

Original Research Article

Effects of tobacco chewing habits on male infertility

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ABSTRACT

Background: It is the fact that, India consists of world's largest tobacco chewer population, more prevalent in low income group. The effects of tobacco chewing on semen parameters have been widely studied. The study aim is to analyze the semen analysis parameters (oligozoospermia, asthenozoospermia, teratozoospermia, oligo-asthenoteratozoospermia -OATS and azoospermia) of tobacco chewer and non chewer infertile patients.

Methods: A retrospective analysis of 639 patients was done out of which 150 were non-chewers and 489 were tobacco chewers. The percentage of population with particular semen abnormalities were compared between the two groups. The same comparison was performed between tobacco chewing primary infertility and secondary infertility patients in order to specifically assess the effect of tobacco chewing in sub-fertile patients.

Results: OATS and azoospermia cases were significantly higher in the tobacco chewing infertile patients as compared to oligozoospermia, asthenozoospermia and teratozoospermia cases. In case of sub-fertile patients also, the percentage of OATS and azoospermia were significantly higher.

Conclusions: This finding suggest that tobacco chewing greatly affects every parameter of sperm i.e. concentration, motility and morphology collectively. Moreover, tobacco chewing may be less affecting the male fertility initially but prolonged exposures affects detrimentally resulting in serious semen parameter abnormalities such as OATS and even azoospermia. And such cases are difficult to treat even with higher and advanced infertility treatment options like ICSI, microfluidics, etc. This reduces the chances of IVF success as well as increases the financial burden on the patients undergoing infertility treatment. Thus, infertility clinics must employ awareness programs for such patients to explain them the effects of tobacco chewing habit and reducing it can definitely enhance the treatment outcomes.

Keywords: Azoospermia, Male infertility, OATS, Semen parameters, Tobacco chewing

INTRODUCTION

The increase in infertility rates today can be correlated with the fact that sperm concentration in the semen of males having childbearing potential has decreased by more than 50% in the past 4 decades.¹

As per the estimates, 12-15% of sexually active couples are infertile and among the causes of infertility in the couples seeking for treatment, male infertility accounts for 40-50%. Around 25% of male infertility patients do not have a specific cause of infertility and these cases are mainly correlated with the incorrect lifestyle habits.² The

current trend of lifestyle includes drug addictions like alcohol, tobacco, heroin, cocaine and others, among which tobacco consumption can be tobacco smoking or tobacco chewing. Moreover, the burden of male infertility is more among the developing countries where the cause of male infertility is predominantly secondary due to high prevalence of drug addictions.³ Studies have been done proving the detrimental effects of heavy smoking and alcohol consumption on semen parameters.⁴

India, a developing country is the second largest producer as well as consumer of tobacco (both smokers and chewers) and it has world's largest tobacco chewers

population.⁵ About 28.6% population in India is tobacco addicted among which 10.7% are tobacco smokers while 21.4% are tobacco chewers.⁶ Tobacco use is considered as an epidemic causing major public health issues which also includes infertility, pregnancy complications, premature births, low birth weight infants, and stillbirths. Tobacco chewing has more addictive effect due to the presence of nitrosamines but it is less harmful than tobacco smoking.^{7,8} It is globally stated that tobacco use is more prevalent in low income population and in India, major population belongs to low income group showing high prevalence and extremely low quitting rates of this addiction.⁹ The use of tobacco generally starts in late adolescence and early adulthood (15 to 24 years of age) due to social impact, peer pressure, career stress which indirectly affects them in reproductive age. Moreover, it is demonstrated that male infertility is more affected by tobacco use than female infertility.¹⁰

Chewing tobacco consists of coarsely crushed tobacco leaf, which is mixed slacked lime paste, areca nuts (pan, gutka and mishri) and consumed, the dissolved tobacco content is then taken up by the gums and soft tissues of mouth. Some of the potent carcinogens present includes N-nitrosamine, N'-nitrosornicotine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and 3-methylnitrosaminopropionaldehyde which have shown many detrimental effects.¹¹

Several studies have shown the negative effects of tobacco chewing on semen quality while some studies have shown no association.¹²⁻¹⁸ Since last decade authors have witness increase in population of male infertility patients as well as tobacco chewers. A study was done in Gujarat state indicated the prevalence of tobacco use in self-employed and low educated population in rural areas.¹⁹ In the present study, we have investigated the cases of male infertility patients visiting our clinic situated in Surat city of Gujarat state. The primary objective of the present study is to compare the semen analysis parameters between tobacco chewers and non-chewers. And secondary objective is to compare the semen analysis parameters between tobacco chewing primary infertility and secondary infertility patients in order to specifically assess the effect of tobacco chewing habits in sub-fertile patients.

METHODS

A retrospective study including semen analysis reports of patients visiting the infertility department from January 2015 to December 2019 was performed. Addiction history of each patient was analyzed from the questionnaire given during the semen analysis test. The addiction detail includes the duration, quantity and frequency of tobacco chewing by the patient. Patients with other addiction habits along with tobacco chewing were excluded. Also patients diagnosed with diabetes mellitus, hernia, varicocele, hydrocele and any other infection were excluded. All the patients provided written

informed consent and ethical approval was obtained from institutional ethics committee. Semen analysis was performed manually by trained andrologist as per the standard WHO 2010 guidelines.²⁰ Sample collection was done by masturbation and sexual abstinence of 3-5 days was confirmed. Sperm counting and motility assessment were done using Makler's chamber (Ast Meditech, India). Sperm morphology assessments were done by Diff-Quik (Hi-Tech Solutions, India) following the standard protocol.²⁰

The patients were divided as control group (non - tobacco chewers) and test group (tobacco chewers). The patients were characterized into normozoospermia, oligozoospermia, asthenozoospermia, teratozoospermia, oligo-astheno-teratozoospermia and azoospermia as per the standard WHO guidelines described in Table 1.

Table 1: Semen Analysis Parameters as per the WHO 2010 guidelines.²⁰

Terminology	Description
Oligozoospermia	Sperm concentration ≤ 15 million/ml
Asthenozoospermia	Sperm Progressive Motility $< 32\%$
Teratozoospermia	Sperm Normal Morphology $< 4\%$
Oligo-astheno-teratozoospermia (OATS)	All the above three parameters
Azoospermia	No sperm detected
Normozoospermia	Normal Sperm Parameters

Comparative study was done between the control and test group in percentage of patients showing different semen parameters. Specific study to compare the semen parameters of patients with primary infertility and secondary infertility in the tobacco chewing population was also done.

RESULTS

A total of 639 patients were included in the study. The patient age ranged from 21 to 48 years. The control group included 150 patients while the test group included 489 patients. A further analysis of the addiction details was not recommended as many responses to the questionnaire were incomplete, inconsistent and not reliable. The primary and secondary infertility patients in the control and test group were compared. The control group consists of more of primary infertility patients than in the test group as summarized in Table 2.

Semen parameters between test and control groups were compared and summarized in Table 3. The normozoospermia and oligozoospermia cases were higher in control group than in the test group. The asthenozoospermia cases were comparable between both

the groups. The OATS and azoospermia cases were significantly higher in the test group compared to the control group.

Table 2: Primary and secondary infertility patients in control and test group.

	Control group	Test group
Primary infertility	83%	64%
Secondary infertility	17%	36%

Table 3: Comparison of semen parameters between control and test group.

Terminology	Control group (n = 150)	Test group (n = 489)
Normozoospermia	53.7%	31.3%
Oligozoospermia	22.8%	12.3%
Asthenozoospermia	10.3%	11.9%
Teratozoospermia	7.5%	12.9%
Oligo-astheno-teratozoospermia (OATS)	4.3%	21.8%
Azoospermia	1.4%	5.8%

Excluding the control group patients, comparison of semen parameters between primary infertility and secondary infertility patients of the test group was done as summarized in Table 4. Oligozoospermia, asthenozoospermia and teratozoospermia cases were higher in primary infertility patients. And OATS and azoospermia cases were significantly higher in secondary infertility patients.

Table 4: Comparison of semen parameters between primary and secondary infertile patients.

Terminology	Primary infertility group	Secondary infertility group
Oligozoospermia	30.9%	18.6%
Asthenozoospermia	35.1%	17%
Teratozoospermia	5.2%	3.5%
Oligo-astheno-teratozoospermia (OATS)	18.3%	34.6%
Azoospermia	10.5%	26.3%

DISCUSSION

In the present study, a comparison was made with respect to the percentage of patients with abnormal semen parameters in the total population. This gives a proper idea about distribution of the specified abnormal semen parameters on a broader perspective.

In the tobacco chewers group the secondary infertility cases were higher which may indicate that prolonged habit of tobacco chewing affects the male fertility. The

OATS and azoospermia cases were significantly higher in the tobacco chewing population as compared to oligozoospermia, asthenozoospermia and teratozoospermia cases. This suggests that the tobacco chewing greatly affects every parameter of sperm i.e. concentration, motility and morphology collectively. If we compare the semen parameters individually, oligozoospermia cases are less while asthenozoospermia and teratozoospermia cases are higher in the tobacco chewing population. A unique pattern is revealed while comparing the primary and secondary infertility patients in the tobacco chewing population, the cases of OATS and azoospermia were significantly higher in the secondary infertile patients. This may suggest that tobacco chewing may be less affecting the male fertility initially but prolonged exposures affects detrimentally resulting in serious semen parameter abnormalities such as OATS and even azoospermia. The cases of OATS and azoospermia are more difficult to treat even employing latest infertility treatment option like ICSI, TESA-PESA.

The main component in tobacco i.e. nicotine has shown to affect the sperm plasma membrane and genetic integrity, also as demonstrated in our study a higher incidence of teratozoospermia in tobacco chewers has been seen.²¹ A defective sperm with respect to its morphology and genetic integrity not only affects normal potential to fertilize the ovum but it can also cause delayed fertilization, abnormal embryo development and increase the chances of spontaneous abortion when highly advanced treatment like intra-cytoplasmic sperm injection (ICSI) is employed as infertility treatment option.²²⁻²⁴ A study has demonstrated the adverse impact of tobacco chewing on sperm morphology (mainly defects in head and cytoplasmic residue) in intensive chewers and also some in mild chewers. Moreover, the normozoospermic tobacco chewer patients showed higher number of morphological abnormalities.²⁵

Many studies have been reported explaining the possible mechanism of detrimental effects of tobacco on sperm parameters. Disturbed hypothalamus-pituitary axis causes reduced testicular microcirculation of testosterone resulting in impaired Leydig cell function, increase in norepinephrine and decreased sperm counts.²⁶⁻³⁰ Mitochondrial genome damage and disturbed mitochondrial enzymatic activities results in impaired seminal vesicle function, prostate function, epididymis function and compromised sperm motility.³¹ It is predicted that certain chemical may cause abnormal development of Golgi body in pro-acrosome and improper attachment to nucleus forming defective head with irregular or absent acrosome in head of the sperm.²⁵ Direct inhibition of primary maturation of germ cells has also been reported.³² Effects of reactive oxygen species have been broadly studied and tobacco chewing also leads to oxidative stress and DNA damage.³³

The treatment for infertile patients along with female parameters mainly depends on the male semen

parameters. As we know, if semen parameters are good, simpler infertility treatment options like intrauterine insemination (IUI) can also help the couple. But compromised semen parameters left the couple with more advanced treatment options like IVF, ICSI which indirectly increases the financial burden on the couple. Many different techniques are still under research for selection of best morphologically normal sperm for ICSI and increasing the chances of success rates.³⁴

CONCLUSION

Tobacco chewing habits has detrimental effects on male infertility as per our study done for the patients visiting our clinic. More studies including larger and geographically distributed patient population must be conducted to make stronger conclusions. It is evident from this study that prolonged tobacco chewing habits leads to serious abnormalities in semen parameters like OATS and azoospermia. And such cases are difficult to treat even with higher and advanced infertility treatment options like ICSI, microfluidics, etc. This reduces the chances of success as well as increases the financial burden on the patients. Thus, infertility clinics must employ awareness programs for such patients to explain them the effects of tobacco chewing habit and reducing it can definitely enhance the treatment outcomes.

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