect on respiratory sinus rhythm, autonomic control): maternal vagal responders more likely to have infants with NAS ($p < 0.05$); NAS: unrelated to substance abuse history, methadone maintenance, exposure to psychotropic drugs; male infants more likely to develop NAS, require medication ($p < 0.05$)	Maternal vagal tone's response to methadone may be a predictor of NAS severity
Fajemirokun-Oduzeyl et al. (2006)	Retrospective study NAS symptoms in infants born to women who used heroin or methadone during late pregnancy	110 newborns from 108 mothers using heroin or on methadone maintenance during late pregnancy	Comparing infants of heroin-using group with methadone group, morphine therapy needed by 40% vs. 19%; length of stay 172 vs. 118 days	Heroin use in late pregnancy is associated with increased need for morphine therapy for the newborn, higher NAS scores, and longer hospital stays when compared with infants born to mothers on methadone maintenance

CI, Confidence interval; MI, Myocardial infarction; OR, Odds ratio. a An opium dependent and a non-dependent group (age- and smoking-matched) of alive poste MI patients were followed up for 12 months.

four.1. Clinical research on sufferers present process revascularization

Some research on coronary artery pass grafting surgical treatment (CABG) applicants have confirmed that opium intake is now no longer correlated with multiplied in-sanatorium mortality rates, postoperative hardship rates, or sanatorium lengths of stay.^{37e40} However, others have proven that opium use is immediately correlated with intra- and post-operative bleeding, forty one readmission,³⁸ and longer sanatorium lengths of stay. forty Recently, we studied 28,691 sufferers who underwent CABG for a mean of fifty six months to assess the results of opium intake and cessation at the long-time period results of those sufferers. forty two In this cohort, 3636 sufferers endured opium intake after surgical treatment, even as 1436 sufferers stopped opium use. After modifications for viable confounders, we discovered that in assessment with the in no way customers of opium, chronic opium intake after CABG changed into related to multiplied 5-12 months all cause mortality (danger ratio [HR]:1.28, 95% CI:1.06 to 1.54; p ¼ 0.009) and 5-12 months important damaging cardiac events (MACE) (HR: 1.25, 95% CI: 1.thirteen to 1.forty; P<0.0001). Still, individuals who quitted opium use after surgical treatment have been now no longer at an multiplied chance of mortality (HR: 1.09, 95% CI: 0.eighty three to 1.forty three; p ¼ 0.514) or MACE (HR: 1.03, 95% CI: 0.88 to 1.21; p ¼ 0.645) at 5 years in comparison with the in no way customers of opium. forty two In a retrospective cohort study, opium intake changed into now no longer related to 12-month MACE amongst male sufferers after optional percutaneous coronary interventions, and not one of the additives of MACE, inclusive of goal vessel revascularization, goal lesion revascularization, CABG, and non-deadly MI, changed into unique among opium customers and non-customers. forty three Nonetheless, it have to be stated that even as age is a vital predictor of MACE, specially mortality, the authors did now no longer make modifications for the confounding impact of age on MACE notwithstanding the extensively lower age of the opium customers via way of means of assessment with the non-customers (55.7 as opposed to 58.four years, respectively; p < 0.001). This bias may probably underestimate MACE withinside the opium consumer group. forty three Altogether, it seems that opium intake now no longer best has no ameliorating impact on sufferers present process coronary revascularization however additionally can also additionally have dangerous results on mid-time period and longer moutcomes

5. Stroke

There are scarce reviews approximately the correlation among opium and stroke (Table 3). In a case control look at, opium abuse was independently related to ischemic stroke.forty four Other studies have established that opium dependancy is related to expanded intima-media thickness, greater atherosclerotic plaques, and a extra pulsatility index and imply go with the drift pace of the middle cerebral artery, which might be the markers of cerebral atherosclerosis.^{45e47} In a look at on male CABG candidates, there has been no distinction in the superiority of enormous carotid artery stenosis among opium-addicted and non-addicted sufferers. forty eight Nonetheless, there's an enormous bias on this look at because the authors said a better incidence of diabetes (17% as opposed to 11.4%) and hypertension (88.6% as opposed to 11.4%) in addition to a decrease incidence of smoking (27.1% as opposed to 65.5%) withinside the non-addicted sufferers than withinside the opium addicted ones, respectively. Indeed, no end may be drawn approximately the affiliation among opium intake and carotid stenosis with out adjusting for such essential confounding factors (Table 3).

forty eight In summary, the presently constrained proof shows the destructive outcomes of opium on cerebral atherosclerosis and hemodynamic abnormalities, and its affiliation with ischemic stroke Nonetheless, in addition research are had to elucidate the association among opium intake and stroke.

6. Peripheral arterial disorder

Despite numerous research assessing the connection among opium intake and CAD, there may be confined facts concerning the affiliation among opium intake and peripheral arterial disorder. In a take a look at on sufferers with peripheral arterial disorder who underwent decrease extremity vascular reconstruction surgery, investigators determined that the patency price changed into extensively decrease in opium customers than non-customers (32% as opposed to 67%, respectively).forty nine However, the authors did not modify this locating for potential confounders. forty nine Future well-designed research have to elucidate the actual position of opium intake in peripheral arterial disorder.

7. Heart failure

The affiliation among opium intake and left ventricular systolic disorder has been evaluated in lots of latest research. The contemporary proof means that opium intake is now no longer related to a reduced practical elegance.^{23,33,34,37e39,50e52} Nonetheless, there are conflicting consequences concerning the affiliation among opium intake and the left ventricular ejection fraction (LVEF). Some research have proven that opium customers, with or with out CAD, are much more likely to have decreased LVEF than nonusers,^{50,51,fifty three, fifty four} whilst others have observed a impartial impact on this regard.^{10,20,23,31,33e35,37-39,43,52,fifty five} A latest meta-evaluation confirmed that opium use changed into related to extensively decrease LVEF in opium customers who have been applicants for CABG (mean variations ¼ 2.15, 95% CI: 3.31 to 1).²⁴ However, this statistically good sized distinction of 2%, perhaps of no or minimum medical importance. Moreover, this correlation did now no longer attain statistical importance in different subgroups of sufferers with CAD (mean variations ¼ 0.29, CI: 0.fifty seven to 1.14).²⁴ Taken these types of strains of proof together, we might also additionally finish that opium intake has impartial outcomes at the LVEF and practical elegance of people with coronary heart failure.

8. Cardiac arrhythmias

Studies have verified that opium use is related to a better occurrence of ventricular arrhythmias withinside the poste MI course, even after changes for confounders.^{52,fifty six} whilst every other take a look at confirmed a impartial impact on this regard.³⁴ Whereas a take a look at confirmed that opium dependancy changed into related with better post-CABG arrhythmias, fifty three every other take a look at observed defensive outcomes for opium use

in phrases of post-CABG atrial traumatic inflammation. fifty seven Despite those controversies in medical research, animal studies²⁷, fifty eight have always indicated a proarrhythmic impact for opium.²⁹ Future well-designed potential medical research have to elucidate the precise position of opium intake in inducing or stopping cardiac arrhythmias.

9. Interactions with cardiovascular tablets

The contemporary proof suggests that opiates can intrude with cardiovascular medicinal drugs via changes of their pharmacokinetics or pharmacodynamics. fifty nine In a massive take a look at, an evaluation of prescriptions for sufferers with non-valvular atrial traumatic inflammation who have been below remedy with warfarin and had a solid international normalized ratio (INR) indicated that the intake of opiates, consisting of herbal opium, buprenorphine, and tramadol, changed into related to an extended INR in those sufferers, which would possibly suggest a clinically crucial interplay.⁶⁰ Furthermore, it's been proven that the concomitant use of opium and digoxin might also additionally boom the danger of digoxin toxicity. sixty one Another clinically applicable interplay of opium is with antiplatelets. Research has proven that the management of opioids inclusive of opium, methadone, and morphine attenuates the antiplatelet moves of aspirin, sixty two ticagrelor,⁶³ prasugrel,⁶⁴ sixty six and clopidogrel.⁶⁷, sixty eight This listing of doubtlessly lethal interactions among opium and cardiovascular tablets shows that cardiologists and cardiac surgeons act carefully while prescribing antiplatelets, digoxin, and warfarin for an opium-abusing patient.

10. Temporal dating among opium intake and cardiovascular diseases

Although the medical research at the affiliation among opium intake, and CAD and stroke have set up a systematic base withinside the proof pyramid, there are not unusual place obstacles of their methodologies that name for warning in decoding their consequences. First, all of those research have case control or cross-sectional designs. Some sufferers with CAD or stroke possibly begin the use of opium due to their signs or their ideals approximately the useful outcomes of opium use on CVDs following the improvement of their diseases. Hence, whilst we have a look at a better incidence of opium intake amongst sufferers with CVDs than healthful people, we can not make a causal interpretation due to the fact the tempora courting among opium intake and CVDs can't be decided in those research. Another problem is the possible occurrence-prevalence bias, which ought to be taken into consideration in cross sectional and case control research. If opium intake affects the survival of sufferers with ischemic coronary heart diseases, then the outcomes of cross-sectional research with popular instead of incident instances might be biased. Community-primarily based totally cohort research can conquer those boundaries and assist us to make causal interpretations of the connection among opium and CVDs. With the growing use of opioids for persistent non-most cancers pain, a huge nested case control examine established that using opioids become related to an expanded danger of MI (OR: 1.28, ninety five% CI: 1.19 to 1.37).⁶⁹

In our opinion, the maximum supportive proof for a possible dangerous function of opium intake in CVDs got here from the Golestan Cohort Study.⁷⁰ The Golestan Cohort Study recruited 50, half human beings elderly 40e75 years from January 2004 to June 2008 from Golestan Province, placed in North Iran. As distinctive exposure data, a scientific follow-up approach, and the ascertainment of the purpose of demise have been available, the investigators evaluated the affiliation among opium intake and all-purpose mortality and predominant categories, consisting of circulatory reasons for mortality after a mean follow-up of 4.7 years. The adjusted HR for all-purpose mortality related to ever use of opium become 1.86 (ninety five% CI: 1.67 to 2.06).

They additionally determined that opium customers have been at an expanded danger of demise from ischemic coronary heart diseases (adjusted HR: 1.90; ninety five% CI: 1.57 to 2.29). Moreover, after apart from the men and women who started opium use after receiving a analysis of predominant illnesses, namely ischemic coronary heart diseases, cerebrovascular occasions, diabetes mellitus, and hypertension, they observed a dose-response affiliation among the period of opium use and cardiovascular in addition to all cause mortality. Unlike preceding cross-sectional and case control research, the Golestan Cohort Study become now no longer problem to the aforementioned predominant boundaries and, therefore, it's far affordable to finish causality primarily based totally on its findings.

11. Association among opium intake and cardiovascular diseases: impartial or confounded through smoking?

Cigarette smoking is one of the predominant danger elements for CVDs. It has been proven in all preceding research that opium abusers smoke cigarettes greater frequently.^{10,36, forty eight} Thus, it isn't always clean whether or not the affiliation among opium intake and CVDs is a dependent affiliation confounded through smoking or opium intake is an impartial danger thing for CVDs. Numerous research have attempted to solution this question. In a propensity rating matched analysis, the examine found out that diabetic opium customers had greater intense CAD than matched diabetic non-customers.^{10A} A huge cross-sectional examine indicated a better occurrence of CAD in opium customers than non-customers, even after the exclusion of cigarette smokers (Table 1).¹⁷ In a nested case control examine, opium dependancy become an impartial danger thing for CAD amongst non-smokers, whilst this affiliation become now no longer great in cigarette smokers.²⁰ Hence, we are able to finish that the courting among opium intake and CVDs is impartial.

12. Why ought to opium intake be related to cardiovascular diseases?

Current understanding is scarce approximately the results of opium on blood glucose, dyslipidemia, and hypertension. seventy one Although animal research show the dangerous results of opium at the aforementioned danger elements, there are a few discrepancies in medical research. seventy one Thus, it requires destiny well-designed medical research to cope with this gap of understanding. Here, we are able to attention on different danger elements and novel mechanisms of opium results on CVD.

Studies have established that opium exerts its dangerous results on CVDs through expanded infection and oxidative pressure, expanded thrombosis, and vascular clean mobileular hyperplasia (Fig. 1). Although there's a complicated courting, we in brief speak those interwoven elements here. Recent research have more and more said that opium addicts have multiplied stages of pro-inflammatory mediators^{15,72e76} and decrease stages of anti-inflammatory cytokines.^{74,seventy five} On the opposite hand, it's been proven in numerous research that morphine and heroin set off systemic oxidative pressure and decrease the full antioxidant potential impartial of cigarette smoking.

Hypotestosteronemia and hypoestrogenemia in opium addicts⁷⁸ can also additionally bring about CVDs through all the aforementioned mechanisms. These hormonal imbalances are related to expanded stages of procoagulant elements and insulin resistance.^{79e86} Studies have additionally established that opium-addicted individuals have remarkably better stages of procoagulant elements than nonaddicted individuals.^{15,87e90} Additionally, studies have validated a country of insulin resistance, much like sufferers with kind 2 diabetes mellitus, ninety one which reasons CVDs.^{79e86,89,92,ninety three} Opium abusers have hyperprolactinemia,^{78,ninety four} which ends up withinside the proliferation of vascular clean muscle cells and CVDs.^{ninety five} Another mechanism is the discount of bodily pastime because of the depressant results of opium at the significant anxious system, ninety six that's related to an expanded danger of CVDs.^{97e100}

Last however now no longer least, is the resistance to aspirin and P2Y₁₂ inhibitors in opium customers. We formerly mentioned that opium intake blunts the pharmacological results of aspirin,⁶² ticagrelor,^{63e65} prasugrel,^{64,sixty six} and clopidogrel.^{67,sixty eight} These findings can also additionally render opium customers with preceding CVDs greater prone to acute thrombotic occasions and is probably a singular justification for better dangers of MI and stroke in those sufferers.

13. Strategies for the remedy of opioid dependence

For the a success remedy of opioid dependence, we ought to rent pharmacological interventions except psychosocial supportive measures. There are techniques towards pharmacological remedy: 1) opioid agonist preservation remedy with long-performing opioids together with methadone or buprenorphine, which is the best and the favored method, and 2) detoxification, observed through remedy with long-performing opioid antagonists together with naltrexone, to save you relapses. Other than those medications, alpha-2 adrenergic agonists together with clonidine for the remedy of opioid withdrawal and naloxone for the remedy of opioid overdose ought to be available.¹⁰¹

14. CONCLUSION

People have used opium for decades now no longer handiest as a habit, however primarily based totally on their conventional ideals approximately its useful results on diabetes mellitus, dyslipidemia, hypertension, and CVDs. Considering the modern-day proof, opium now no longer handiest has no ameliorating impact on CVDs, however the medical, animal, and potential cohort research continuously suggest that opium intake is associated with CVDs and cardiovascular mortality. Moreover, the rapidly developing organic motives for a causal courting among opium intake and CVDs underscore the caution that opium intake ought to be taken into consideration a danger thing for CVDs. Unfortunately, fake ideals concerning the useful results of opium are common, and it's far the duty of fitness professionals¹⁰² and fitness government to warfare in opposition to those fake beliefs. Healthy people, in addition to cardiac and diabetic patients, need to be informed and knowledgeable approximately the dangerous results of opium consumption on cardiovascular and different continual diseases

Highlight

- There is regular proof helping the affiliation among opium intake and strong coronary artery disease.
- Persistent opium intake after coronary artery pass grafting surgical treatment is related to increased long-time period dangers of mortality and primary destructive cardiac events.
- The presently confined proof indicates the detrimental outcomes of opium on cerebral atherosclerosis, and hemodynamic abnormalities and its affiliation with ischemic stroke.
- A dose response affiliation exists among the duration of opium use and all-motive and cardiovascular mortality.
- Opium intake must be taken into consideration a chance factor for cardiovascular diseases.
- Physicians must war towards fake ideals approximately the useful outcomes of opium.

REFERENCES

1. Masoudkabar F, Sarrafzadegan N, Eisenberg MJ. Effects of opium intake on cardiometabolic diseases. *Nat Rev Cardiol*. 2013;10:733e740.
2. UNODC. World Drug Report. 2019.
3. Amin-Esmaili M, Rahimi-Movaghar A, Sharifi V, et al. Epidemiology of illicit drug use problems in Iran: prevalence, correlates, comorbidity and service usage outcomes from the Iranian Mental Health Survey. *Addiction*. 2016;111:1836e1847.
4. Mohammadi A, Darabi M, Nasry M, Saabet-Jahromi MJ, Malek-Pour-Afshar R, Sheibani H. Effect of opium dependency on lipid profile and atherosclerosis formation in hypercholesterolemic rabbits. *Exp Toxicol Pathol*. 2009;61:145e149.
5. Karam GA, Reisi M, Kaseb AA, Khaksari M, Mohammadi A, Mahmoodi M. Effects of opium dependency on a few serum elements in addicts with non-insulindependent diabetes mellitus. *Addiction Biol*. 2004;9:53e58.
6. Sadr Bafghi SM, Rafiei M, Bahadorzadeh L, et al. Is opium dependency a danger aspect for acute myocardial infarction? *Acta Med Iran*. 2005;43:218e222.
7. Farahani MA, Mohammadi E, Ahmadi F, Maleki M, Hajizadeh E. Cultural boundaries withinside the schooling of cardiovascular ailment sufferers in Iran. *Int Nurs Rev*. 2008;55:360e366.

8. Richards JF. Opium and the British Indian Empire: The Royal Commission of 1895. Opium and the British Indian Empire: The Royal Commission of 1895. Cambridge University Press; 2001.
9. Chopra RN, Chopra IC. Quasi-clinical Use of Opium in India and its Effects. UNODC; 1955.
10. Hosseini SK, Masoudkabar F, Vasheghani-Farahani A, et al. Opium intake and coronary atherosclerosis in diabetic sufferers: a propensity score-matched look at. *Planta Med.* 2011;77:1870e1875.
11. Schiff Jr PL. Opium and its alkaloids. *Am J Pharmaceut Educ.* 2002;66:186e194.
12. Buchbauer G, Nikiforov A, Remberg B. Headspace components of opium. *Planta Med.* 1994;60:181e183.
13. Traynor J. mu-Opioid receptors and regulators of G protein signaling (RGS) proteins: from a symposium on new ideas in mu-opioid pharmacology. *Drug Alcohol Depend.* 2012;121:173e180.
14. Kalant H. Opium revisited: a quick assessment of its nature, composition, nonmedical use and relative risks. *Addiction.* 1997;92:267e277.
15. Asgari S, Sarrafzadegan N, Naderi GA, Rozbehani R. Effect of opium dependency on new and conventional cardiovascular danger elements: do period of dependency and course of management matter? *Lipids Health Dis.* 2008;7:42.
16. Marmor M, Penn A, Widmer K, Levin RI, Maslansky R. Coronary artery ailment and opioid use. *Am J Cardiol.* 2004;93:1295e1297.
17. Sadeghian S, Darvish S, Davoodi G, et al. The affiliation of opium with coronary artery ailment. *Eur J Cardiovasc Prev Rehabil.* 2007;14:715e717.
18. Sadeghian S, Graill P, Salarifar M, Karimi AA, Darvish S, Abbasi SH. Opium intake in guys and diabetes mellitus in girls are the maximum important danger elements of untimely coronary artery ailment in Iran. *Int J Cardiol.* 2010;141:116e118.
19. Masoumi M, Shahesmaeili A, Mirzazadeh A, Tavakoli M, Ali AZ. Opium dependancy and severity of coronary artery ailment: a case-manipulate look at. *J Res Med Sci.* 2010;15:27e32.
20. Masoomi M, Arash Ramezani M, Karimzadeh H. The courting of opium dependancy with coronary artery ailment. *Int J Prev Med.* 2010;1:182e186.
21. Hosseini SA, Abdollahi AA, Behnampour N, Salehi A. The courting between coronary danger elements and coronary artery involvement primarily based totally on angiography findings. *Koomesh.* 2012;14:7e12.
22. Rahimi Darabad B, Vatandust J, Pourmousavi Khoshknab MM, Hajahmadi Poorrafsanjani M. Survey of the impact of opioid abuse at the volume of coronary artery diseases. *Global J Health Sci.* 2014;6:83e91.
23. Rezvani MR, Ghandehari K. Is opium dependancy a danger aspect for ischemic heart ailment and ischemic stroke? *J Res Med Sci.* 2012;17:958e961.
24. Nakhhae S, Amirabadizadeh A, Qorbani M, Lamarine RJ, Mehrpour O. Opium use and cardiovascular diseases: a scientific assessment and meta-analysis. *Crit Rev Toxicol.* 2020;50:201e212.
25. Esmaeili Nadimi A, Pour Amiri F, Sheikh Fathollahi M, Hassanshahi G, Ahmadi Z, Sayadi AR. Opium dependancy as an impartial danger aspect for coronary microvascular dysfunction: a case-manipulate look at of 250 consecutive sufferers with slow-float angina. *Int J Cardiol.* 2016;219:301e307.
26. Masoumi M. Opium Is an Important Risk Factor for Coronary Artery Ectasia; a Cross-Sectional Study. PREPRINT (Version 1) to be had at: Research Square; 04 November 2019. <https://doi.org/10.21203/rs.2.16809/v1>.
27. Najafipour H, Joukar S. Combination of opium smoking and hypercholesterolemia augments susceptibility for deadly cardiac arrhythmia and atherogenesis in rabbit. *Environ Toxicol Pharmacol.* 2012;34:154e159.
28. Joukar S, Najafipour H, Malekpour-Afshar R, Mirzaeipour F, Nasri HR. The impact of passive opium smoking on cardiovascular indices of rabbits with regular and ischemic hearts. *Open Cardiovasc Med J.* 2010;4:1e6.
29. Nakhhae S, Ghasemi S, Karimzadeh K, Zamani N, Alinejad-Mofrad S, Mehrpour O. The results of opium at the cardiovascular system: a assessment of aspect results, uses, and capability mechanisms. *Subst Abuse Treat Prev Pol.* 2020;15:30.
30. Niaki MRK, Mahdizadeh H, Farshidi F, Mohammadpour M, Omran MTS. Evaluation of the position of opium dependancy in acute myocardial infarction as a danger aspect. *Caspian J Int Med.* 2012;4:585e589.
31. Roohafza H, Talaei M, Sadeghi M, Haghani P, Shokouh P, Sarrafzadegan N. Opium decreases the age at myocardial infarction and unexpected cardiac death: a long- and short-time period final results evaluation. *Arch Iran Med.* 2013;16: 154e160.
32. Azimzade-Sarwar B, Yousefzade G, Narooey S. A case-manipulate look at of impact of opium dependancy on myocardial infarction. *Am J Appl Sci.* 2005;2:1134e1135.
33. Dehghani F, Masoomi M, Haghdoost A. Relation of opium dependancy with the severity and extension of myocardial infarction and its associated mortality. *Addict Health.* 2013;5:1e7.
34. Javadi HR, Allami A, Mohammadi N, Alauddin R. Opium dependancy and inhospital final results of acute myocardial infarction. *Med J Islam Repub Iran.* 2014;28:122.
35. Davoodi G, Sadeghian S, Akhondzadeh S, Darvish S, Alidoosti M, Amirzadegan A. Comparison of specifications, short-time period final results and diagnosis of acute myocardial infarction in opium based sufferers and non-dependents. *Ger J Psychol.* 2005;8:33e37.
36. Harati H, Shamsi A, Moghadam MF, Zadeh FSS, Ghazi A. The mortality fee of myocardial infarction sufferers with and with out opium dependen. *Int J High Risk Behav Addiction.* 2015;4.
37. Safaei N. Outcomes of coronary artery pass grafting in sufferers with a records of opiate use. *Pakistan J Biol Sci.* 2008;11:2594e2598.
38. Safaii N, Kazemi B. Effect of opium use on short-time period final results in sufferers present process coronary artery pass surgical treatment. *Gener Thoracic Cardiovascular Surgery.* 2010;58:62e67.
39. Azarasa M, Azarfarin R, Changizi A, Alizadehasl A. Substance use amongst Iranian cardiac surgical treatment sufferers and its results on short-time period final results. *Anesth Analg.* 2009;109:1553e1559.