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Evaluation of the Effects of PAKDAM, an Invented Device to Get Nitrous Oxide and Oxygen, in the Consumers: A Report of Pilot Study

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Background: Since last decade, a device called PAKDAM (means clean inspiration) was invented in Iran which has been used in some cafe to prepare N_2O and O_2 as a new instrument instead of using water pipe. This study aimed to evaluate the respiratory and health effects of Pakdam and investigate its short and midterm side effects in users.

Materials and Methods: In a case-control pilot study between September 2021 and March 2022, 152 individuals were divided into two groups: 76 consumers (case) and 76 non- consumers (control). Both groups were divided into two groups of 36 smokers and 36 non-smokers. Participants signed the participation form and filled out the demographic data questionnaire, and then their vital signs, O_2 saturation, expiratory CO, and spirometry tests were recorded.

Results: The subjects who used the device had a mean blood pressure of 123.71±16.11 mmHg, oxygen saturation of 97.2±1.9, exhaled carbon monoxide of 9.8±5.5, and an FVC / FEV1 ratio of 88.5±7.9. These figures in control group were (137.79±18.15) - (94.1±4.2) - (14.3 ± 9.3) and (83.9 ± 10.4), respectively. In addition to the effects on the respiratory system, consumers had lower heart rates and lower systolic and diastolic blood pressures.

Conclusion: The blood oxygen level and FEV1/FVC ratio were higher in subjects using Pakdam and the amount of exhaled carbon monoxide and blood pressure were lower. This condition was more common in smokers and less in non-smokers. It is possible to see the favorable effects of using Pakdam device on people especially in smokers.

Keywords: Water pipe; Oxygen; Nitrous Oxide (N_2O)

INTRODUCTION

Nitrous oxide or N_2O gas, also known as laughing gas or sweet air, has been used since the mid-seventeenth century. It took about a hundred years to be obtained purely by Joseph Priestly in 1774. At that time, this gas was used for entertainment in parties, but in 1800, Sir Humphry Davy mentioned the properties of N_2O and its efficiency in surgery for pain relief until late 19th century. Horace Wells realized its analgesic effect in dentistry but unfortunately could not prove his discovery (1). Twenty years later, Gardner Quincy Colton reduced the risk of subsequent death by adding oxygen to N_2O gas, reporting 25,000 successful use cases (2).

Oxygen therapy is offered as a method of respiratory care when there is a respiratory problem. In this method, oxygen flow is delivered to the patient's vital organs with a

higher concentration than usual. The lungs normally absorb oxygen from the air. However, some diseases and circumstances may prevent getting enough oxygen. Oxygen therapy ensures better and more active function. Oxygen concentrators (sometimes known as oxygen generators) are devices that absorb room air through filters that remove dust, bacteria, and other particles (3).

Nitric oxide is an N-methyl aspartate receptor antagonist which reduces chronic postoperative pain. Its analgesic mechanism has been confirmed by the release of endogenous endorphins at the supraspinal level and the inhibition of NMDA receptors in the spinal cord. The analgesic effects start at a concentration of 20 to 30% and can continue without increasing severe unconsciousness by increasing the concentration to 70%, which is the limit of anesthesia. However, not paying attention to the time and environment and difficulty in remembering recent events that occur at this rate of consumption, will make patients satisfied with this pain-killing method (4).

The use of this combination in dentistry, obstetrics, gynecology, and during general anesthesia in combination with other anesthetic agents was welcomed. Its advantages include analgesic and amnesia properties, rapid induction and healing properties, reducing the need for other anesthetic agents, and being non-flammable (5). Systematic studies on the effectiveness of this gas in analgesia and anti-anxiety in childbirth showed that the combination of N_2O and O_2 led to a reduction in labor pain, greater patient satisfaction, and a request for its use in future deliveries (6, 7).

In several hospitals, this combination has been used to tranquilize children in minor and painful treatments. The major advantage of this combination was the shorter recovery time for patients compared to other active drugs. Besides, no serious complications were reported in these children (8).

The first clinical trial of N_2O in refractory major depression was based on the amazing efficacy of ketamine in providing rapid antidepressant effects, even in patients who failed several antidepressant treatments known as refractory depression. Ketamine and N_2O exert their antidepressant effect by inhibiting N-methyl-D-aspartate (NMDA) glutamate receptors. The antidepressant effect of N_2O occurs immediately and persists after gas administration (9-11).

About a decade ago, a device called PAKDAM (means clean inspiration) was invented in Iran and was used in some café to prepare N_2O and Oxygen as a new hobby instead of water pipe (Appendix 1-3). (12, 13)

Mechanism and Structure of Pakdam Device

In Pakdam device, an oxygen source is installed instead of tobacco product. Using this device, instead of releasing carbon dioxide and tobacco into the air, oxygen is released creating clean air in the surrounding places.

Pakdam consists of three parts:

Balloon: In the upper part of the fireplace, there is a balloon that is attached to the oxygen capsule and adjusts the amount of oxygen consumption.

Oxygen hose: The oxygen transport tube from the balloon to the water source is made of nylon, steel or bronze which is not oxidized by oxygen.

Water jar: The water jar increases the moisture of oxygen and can be used by adding essential oils or essences of mint, basil, cactus, or eucalyptus for flavoring and respiratory health.

How the device works:

This device is similar to ordinary hookahs. It contains a water jar in which oxygen is moistened before leaving the device and is directed to the hose. The water temperature can be adjusted to release hot or cold steam.

The balloon has a capacity of 4 liters which simulates the lung. In this balloon, oxygen is mixed with N_2O through a mixer. This inlet capacity is adjustable and there is no other compartment for oxygen to enter the balloon. The hose is similar to a hookah hose. With each suction oxygen enters the mouth and lungs of the consumer. No smoke is generated or emitted from this balloon. N_2O output percentage and lung capacity are determined by the

mixer. The air leaving the balloon gets enough moisture to pass through the water jar.

There is a safety valve in the mixer path. Whenever the oxygen gas in the balloon runs out, the N_2O outlet closes automatically and N_2O is not used alone. Besides, the percentage and rate of N_2O output is adjustable. The amount of N_2O output cannot be manipulated or changed by the consumer and just the physician or the trained operator can adjust the output. However, oxygen can be adjusted and increased. This compartment has been approved by the Food and Drug Administration of the Iranian Ministry of Health (12). The goal of this study was to evaluate the effects of Pakdam and investigating short and midterm side effects in users.

MATERIALS AND METHODS

It was a case-control study which was done between September 2021 and March 2022. Subjects were divided into two groups: consumers (case) and non- consumers (control). In terms of smoking, both groups were divided into two groups (according to Figure 1). For the pilot study, it was decided to evaluate 38 subjects in each group and the whole 152 subjects. Adaptation was considered in 4 groups based on random selection, homogeneity of age and sex, social status, and medical history.

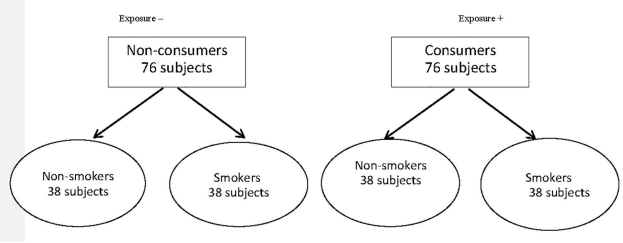

Figure 1. Case control study flow

Inclusion criteria:

Willingness for participation, having no disease, no medication, the smoking status: in the group of consumers for at least 1 year and once a week and in the group of smokers for at least 1 year with 10 cigarettes per day or once a week for hookah users.

Subjects who were found at Pakdam cafes, read and signed the participation form and filled out the questionnaire. Demographic data and survey questions about the device were collected and vital signs were recorded. Subjects were justified about the respiratory test and an appointment was made for each subject to attend the Masih Daneshvari hospital. Subjects were referred on the appointed day and tests were performed.

Measured indicators: blood pressure, pulse rate, respiratory rate, oxygen saturation, expiratory CO, and spirometer test including FEV1 / FVC.

A relevant database was created and evaluated by SPSS software version 20. First, the case and control groups were matched based on demographic indicators while no significant difference was observed in the indicators. Then, the frequency of variables was reported and both groups were compared using independent chi-square and t-tests. In order to use the independent t-test, quantitative variables were examined using the Kalmogorov-Smirnov and Shapiro tests at a significance level of less than 0.05. If they were significant, instead of a t-test, its non-parametric equivalent, the Mann-Whitney test, was used. Also, a generalized linear regression model was used.

RESULTS

Totally, 76 subjects were included in both case and control groups according to Pakdam device consumption. 38 subjects in 4 groups (according to smoking status) were divided into case and control groups. Information about demographic indicators and comparison of case and control groups are given in Table 1. No significant difference was observed between case and control groups regarding these indicators.

To compare the variables of systolic and diastolic blood pressure, oxygen saturation, expiratory carbon monoxide, and FEV1 to FVC ratio, Kalmogorov-Sperenov normality test was performed. Then, the non-parametric Mann-Whitney test was conducted. Since the normality results allowed the comparison of the two groups, this was done

using the independent t-test, the results of which are shown in Table 2.

In addition, a comparison of the two groups based on smoking status using the independent t-test can be seen in Table 3. Blood pressure and exhaled carbon monoxide were significantly lower in consumers while the FEV1/FVC ratio and oxygen saturation were higher. In the case group (consumers), it was observed that in smokers, exhaled carbon monoxide and FEV1/FVC ratio had a less increase (Table 4). Regression analysis in Table 5 shows that oxygen saturation and FEV1/FVC ratio are higher in smokers using the device.

Table 1. Frequency and comparison of case and control groups of Pakdam study

	Variable	Control Numbers (% - mean)	Case Numbers (% - mean)	Significance
Gender	Male	57 (52.3)	52 (47.7)	0.472
	Female	19 (44.2)	24 (55.8)	
age		76 (28.3±9.8)	76 (28±8.3)	0.83
Occupation	Employee	15 (40.5)	22 (59.5)	0.616
	Self-employment	32 (50)	33 (50)	
	Student	12 (52.2)	11 (47.8)	
	Housewife	2 (66.3)	1 (33.3)	
	Other	14 (60.9)	9 (39.1)	
	Missing	1	0	
Education	High school	16 (72.2)	6 (27.3)	0.056
	High school diploma & BA degree	47 (43.9)	60 (56.1)	
	Over BA degree	13 (56.5)	10 (43.5)	
	Missing	0	0	
Monthly income	Less than 100 million IRR	40 (48.2)	43 (51.8)	0.88
	100-150 million IRR	20 (44.4)	25 (55.6)	
	More than 150 million IRR	8 (50)	50 (8)	
	Missing	8	1	

Table 2. Independent t-test to compare blood and respiratory indices according to Pakdam device consumption

Group Statistics						
	Pakdam	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**Sig**
Systole	1.00	76	123.9342	16.14132	1.85154	0.00
	2.00	76	137.0395	18.72214	2.14758	
Diastole	1.00	76	71.7105	11.63307	1.33441	0.00
	2.00	76	79.0132	15.52073	1.78035	
HR	1.00	76	83.0789	14.35434	1.64656	0.09
	2.00	76	79.1974	14.45270	1.65784	
O2saturation	1.00	76	97.2632	1.94846	.22350	0.00
	2.00	76	94.1184	4.20782	.48267	
PICO	1.00	76	9.8816	5.57845	.63989	0.00
	2.00	76	14.3684	9.33216	1.07047	
FEV1	1.00	76	81.1447	7.53428	.86424	0.017
	2.00	76	77.8684	9.17728	1.05271	
FVC	1.00	76	91.6447	2.78426	.31938	0.00
	2.00	76	92.8026	2.28631	.26226	
Ratio FEV1/FVC	1.00	76	88.5559	7.90355	.90660	0.00
	2.00	76	83.9969	10.45023	1.19872	

1 = Consumer; 2 = Non-consumer

Table 3. Independent t-test to compare blood and respiratory indices according to smoking status

	Group Statistics					Sig
	Smoker	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	
Systole	Yes	76	134.0395	21.33132	2.44687	0.01
	No	76	126.9342	14.74705	1.69160	
Diastole	Yes	76	79.2237	15.56971	1.78597	0.00
	No	76	71.5000	11.42804	1.31089	
HR	Yes	76	86.5526	13.46640	1.54470	0.00
	No	76	75.7237	13.48342	1.54665	
O2saturation	Yes	76	93.9474	3.78733	.43444	0.00
	No	76	97.4342	2.45132	.28119	
PICO	Yes	76	18.3553	5.70311	.65419	0.00
	No	76	5.8947	4.14915	.47594	
FEV1	Yes	76	72.9211	5.56121	.63791	0.00
	No	76	86.0921	5.25402	.60268	
FVC	Yes	76	92.1579	2.63845	.30265	0.75
	No	76	92.2895	2.58620	.29666	
Ratio	Yes	76	79.2096	6.65368	.76323	0.00
	No	76	93.3431	6.05990	.69512	

Table 4. Independent t-test to compare blood and respiratory indices in the case group (with Pakdam device) according to smoking status

	Group Statistics					Sig
	Smoker	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	
Systole	Yes	38	126.0526	16.64729	2.70055	0.25
	No	38	121.8158	15.54915	2.52240	
Diastole	Yes	38	72.8421	12.47381	2.02352	0.40
	No	38	70.5789	10.77442	1.74784	
HR	Yes	38	85.4211	14.13952	2.29373	0.15
	No	38	80.7368	14.36904	2.33097	
O2saturation	Yes	38	96.7895	2.02895	.32914	0.03
	No	38	97.7368	1.76580	.28645	
PICO	Yes	38	14.3158	3.94630	.64017	0.00
	No	38	5.4474	2.66810	.43282	
FEV1	Yes	38	75.5000	5.82979	.94572	0.00
	No	38	86.7895	3.95350	.64134	
FVC	Yes	38	91.1316	2.79160	.45286	0.10
	No	38	92.1579	2.71658	.44069	
Ratio	Yes	38	82.8987	6.48416	1.05187	0.00
	No	38	94.2130	4.34049	.70412	

Table 5. Evaluation of the effect of Pakdam consumption on the studied factors, separately for two smokers groups, using the generalized linear regression model GLM at a significance level of 0.05

Dependent Variable: Ratio FEV1/FVC

Smoker 100		B	Std. Error	t	Sig.	95% Confidence Interval		Partial Eta Squared
						Lower Bound	Upper Bound	
Yes	Intercept	75.520	0.902	83.759	0.000	73.724	77.317	0.990
	[pakdam2=1.00]	7.378	1.275	5.786	0.000	4.838	9.919	0.312
	[pakdam2=2.00]	0[a]						
No	Intercept	92.473	0.979	94.430	0.000	90.522	94.425	0.992
	[pakdam2=1.00]	1.740	1.385	1.256	0.213	-1.020	4.499	0.021
	[pakdam2=2.00]	0[a]						

Dependent Variable: O2 Saturation

Smoker 100		B	Std. Error	t	Sig.	95% Confidence Interval		Partial Eta Squared
						Lower Bound	Upper Bound	
Yes	Intercept	91.105	0.405	224.791	0.000	90.298	91.913	0.999
	[pakdam2=1.00]	5.684	0.573	9.917	0.000	4.542	6.826	0.571
	[pakdam2=2.00]	0[a]						
No	Intercept	97.132	0.397	244.522	0.000	96.340	97.923	0.999
	[pakdam2=1.00]	0.605	0.562	1.077	0.285	-0.514	1.725	0.015
	[pakdam2=2.00]	0[a]						

DISCUSSION

In this study, it was found that blood oxygen level and FEV1 / FVC ratio were higher in people using Pakdam and the amount of exhaled carbon monoxide was lower. This condition was more common in smokers and less common in non-smokers. It can be considered that the desired effects of the device were greater for smokers.

Due to the innovation of this device, there are limited similar studies on it; so, it is not easy to compare the results. However, regarding the effect of oxygen and nitrogen on humans, available studies show similar results (3-6). As shown in Figures 2 and 3, the subjects who used the device had a mean blood pressure of 123.71±16.11, oxygen saturation of 97.2±1.9, exhaled carbon monoxide of 9.8±5.5, and an FVC / FEV1 ratio of 88.5±7.9. These results for people who did not use the device were (137.79±18.15) - (94.1±4.2) - (14.3 ± 9.3) and (83.9 ± 10.4), respectively. In addition to the effects on the respiratory system, consumers had lower heart rates and lower systolic and diastolic blood pressures, as seen in the study of Harford et al. and Djarova et al. (14, 15), which may be due to the effect of oxygen on the blood and vascular system.

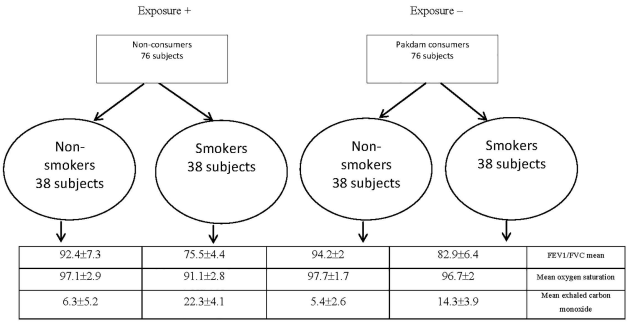

Figure 2. Results of respiratory indexes of subjects in terms of using Pakdam device and smoking status

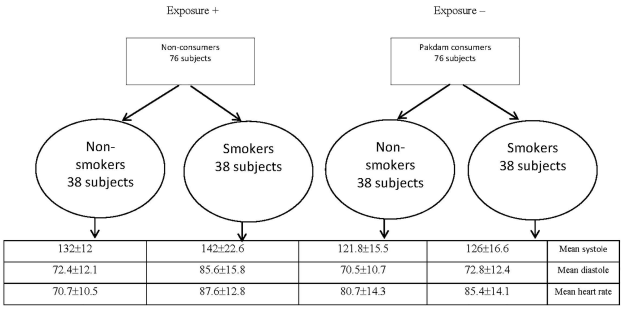

Figure 3. Results of blood indexes of subjects in terms of using Pakdam device and smoking status

Table 3 shows how important is the effect of smoking on the above indices: in smokers, blood pressure, exhaled

carbon monoxide, and heart rate are higher, while oxygen saturation and FEV1 / FVC ratio are lower. It is similar to the results of other studies (16- 17). However, when we compared these indicators in the case group in terms of smoking (Table 4), we found that smokers who used the device were in a healthier condition than smokers who did not use it because they had lower blood pressure, more oxygen, and higher FEV1 / FVC ratio. This means that the effects of Pakdam will be probably more in smokers, but this issue should be considered in further studies.

It was also observed that the mean FEV1 / FVC ratio in non-smokers who used the device was 94.21 ± 4.3, in non-smokers who did not use the device was 92.47 ± 7.7, in smokers who used the device was 82.9 ± 6.4, and in smokers who did not use the device was 75.5 ± 4.4. These findings could show the possible protective effects of Pakdam device on respiratory capacity.

Moreover, in the regression analysis, the effect of the device on the volume of FEV1 / FVC was significant and 7 times positive in the smoking group, while no difference was seen in the non-smoking group (Table 5). The same condition was observed for oxygen saturation in the smoker group so that the effect of the device was significant and 5 times positive.

Another point observed in this study was the possibility of replacing this device with Water pipe considering having the same shape and method of using and does not have the harmful effects of tobacco consumption. It may be investigated in a new study to be used as an alternative device to Water pipes in some public serving places. Nowadays, the demand for Water pipe smoking is increasing, and even given the implementation of tobacco control programs in many countries, this social and health problem still exists. Therefore, it is very critical to find a solution that can be a healthy alternative behavior to reduce or eliminate hookah smoking.

CONCLUSION

We saw that blood oxygen level and FEV1 / FVC ratio were higher in people using Pakdam and the amount of exhaled carbon monoxide was lower. This condition was more common in smokers and less in non-smokers. It can be considered that the desired effects of the device were greater for smokers. Considering the small sample size in this pilot study and to generalize the results, further studies should be conducted in larger sample sizes with different demographic variables.

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