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Research Article

Impact of Nyaope Use on Erectile Function of the Users: An Exploratory Study in Three Townships of Tshwane District, South Africa

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Abstract

The widespread abuse of Nyaope, a novel psychoactive substance (NPS) commonly used in South Africa, has become a major health and socio-economic challenge. Anecdotal evidence suggests that Nyaope use affects male sexual function. A cross sectional quantitative design was used to collect data from fifty adult men who use Nyaope to explore the impact of Nyaope on the sexual function of male users. The International Index of Erectile Function (IIEF-5) scale was used to assess sexual function and blood tests were conducted to assess gonadal function and hormonal levels. The duration of use of Nyaope ranged from 4 to 26 years, with a mean of 11.86. Ninety-two percent (n=46) of the participants reported some degree of erectile dysfunction. The mean score on the IIEF-5 scale was 13.52, which indicates mild to moderate erectile dysfunction. The use of Nyaope has a negative clinical and biochemical effect on male sexual function.

Keywords

Erectile Function, Moderate erectile dysfunction

1. Introduction and Background to the Study

The global increase in the use of psychoactive substances has also resulted in an increase in the introduction of cocktail, designer or novel psychoactive substances (NPS) on the recreational drug market. Novel psychoactive substances (NPSs) are recreational and illicit psychoactive substances that consists of various components mixed together [1]. Although the composition of NPSs varies, they have been found to be toxic to various organs and systems of the body [2-4] and their use is markedly motivated by access, habit and addiction. This category of substances is profiled by the continuous introduction of new compounds and diversity, and their names are area- specific [5]. Because there is limited data on their metabolism and toxicity [6], studies on their effects on organs and systems of the body remain continuous, which contributes to challenges for clinical management of the patients.

Nyaope is South Africa's version of NPS, and is commonly used in many black townships in South Africa. According to several media publications, it emerged in the early 2000s in Pretoria, specifically in Soshanguve and Mamelodi townships, and over the years, many young black and poor people have become addicted to the drug. In other provinces such as Mpumalanga and Limpopo it is known as "pinch" while in the Western Cape it is known as "unga", and "whoonga" in the Kwa-Zulu Natal province [7].

Nyaope has been found to contain several drugs and its ingredients vary from sources of sellers. Its main ingredient is low grade heroin, to which compounds such as caffeine, drugs of abuse like opiates, methyl-dioxy amphetamine (MDA), antibiotics, antiretroviral drugs, central nervous system depressants (like phenobarbitone and benzodiazepines), stimulants such as pipradol, and antitussive syrups like dextromethophan) are added [8,9]. The mixture is commonly distributed in powder form, wrapped with cannabis and smoked [1]. The latest trend is that an increasing number of users dissolve the mixture in water and inject it intravenously [10], with additional risks related to the spread of blood borne diseases and infections associated with the use of unsterilized needles.

Although the use of Nyaope is increasing, there is dearth of literature on its impact on physical health. However, anecdotal evidence from the users suggests that Nyaope has negative impacts on sexual function in men, specifically penile erection, which can be explained

by a previous study which found that nyaope use affects gonadal function in men [11]. Male sexual dysfunction is a complex entity that can result from multifactorial causes that can be psychogenic, organic, or both. Organic causes can be neurogenic, endocrinological and vasculogenic in origin [12]. Erectile dysfunction, which is defined as the inability to achieve or maintain an erection satisfactory for the completion of sexual activity, is among the most studied phenomenon in urology. Its prevalence on adult males is reported to be between 10% and 20% worldwide [13].

Because there is dearth of studies on the effects of Nyaope on erectile dysfunction, the purpose of this exploratory study was to explore the impact of nyaope on erectile function of adult males. As far as we know, this is the first study conducted with a specific aim to study this relationship. The current study is a subset of a broader study to determine the impact of nyaope on organs and body systems, and will thus contribute to the body of knowledge specific to male reproductive system.

2. Objective of the study

The purpose of this study was to assess erectile function amongst male Nyaope users.

3. Methodology

3.1 Study design

This study used a quantitative and cross-sectional design

3.2 Study setting

Study participants were recruited from Mabopane, Ga-Rankuwa and Ga-Rankuwa View, which are townships in the North of Pretoria, and they were transported to Sefako Makgatho Health Sciences University for data collection. These townships were selected because of a high prevalence of Nyaope use. In addition, the current study was part of a larger study about the health impacts of Nyaope, which is being conducted in the same communities.

3.3 Study population

The population consisted of adult men who were using Nyaope, and who reside in the identified communities.

3.4 Recruitment

A recruitment strategy previously used for the main study was repeated, where the research assistants approached Nyaope users from where they usually assemble. These places included shopping centres, parks, entrances of malls and/or taxi ranks. Potential participants were randomly approached and a brief explanation of the purpose and procedure of the study was given, following which they were requested to participate. Those who agreed to participate were then transported by a car to a data collection laboratory at Sefako Makgatho Health Sciences University where data collection took place. Initial screening to confirm nyaope use and the age of the participants was conducted at the place of recruitment.

3.5 Sampling and sample size

As this was an exploratory study, a sample of 50 was decided upon. This sample size was determined based on the costs of conducting the laboratory tests and the time of the principal investigator, who was a postgraduate student at the time of data collection. The sample of convenience was determined by the availability and willingness of users from the recruitment venues. Being an exploratory study in which a trend would be established, a sample size of 50 was used in order to explore the trend, the feasibility and viability of the study. The limited sample size was also informed by the exploratory phase of the study, and the costs of conducting the required tests. Men who were 18 years and older were recruited to participate in the study.

3.6 Inclusion criteria

Participants were screened for inclusion by both the research assistants during the recruitment process and the researcher at the data collection venue. Only participants who were 18 years of age or older, who were alert enough to understand the purpose and procedures of the study, and were able to provide informed consent were included in the study.

3.7 Data collection

On the day of data collection, each participant was confirmed to be eligible for participation by the research assistant. The purpose and process of the study was explained and the participant was given an opportunity to ask questions or seek clarifications. The informed consent process was administered, which was followed by data collection in the following sequence:

a) A researcher-developed demographic questionnaire was administered by the research assistants. This questionnaire included history of nyaope use and other socio-demographic variables.

b) The International Index of Erectile Function Questionnaire (IIEF-5) was completed by the participants with the assistance of the researcher.

c) Blood samples were collected from the participants, to measure testosterone, SHBG, Prolactin, LH, and FSH levels.

3.8 Data analysis

The socio-demographic data were descriptively analysed and presented as percentages and proportions.

The prevalence and severity of erectile dysfunction was calculated from the International Index of Erectile Function-5 scores. The International Index of Erectile Function Questionnaire (IIEF-5) consists of five questions, and each question has 5 options or responses for the patient or participant. It has a total cumulative score of 25, and the total score is used to classify the erectile functionality of the participants as follows:

A. Scores 22 to 25: normal erectile function

B. Scores 17 to 21: mild erectile dysfunction

C. Scores 12 to 16: mild to moderate erectile dysfunction

D. Scores 8 to 11: moderate erectile dysfunction

E. Scores 5 to 7: severe erectile dysfunction

Hormone levels were measured from the blood samples, and the levels of each hormone were classified, level frequencies were calculated and results were displayed using distributive charts, a graph and frequency tables. Multivariate analysis was performed to explore associations between presence of erectile dysfunction duration of Nyaope use, and levels of serum hormone.

4. Validity and Reliability of Results

The International Index of Erectile Dysfunction (IIEF) is a globally validated instrument for assessment of presence and severity of erectile dysfunction [14-16]. The validity and reliability of the blood analysis was enhanced by the use of the National Health Laboratory Services, which is a nationally accredited laboratory.

5. Ethical Considerations

The study obtained ethics clearance from the Research and Ethics Committee of Sefako Makgatho Health Sciences University. Permission to conduct the study was given by the management of DGMAH and all participants provided informed consent. The right to privacy was ensured by using codes that uniquely identified each participant, and this enabled the linking of the IIEF interview results and the blood results. Participants were compensated for their time with a food voucher after data collection was completed.

6. Results

6.1 Socio-Demographic Characteristics of Participants

A total of fifty male participants with ages that ranged between 19 and 42, and a mean of 30.7 years (SD 4.82) participated in the study. Fifty percent (n=25) of the participants resided in Ga-Rankuwa, 30% (n=15) in Mabopane and the remainder (20%) resided in Ga-Rankuwa-View. Fifty-six percent (n=28) of the participants had primary school education, 30% (n=15) received some form of secondary school education, and the rest had tertiary level education (14%). The majority (96%, n=48) were unemployed (96%), none were married and 56% (n=28) were in relationships (Table 1).

The duration of Nyaope use ranged from four to twenty-six years, with a mean of 11.86 years (SD: 5.11), and for those who previously attended substance abuse rehabilitation interventions, the average duration of sobriety was 5.2 months (SD: 5.57) before they relapsed. The rest of the information on substance use are shown on Table 2.

7. IIEF-5 Questionnaire Scores

Figure 1 below shows the presence and severity of erectile dysfunction in Nyaope users. The average erectile function score reported by users was 13.52, which indicated mild to moderate erectile dysfunction. Ninety-two percent (n=46) of the participants reported having erectile dysfunction. Fourteen participants (28%)

Table 1: Socio-demographic characteristics of the participants (n=50)

Variable	Category	Frequency (n)	Percentage (%)
Age			
	20-30	27	54
	31-40	22	44
	>40	1	2
	Total	50	100
Township			
	Ga-Rankuwa	25	50
	Mabopane	15	30
	Ga-Rankuwa view	10	20
	Total	**50**	**100**
Level of education			
	Primary	28	56
	Secondary	15	30
	Tertiary	7	14
	Total	**50**	**100**
Employment status			
	Employed	2	4
	Unemployed	48	96
	Total	**50**	**100**
Relationship status			
	Single	22	44
	In relationship	28	56
	Married	0	0
	Total	**50**	**100**

Table 2: Substance use related information of participants

Variable	Frequency	Percentage
Drug use in the family		
Yes	22	44
No	28	56
	50	**100**
Substances previously used		
Alcohol	12	24
Cigarettes	6	12
Cannabis	4	8
Heroin	4	8
None	24	48
	50	**100**
Substances co-using with nyaope		
Alcohol	9	18
Cigarettes	20	40
Cannabis	15	30
Cocaine	11	22
Mandrax	6	12
	50	**100**

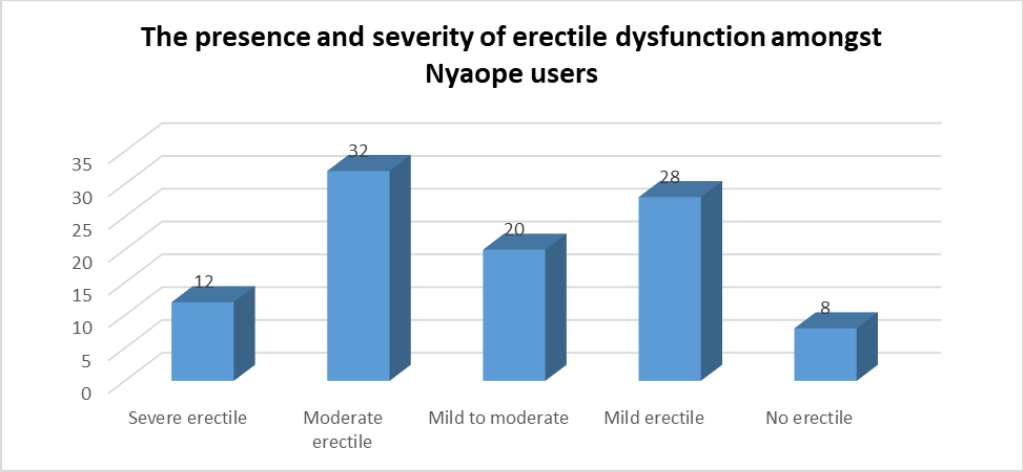

Figure 1: The presence and severity of Erectile Dysfunction amongst Nyaope users.

had mild erectile dysfunction. Ten participants (20%) had mild to moderate erectile dysfunction. Sixteen participants (32%) had moderate erectile dysfunction. Six participants (12%) had severe erectile dysfunction and four participants (8%) did not report erectile dysfunction.

8. Results of Hormone Testing

Table 3 below shows the results of hormonal levels of the participants for serum testosterone, sex hormone binding globulin and prolactin.

8.1 Testosterone (T)

Testosterone is available in the plasma in three different forms: free, albumin-bound and SHBG bound and it determines libido and sexual function [17]. The normal reference range (4.9-32.0 nmol/L) that was used to assess testosterone levels was advised by the NHLS. The study showed that nine (18%) of the fifty participants had low testosterone levels which denotes hypogonadism. Thirty-eight participants (76%) had normal testosterone levels. The mean testosterone level was 14.36 (SD: 9.63) which fell within the normal parameters for the 50 participants.

8.2 Sex Hormone Binding Globulin (SHBG)

Sex hormone binding globulin is a plasma protein and its function is to transport testosterone to its target organs. An increase in plasma levels of SHBG may result in the decrease of bioavailable (free) testosterone [18]. The normal reference range (17.1-76.6 n mol/L) which was used to assess SHBG levels was advised by the NHLS. Twenty participants (40%) had increased SHBG levels, while two participants (4%) had decreased levels of SHBG. The majority of the participants (56%) had serum levels within normal parameters. The calculated mean of the group was 69.14 n mol/L (SD: 31.59).

8.3 The presence and severity of ED with Testosterone, SHBG and LH levels

Table 4 shows the comparison of Testosterone, SHBG and LH and the IIEF scores that were obtained by interviews. Twenty participants (40%) had elevated SHBG and 17 of the 20 participants demonstrated various degrees of

Table 3: Comparison of the presence and severity of ED with hormone levels.

Testosterone				
ED Category	**Increased**	**Decreased**	**Normal**	**Total**
Severe	0	2	4	6
Moderate	1	3	12	16
Mild to moderate	0	2	8	10
Mild	2	1	11	14
No erectile dysfunction	0	0	4	4
Total	3	8	39	50
Sex hormone binding globulin				
ED Category	**Increased**	**Decreased**	**Normal**	**Total**
Severe	1	1	4	6
Moderate	5	0	11	16
Mild to moderate	5	1	4	10
Mild	6	0	8	14
No erectile dysfunction	3	0	1	4
Total	20	2	28	50
Prolactin				
ED Category	**Increased**	**Decreased**	**Normal**	**Total**
Severe	1	0	5	6
Moderate	7	1	7	16
Mild to moderate	6	1	4	10
Mild	8	1	5	14
No erectile dysfunction	1	0	3	4
Total	23	3	24	50

Table 4: Evaluation for ED and assessment of hormonal profile in participants with low testosterone levels.

Testosterone	SHBG	LH	ED Score
0.7	53	0.9	Moderate
1.6	71.8	2.5	Severe
1.7	56.3	1.9	Moderate
2.1	56.6	0.9	Moderate
2.8	46.6	6.3	Severe
3.3	4.3	1.5	MTM
3.3	32.8	3.3	MTM
3.6	26.4	1.9	Mild

erectile dysfunction. These findings are indicative of a positive correlation between high serum SHBG and erectile dysfunction.

8.4 Luteinising hormone (LH)

Luteinising hormone is a hormone produced by the pituitary gland which stimulates the Leydig cells in the testicles to produce testosterone. Decreased plasma levels of LH can lead to decreased production and secretion of testosterone in the testes and this may result in sexual dysfunction [17]. The normal reference range (0.6-12.1 IU/L) which was used to assess LH levels was advised by the NHLS. All the participants had normal plasma LH levels. The calculated mean was 3.65 IU/L (SD:2.17).

8.5 Follicle stimulating hormone (FSH)

Follicle stimulating hormone is a hormone that, together with LH, is produced by the pituitary gland under the influence of GnRH released by the hypothalamus. Both hormones act on the testes to induce its hormonal and spermatogenic function [17]. The normal reference range (1.0-12.0 IU/L) which was used to assess FSH levels was advised by the NHLS. The results showed that eight percent (8%) of the participants had increased FSH levels, whilst two percent (2%) had a decreased level. The majority (90%) had normal FSH levels. The calculated mean was 5.22 IU/L (SD:3.84).

8.6 Prolactin

Prolactin is a hormone produced in the pituitary gland. It plays an important role in the regulation of the immune system, metabolism and development of the pancreas. Although it has no definitive role in the physiological

control of human sexual behaviour, its increase may lead to the impairment of the pulsatile secretion of LH. This can result in the decline of testosterone secretion in the testicles and subsequently, sexual dysfunction [19,20]. The normal reference range (3.5-19.4 ug/L) that was used to assess prolactin levels was advised by the NHLS. The results showed that twenty-three (46%) of the participants had a raised prolactin level, three (6%) had decreased levels and twenty-four (48%) had normal prolactin levels. The mean prolactin value was 22.72ug/L (SD: 17.76) which was elevated.

Twenty-three (46%) participants had hyperprolactinemia and 22 (95.7%) of these participants demonstrated various degrees of erectile dysfunction ranging from mild to severe. These results are indicative of a positive correlation between increased serum prolactin levels and the presence of erectile dysfunction. Twenty-four (48%) of the participants had normal prolactin levels. Twenty-one (87.5%) of this sub-group had erectile dysfunction. Three participants (6%) had low serum prolactin levels and all of them showed various degree of erectile dysfunction.

8.7 Prolactin, LH and testosterone levels and erectile dysfunction

The results indicate that the hormone profile and erectile function scores tend to align with low testosterone levels (hypogonadism). Of the fifty participants, nine (18%) had hypogonadism. The participants with hypogonadism had normal serum SHBG and LH levels. However, all of them (n=9) showed various degrees of erectile dysfunction, as shown in Table 5.

8.8 Erectile function scores in participants with hyperprolactinemia

Twenty-three of the 50 participants had high serum prolactin levels (hyperprolactinemia). Various degrees of erectile dysfunction were present in 22 of these participants (95.6%). Low serum testosterone (hypogonadism) was only present in two of the participants with hyperprolactinemia. There were no abnormal serum LH levels in this sub-group. Both of these participants had erectile dysfunction. In all the participants with hyperprolactinemia, the serum LH levels were found to be normal.

8.9 Duration of nyaope use and hormonal levels

The duration of Nyaope use was positively associated ($p<0.05$) with an increase in serum Prolactin levels (95%CI, 0.337-0.623) and SHBG levels (95% CI, 0.375-0.642). On the other hand, the average duration of use of Nyaope was positively associated ($p<0.05$) with a decrease in serum testosterone levels (95% CI, 0.300-0.517). These findings reflected on Table 6.

9. Discussion

The ages of the participants in this study ranged from 19 to 42 years (mean 30.7 years, SD 4.8), with the majority being between 20 and 30 years. Although this could support previous studies that typify Nyaope users as young adults [21], 16% of the users in this sample were above 35 years of age, which suggests that the Nyaope using population is getting older and is not limited to young people. It is also important to note that users under the age of 18 were excluded from the study (due

Table 5: ED and hormonal profile of participants with elevated Prolactin.

Prolactin level	LH level	Testosterone level	ED score
28.4	1.9	6.9	Mild
32	3.5	>35	Mild
30.2	2.4	13.2	No ED
21.7	5	22.3	Severe
89	6.1	28.7	MTM
53.3	2.1	10.9	Mild
28.4	1.9	1.7	Mod
28.5	1.5	3.3	MTM
32.9	1.2	5.8	Mod
59.3	2.9	14.5	Mod
33.4	3.5	6.2	Mild
35.2	1.6	24.5	MTM
35	1.8	8.8	Mild
43	5.3	6.5	MTM
30.5	1.2	34.8	Mild
25.6	2.9	30.5	MTM
54.2	2	8.2	Mild
41.1	2.4	21.7	Mod
51.9	5.1	21.2	Mild
34.6	1.8	8.7	Mod
29.2	9.9	29.4	Mod
28.7	3.8	5.9	Mod
23.7	1.1	7.5	Mild

Table 6: Linear relationship between multiple variables.

Average duration of Nyaope use			
Hormone level	**p>t**	**95% (Confidence interval)**	**R-squared**
Testosterone	0.000	0.300-0.517	0.893
SHBG	0.00	0.375-0.642	0.896
Prolactin	0.00	0.337--0.623	0.887

to ethical considerations) because they could not provide informed consent. However, anecdotal evidence suggests that there are many users who are under the age of 18, which was confirmed by the participants reporting that they started using Nyaope and other drugs when they were teenagers. The vast majority were unemployed, which supports previous studies that the majority of nyaope users are unemployed, primarily because the drug has taken over their lives [1], which places them at risk of committing crime. The unmarried status of all the participants is also similar to other studies which reported that substance abusers are often unmarried or divorced [1,22]. A number of the participants used other substances, which is in contrast to the previous findings which found that the majority of Nyaope users [1].

Based on the IIEF scores, 92% (n=46) of the participants reported baseline erectile dysfunction, which suggests a high prevalence of erectile dysfunction among the sample, which is way above the global prevalence of 10 to 20% in the general population. This high prevalence of erectile dysfunction confirms previous findings which reported hypogonadism among nyaope users [11]. Although previous studies have reported that prolonged use of amphetamines and heroin were associated with erectile dysfunction [23,24], this study is the first to directly associate nyaope use with erectile dysfunction.

All the eight participants (16%) with hypogonadism (as indicated by low serum testosterone levels), showed various degrees of erectile dysfunction, which concur with the results of the study that reported that hypogonadism may lead to erectile dysfunction [19]. In humans, the direct physiological role of testosterone for erectile function is not clear and remains a topic of debate [25-28]. However, many studies on participants with both erectile dysfunction and hypogonadism demonstrated an improvement of the erectile dysfunction with testosterone replacement [29-31], which confirmed the significance of testosterone in the process of erections. This implies that although testosterone's role in erectile physiology is not well defined, it has an important role in the process of erection.

All of the participants with hypogonadism had normal levels of serum luteinising hormone (LH), which suggests that the low testosterone may be from hypothalamic pituitary failure (secondary hypogonadism). Other studies have reported that hypogonadism with normal serum LH levels is of a secondary nature [32], which implies that Nyaope may have negative impact on the hypothalamus or pituitary gland function. Contrary to findings that elevated SHBG could lead to low testosterone and result in erectile dysfunction [18,33,34], none of the participants in our study with low testosterone had elevated SHBG, implying that the hypogonadism in this study is not associated with elevated SHBG.

The results showed that 40% of the participants had elevated serum SHBG levels, and of these, 85% had some erectile dysfunction. This confirms previous findings that the use of caffeine, morphine and heroin is associated with elevated SHBG, which may result in decreased bioavailable testosterone [35]. Although the total testosterone levels were not decreased in participants who had elevated SHBG levels, the bioavailable testosterone was not calculated, which was one of the limitations of the study.

The majority of the study participants with hyperprolactinemia reported erectile dysfunction, despite the normal levels of their serum LH. Hyperprolactinemia may lead to the inhibition of most aspects of male sexual performance by impairing the rhythmic secretion of LH by the pituitary gland [17,19], which can result in the decline of serum testosterone levels. This suggests that the erectile dysfunction in these participants may not be associated with hypogonadism due to low LH secondary to hyperprolactinemia, but that their hyperprolactinemia could be causing erectile dysfunction via another mechanism or that the erectile dysfunction has an alternative pathophysiological cause. However, almost half of the participants (n=24) had normal prolactin levels and 91.7% of this sub-set had erectile dysfunction, which suggests an additional separate reason for erectile dysfunction in this population.

10. Conclusion

The majority of the participants of this study reported erectile dysfunction, which was corroborated by hormone testing, thus confirming that nyaope use is associated with erectile dysfunction, although the exact mechanism needs further investigation. The results therefore confirm that the use of Nyaope has negative clinical and biochemical effect on sexual function. Erectile dysfunction was largely detected amongst participants with hyperprolactinemia and hypogonadism. The study has therefore expanded areas of focus in the clinical treatment of nyaope users, and has contributed to the body of knowledge regarding the effects of nyaope use.

11. Limitations of the study

Bio-available testosterone levels were not calculated but total testosterone was used as a proxy for erectile function, which may have underestimated the presence of hypogonadism. As this was an exploratory study, a limited sample size of 50 was used.

12. Recommendations

It is recommended that a study with a larger sample size will better identify significant relationships between Nyaope use and erectile dysfunction, and that future studies make use of bio-available testosterone as it is a more accurate and reliable marker for the diagnosis of hypogonadism.

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