CLINICAL ALERT

Secondary polycythaemia with elevated carbon monoxide levels due to hookah pipe smoking: A public health concern

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Hookah pipe (HP) smoking is perceived as a harmless activity, enjoyed by young adults and high school-going children. Awareness of the health impact of recreational habits, and their intersection with new social norms in the COVID-era, requires critical review. We describe a case series of young HP smokers presenting with secondary polycythaemia with significant clinical sequelae necessitating extensive work-up. HP smoking may lead to acute and chronic carbon monoxide intoxication, with resultant secondary polycythaemia and complications including provoked thrombosis.

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Hookah pipe (HP) smoking, also known as hubbly bubbly, waterpipe, shisha and narghile, has become a popular way of smoking tobacco over the past decade.[1] HP smoking was previously limited to older males in the Middle East, but has emerged as a trendy practice among youth all over the world, including South Africa (SA).[1] A recent cross-sectional study in Johannesburg, SA, showed that ~26% of grade 8 and 70% of grade 12 learners have smoked an HP.[2] The current widespread use is attributable to lack of knowledge about the dangers of HP smoking, the popular café culture, and the availability of attractive flavours.[3]

Surveys suggest that many people perceive HP smoking as less harmful and less addictive than cigarette smoking, but this is not supported by the literature.[3] Misperceptions include that inhaled smoke has been 'detoxified' by the 'filtering' effects of the water and that smoke from an HP contains less nicotine. There is also a lack of information in the media regarding the dangers of HP smoking.[3-5] Behavioural patterns of tobacco smoking dependence have been observed among HP smokers, such as unsuccessful attempts to stop HP smoking, increased use of the HP, and habits to appease cravings.[3] In view of the prolonged nature of an HP smoking session, the cumulative nicotine exposure is substantially higher than that of cigarette smoking.[6,7] The HP apparatus is complex, and the manufacturing process is non-standardised, leading to variable exposure to smoke byproducts, as well as the harmful effects of second-hand HP smoke. There is also no known regulation of the composition of HP tobacco products.[7-10]

We present a case series of patients who underwent bone marrow investigations for polycythaemia, in whom chronic HP smoking was identified as the underlying cause. These patients represent an unusual secondary polycythaemia cohort in that they were young and a subpopulation had documented venous thromboembolism (VTE). The findings highlight some of the potential risks of HP smoking and the need to elicit a full smoking history.[11]

Case presentation

We describe 7 patients with secondary polycythaemia due to HP smoking, identified over a 2.5-year period (June 2018 - November 2020), from private hospitals in the Johannesburg area in SA. The clinical information in Table 1 was obtained from the treating doctors, and the laboratory data in Table 2 were collated from the access-controlled Meditech software system at Lancet Laboratories. Informed written consent was obtained from all the patients to use their information anonymously.

All the patients were male, with ages ranging from 28 to 47 years. Five of the patients presented with nonspecific symptoms and polycythaemia as an incidental finding. Two of the patients experienced a thromboembolic event.

The patients' HP smoking history ranged from 3 months to 12 years. All 7 patients smoked an HP on a daily basis, with the duration of the smoking sessions being 10 minutes to ~3 hours per day. The frequency of the smoking sessions was 2 - 5 times per day. The hookah pack-year calculation estimated the cigarette consumption per HP smoking session to be between 19 cigarettes in a 15-minute session and 225 cigarettes in a 3-hour session. The equivalent cigarette pack-year history ranged from 1 to 34 pack-years.

Laboratory investigations (Table 2) revealed an elevated red cell count and haemoglobin and haematocrit concentrations in all 7 patients, reflecting polycythaemia according to the reference ranges used. The white cell count and platelet values were not elevated. Carboxyhaemoglobin levels were available for 3 patients, 1 of which was in the toxic range (36.8%) and the other 2 in the range of a cigarette smoker with a 1 - 2-year pack-year history. Serum ferritin levels were normal in 6 patients, but elevated in 1. Erythropoietin levels were lower than the reference interval in only 1 patient. The others were all in range.

Bone marrow investigations, performed in all the patients, revealed no morphological features to suggest a myeloproliferative neoplasm, and molecular investigations did not detect the *JAK2* (Janus kinase 2) V617F mutation. Cytogenetic studies, performed on 3 of the patients, indicated a normal male chromosome pattern. Next-generation sequencing, performed on 2 of the patients, detected no fusions or somatic variants. In view of these findings, none of the cases meet the World Health Organization criteria for polycythaemia vera.[15]

Table 1. Patient clinical information

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age (years)	28	29	29	47	28	31	34
Sex	M	M	M	M	M	M	M
Clinical presentation	Fever for 3 days, pulmonary emboli	Lethargy, progressive polycythaemia	Pruritus, chronic urticaria Blood donor	DVT left calf	Haematuria	Pica, restless legs	Headache, fatigue
HP smoking history							
Frequency	Daily	Daily 2 - 3 ×/day	Daily 2 - 3 ×/day	Daily 2 ×/day	Daily 2 - 3 ×/day Weekends 3 - 5 ×	Daily 3 - 5 ×/day	Daily
Duration/ session	~45 minutes	~60 - 90 minutes	~35 minutes	~60 minutes	~15 minutes	~30 - 45 minutes	~180 minutes per day
History of HP smoking	>10 years	>5 years	>12 years	12 months	>11 years	3 months	3 years, stopped 2 months before hospital admission
Cigarette smoking	None	Not known	Not known	None	2 years, stopped 10 years ago	18 years, stopped 2 months before hospital admission	None
HP pack-year calculation[12-14]	~56 cigarettes per 45-minute session 28 cigarette pack-year equivalent	~75 cigarettes per 60-minute session 19 cigarette pack-year equivalent	~44 cigarettes per 35-minute session 26 cigarette pack-year equivalent	~75 cigarettes per 60-minute session 4 cigarette pack-year equivalent	19 cigarettes per 15-minute session 10 cigarette pack-year equivalent	56 cigarettes per 45-minute session 1 cigarette pack-year equivalent	~225 cigarettes per 3-hour session 34 cigarette pack-year equivalent

M = male; DVT = deep-vein thrombosis.

Table 2. Laboratory investigations

Variables (reference ranges)	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
FBC							
RCC (4.5 - 6.5 × 10^{12}/L)	6.80	6.28	7.33	7.46	6.22	6.25	6.73
Hb (13.8 - 18.8 g/dL)	20.5	18.9	20.9	21.5	22.0	19.4	22.2
Hct (0.40 - 0.56 L/L)	0.60	0.53	0.62	0.65	0.60	0.55	0.61
MCV (79 - 100 fL)	88	84.2	84.3	86.6	95	87.5	90
WCC (4.0 - 12.0 × 10^{9}/L)	2.34	6.44	10.15	6.45	5.0	7.09	4.22
Platelet count (150 - 450 × 10^{9}/L)	120	227	263	169	210	260	206
BG and COHb (%)*	Not performed on hospital admission	COHb-BG instrument unable to calculate parameter (see 'Discussion')	Not performed on hospital admission	Not performed on hospital admission	COHb 36.8	*First:* BG normal with no COHb measured *Second:* BG done 1 month after stopping HP smoking. ONLY COHb was measured (4.4)	COHb 3.8 Stopped HP smoking 2 months before hospital admission
Serum ferritin (20 - 300 ng/mL)	Not done	207	112	Not done	145	18	599
Erythropoietin (4.3 - 29 mIU/mL)	4.6	8.2	22	Not done	3.3	11.4	13.7

FBC = full blood count; RCC = red cell count; Hb = haemoglobin; Hct = haematocrit; MCV = mean cell volume; WCC = white cell count; BG = blood gas; COHb = carboxyhaemoglobin; HP = hookah pipe.
*Reference range for COHb: non-smokers 0.5 - 1.5%; smokers 1 - 2 packs/day 4.0 - 8.0%, >2 packs/day 8.0 - 9.0%; toxic >20%, lethal >50%.

Table 3. Radiological investigations

Investigation	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
CT scan	CT chest angiogram: small filling defects in descending pulmonary arteries suggestive of thromboemboli	Not performed	Not performed	Not performed	Not performed	Not performed	Not performed
CXR	Not performed	Not performed	Not performed	Not performed	Hyperinflation, prominent vessels in pulmonary hilum, coarse bronchovascular markings in lung bases	Normal findings	Normal findings
Venous Doppler US	Not performed	Not performed	Not performed	Positive for DVT	Not performed	Not performed	Not performed
Abdominal US	Normal spleen size	Normal spleen size	Normal spleen size	Not performed	Normal spleen size	Normal spleen size	Normal spleen size

CT = computed tomography; CXR = chest radiograph; US = ultrasound; DVT = deep-vein thrombosis.

Radiological investigations (Table 3) confirmed the thromboembolic events in 2 patients (patients 1 and 5). The chest radiographs performed indicated normal lung features in 2 of the patients, and showed hyperinflation with prominent hilar pulmonary vessels in 1 patient.

No causes of secondary polycythaemia other than HP smoking were identified.

Discussion

The patients in this series illustrate the potential adverse effects of HP smoking, which include acute carbon monoxide intoxication, thromboembolic events, and secondary polycythaemia.

Carbon monoxide toxicity

The secondary polycythaemia caused by HP smoking develops as a result of tissue hypoxia from chronic exposure to elevated levels of carbon monoxide (CO). CO is a product of the ignited charcoal used to heat the tobacco in the water pipe, and studies have shown plasma levels of carboxyhaemoglobin to be 10 times higher than those observed in cigarette smokers.[16]

Acute CO intoxication is also a possibility. This is associated with a left shift of the oxygen-dissociation curve due to hypoxia. The elevated CO levels cause mitochondrial dysfunction at a cellular level, resulting in myocardial and neuronal necrosis.[17] This process explains the acute cardiac and neurological symptoms that patients develop. Symptoms and signs can be nonspecific and include loss of consciousness and confusion, headache, malaise and nausea. Severe cases may result in seizures, coma, acute myocardial ischaemia and ventricular arrhythmias.[7,16]

The carboxyhaemoglobin levels measured in our case series were quantified on a point-of-care instrument available at Lancet Laboratories, using a lithium heparinised whole-blood sample transported on ice to the laboratory.[18] The carboxyhaemoglobin level is a calculated parameter, calibrated on the point-of-care instrument, and is part of the co-oximetry function of the blood gas instrument. Availability of this function should be confirmed with the laboratory used. Co-oximetry evaluates the total haemoglobin and determines the percentage of functional (e.g. oxyhaemoglobin) and dysfunctional haemoglobin species such as carboxyhaemoglobin and methaemoglobin.[18] Heparinised syringes and blood tubes can be used for blood gas and carboxyhaemoglobin analysis using small volumes (microlitres) of arterial, venous or capillary blood, but are subject to pre-analytical and analytical variables.[19] These blood samples are stable at room temperature for up to a month at 22°C and refrigerated for several years at 4°C.[20,21]

Thromboembolic risk

Although our cohort is small, 2 of our patients (28%) presented with a VTE (pulmonary emboli and lower-limb deep-vein thrombosis). Secondary polycythaemia from any cause has been associated with an increased risk of thrombosis. In addition, acute exposure to HP smoke in animal models demonstrated platelet activation and thrombogenesis.[11,16]

Secondary polycythaemia

Erythrocytosis results in increased blood viscosity. Symptoms of hyperviscosity include headaches, visual disturbances, dyspnoea, abnormal bleeding and severe neurological fall-out such as seizures and coma. These symptoms are alleviated by therapeutic venesection.[16]

Other adverse effects

Non-haematological effects associated with HP smoking include nicotine addiction; exposure to other carcinogens; infection risk (e.g. SARS-CoV-2, herpesvirus, Epstein-Barr virus) by means of a shared mouthpiece, as well as the water in the bowl of the HP apparatus acting as a reservoir for bacterial, mycobacterial and fungal growth; oral and gastrointestinal sequelae such as periodontal disease and oesophageal reflux disease; and cardiovascular and/or cardiopulmonary changes akin to those described with cigarette smoking.[6,7,22,23] Effects in pregnancy have been documented to increase the risk of intrauterine growth restriction and preterm labour.[11,24]

The perceived harmlessness of HP smoking has resulted in children, adolescents and young adults of all socioeconomic backgrounds increasingly adopting this dangerous but seemingly socially acceptable practice. In view of these misconceptions, there is a need for increased public awareness and education on the adverse effects of HP smoking to prevent an additional burden on our already pressured healthcare system.[23-26]

Teaching points

- HP tobacco products do not appear to be under the same regulatory scrutiny as traditional tobacco products, which requires review.
- HP-related polycythaemia should be considered in the younger patient with nonspecific symptoms.
- Recreational history is important. Smoking is no longer limited to cigarettes, and a full smoking history should include HP smoking. A calculator for HP pack-year history is available online.[12]
- In the event of a thromboembolic presentation, exclusion of polycythaemia is recommended in addition to eliciting the traditional risk factors and family history.
- A formal carboxyhaemoglobin measurement, or blood gas co-oximetry that is quality controlled, is recommended in the evaluation of polycythaemia, together with the patient history.

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