

Drug Corner

Consensus Statement : The Need for Tobacco Harm Reduction in India

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Cigarette smoking is a major public health issue in India and leads to significant morbidity and mortality. Addressing the issue of smoking is a major challenge to public health, as the addiction is hard to break. Counseling smokers regarding smoking cessation is the first step to achieving cessation, but the quit rates remain low. Several pharmacological interventions have been developed over the years. Nicotine replacement therapy is available in a variety of formulations, each with different advantages, drawbacks, acceptability among smokers and quit rates. In addition, a range of novel nicotine and tobacco products, including Heated Tobacco Products (HTPs), have been developed which leverage nicotine to aid in smoking cessation. A group of medical experts convened to review the evidence on the burden of smoking, the concept of Tobacco Harm Reduction (THR), novel nicotine and tobacco products for THR, and the potential of HTPs to aid in smoking cessation. This paper outlines the findings and recommendations regarding THR in the Indian context. The panel opined that tobacco cessation centers and counseling remain the foundation of tobacco cessation in India. At the same time, there appears to be potential for the application of THR products in India. The relevant authorities must review the potential of THR products, and make these available, to provide the best possible cessation strategy for the Indian population that is currently at risk of mortality and severe morbidity.

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Key words : Cigarette smoking, Nicotine, Tobacco, Tobacco harm reduction, Heated tobacco products, Novel nicotine, Tobacco products.

The epidemic of smoking looms large over the Indian population, with millions of adult smokers at risk of developing life-threatening diseases. Overcoming the nicotine addiction is the key to preventing morbidity and mortality associated with smoking¹. Several modalities are available to aid in smoking cessation, including non-pharmacological and pharmacological therapies. These have varied acceptability among smokers, and varied efficacy of cessation and impact on risk of disease^{2,3}. Over the years, a number of Nicotine Replacement Therapies (NRTs) have been introduced as smoking cessation aids⁴. In addition, a class of Noncombustible Nicotine and Tobacco Products (NNTPs) has been developed, which present lower health risks than conventional cigarettes⁵. A process of regulatory approval is required before

introduction of any smoking cessation interventions, which follows a thorough review of the science of a given intervention. Products such as electronic cigarettes (e-cigarettes) and heated tobacco products (HTPs) are not approved for use in India, thus depriving the at-risk groups from potentially life-saving therapies. The consensus statement presented in this paper describes the opinion of Tobacco Harm Reduction (THR) products of a panel of experts, in the Indian context.

Methodology :

A group of medical experts convened to review the evidence on the burden of smoking, the concept of Tobacco Harm Reduction (THR), novel nicotine and tobacco products for THR, and the potential of Heated Tobacco Products (HTP) to aid in smoking cessation. The HTPs are currently not approved for use in India. The group of experts reviewed the available evidence and presented their conclusions on the same. The objective was to discuss the current scientific evidence on novel nicotine and tobacco products to develop a consensus on potential of THR to alleviate the health burden faced by smokers.

Panelists :

The group included Dr Subhrojyoti Bhowmick (Clinical Director at Peerless Hospital & B K Roy Research Center), Dr Sunil K Khetarpal (Director, Association of Healthcare Providers), Dr Jijo Joseph John (Professor and Head of Department, Pediatrics,

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Dean of Research, Believers Church Medical College), Dr Shubhra Jain (Assistant Professor, Chest and TB Hospital, Jaipur), Dr Jitendra Mohan Hans (Chairman & Director Dr Hans Centre for ENT and Cochlear Implant), and Dr Anirban Dalui (Public Health Specialist, Assistant Finance Secretary, Indian Medical Association, Bengal). The discussion was moderated by Dr Shashikant Pawar (General Manager, Dr L H Hiranandani Hospital).

FINDINGS AND RECOMMENDATIONS

- *Establishing a tobacco cessation center at every medical college including the district medical college is a useful approach to address the issue of counseling and should be made mandatory.*
- *Counseling of youth is a crucial aspect in reducing the dependence on tobacco. Towards this, counseling centers should be established which focus on preventing initiation of smoking among youth. Furthermore, the use of social media could also prove useful.*
- *Patients at high risk must be made aware of the need for smoking cessation and the risks of continuing to smoke. Regular follow-up of these patients is required to ensure continued abstinence from smoking.*
- *Stringent implementation of laws prohibiting smoking in public places should be taken up with the relevant authorities.*
- *Relevant authorities must review the potential of THR products, and make these available, to provide the best possible cessation strategy for the Indian population.*
- *Regulatory aspects regarding sale of tobacco products, such as high cost, should be addressed.*

THE SMOKING EPIDEMIC : INDIAN SCENARIO AND IMPACT OF SMOKING

India has the second highest burden of tobacco consumption in the world, second only to China. Tobacco smoking remains a significant concern, with nearly 100 million adults smoking tobacco, and over one million adult deaths attributed to tobacco consumption each year. The maximum prevalence among men is estimated to be 17.5% while that among women is estimated to be 1.2%^{1,6}.

Smoking is known to significantly impact health, causing more deaths from vascular, respiratory, and other causes than from cancer. Worldwide, the annual deaths attributed to tobacco smoking are 4-5 million, with over 1 million deaths attributed to tobacco smoking in India^{6,7}. It is concerning that a majority of the projected tobacco-related deaths are from middle- and

low-income countries such as India, and these countries are expected to carry the majority of the burden of tobacco-related deaths until 2035⁷.

Tobacco is a potent carcinogen and is associated with cancers at various sites. Over 90% of lung cancers are due to tobacco smoking, with a risk ratio of 15-30. Similarly, the risk ratio for cancer of the urinary tract is 3, that of the pancreas, nasal cavity and liver is 1.5-2.5, and that of the kidney is 1.5-2.0. Alarmingly, about one-third of deaths from cancer are due to tobacco smoking. The risk of death from lung cancer is highest among current smokers compared with never smokers, and smoking cessation reduces the risk of death from lung cancer in an age-dependent manner⁷.

A comprehensive analysis on the burden of tobacco use in India revealed a higher risk of all cause-mortality from smoked tobacco rather than smokeless tobacco (relative risk [RR] 1.67 versus 1.16 among men; RR 1.53 versus 1.30 among women). When analyzed by cause of death, the trend remained constant for deaths from Respiratory Diseases, Tuberculosis, Cardiovascular Disease (CVD), and cancer. Economic analysis indicated that smoked tobacco accounted for 78% of the total cost attributed to tobacco use, with higher costs reported among men than women. For all diseases attributed to smoking, the share of the cost was higher among men than women⁸.

Conclusion :

Even after varied awareness campaigns and traditional nicotine replacement methods, the number of smokers is >100 million. What measures can be taken to improve individual and public health?

- *As compared to the burden of tobacco smoking, there are very few tobacco cessation centers and counseling centers in India. The knowledge deficit regarding the harms of smoking, and addiction itself also play a role in the low rates of quitting. *Establishing a tobacco cessation center at every medical college including the district medical college is a useful approach to address the issue of counseling and should be made mandatory.**
- *There is a need to address smoking among the younger population, and target prevention of initiation of smoking among the youth. The harms are noted in the long-term, and therefore, preventing the initiation of smoking is important. *Counseling of youth is a crucial aspect in reducing the dependence on tobacco. Towards this, counseling centers should be established which focus on preventing initiation of smoking among youth. Furthermore, the use of social media could also prove useful.**

- Counseling of patients at higher risk, such as those with Chronic Obstructive Pulmonary Disease (COPD) should be mandatory. *Patients at high risk must be made aware of the need for smoking cessation and the risks of continuing to smoke. Regular follow-up of these patients is required to ensure continued abstinence from smoking.*
- The Cigarettes and Other Tobacco Products Act (COTPA) is existent but is not implemented in mass gathering places. *The issue of stringent implementation of laws should be taken up with the relevant authorities.*
- There are several THR products available across the globe. These products are proven to be successful in achieving smoking cessation. *Relevant authorities must review the potential of THR products, and make these available, to provide the best possible cessation strategy for the Indian population.*
- Lastly, *regulatory aspects regarding sale of tobacco products, such as high cost, should be addressed.*
- THR can be an alternative to reduce the harm caused by smoking tobacco. The options available in India are limited at the current time. There is therefore scope for expanding the portfolio of available options to lower the risk of disease among the population of smokers in India.
- *Although the use of e-cigarettes is banned in India, it may be necessary to re-consider this decision. The availability of a THR product on prescription as a smoking cessation aid has the potential of achieving the target of reduction of the risk of disease.*
- *The evidence in favor of HTPs could be presented to regulatory authorities in India, for consideration as use as a smoking cessation therapy.*
- *There is a need to test HTPs in India to understand the efficacy, safety, and viability of use in the Indian population. To successfully carry out a study, the product must be in sustained use for a prolonged period, in order to evaluate the effects on the users and the community.*

TOBACCO HARM REDUCTION

Cigarette smoke is generated when tobacco is burned at high temperatures (600-900°C). This complex mixture consisting of solid particles and liquid droplets has over 6,000 known chemicals. There are several Harmful and Potentially Harmful Constituents (HPHCs) in cigarette smoke and are responsible for the development of chronic smoking-related diseases⁹.

Tobacco Harm Reduction (THR) is considered to minimize the harm of exposure to tobacco. National Institute for Health and Care Excellence (NICE) defines

Tobacco Harm Reduction (THR) as “reducing the illnesses and deaths caused by smoking tobacco—among people who smoke and those around them”³. The WHO Framework Convention on Tobacco Control defines “tobacco control” as a range of supply, demand and harm reduction strategies that aim to improve the health of a population by eliminating or reducing their consumption of tobacco products and exposure to tobacco smoke¹⁰. The concept of harm reduction is not new, and has been used in medicine and social policy in cases where hazardous behaviors cannot be completely avoided. This concept aims to minimize the harm to individuals and society when certain harmful behaviors cannot be prevented. In the context of tobacco, it is hoped that THR would allow smokers to gain some control of their addiction to nicotine^{3,11}.

This approach has gained traction in several countries, including USA, UK, Japan, and Sweden (among many other countries), where less toxic nicotine-containing products are available as alternatives to smoking. The purpose is to reduce death and disease caused by cigarette smoking. In fact, the use of snus in Sweden is a prime example of the potential of THR. The availability of snus has reduced the prevalence of smoking among males in Sweden, resulting in one of the lowest rates of smoking-related deaths across Europe³.

Addiction to nicotine stems from nicotine content rather than tobacco. Regular cigarette smoking creates a pleasurable sensation mediated by the Central Nervous System (CNS), leading to nicotine addiction. When a person abstains from nicotine exposure for a few hours, withdrawal symptoms arise which sustain the nicotine addiction. To overcome this addiction, Nicotine Replacement Therapies (NRTs) have been developed which deliver steady but lower concentrations of nicotine. This allows for blunting of the pleasurable effect of nicotine and reduction of the intensity of withdrawal symptoms. Cigarettes rapidly deliver nicotine to the brain, thus creating an immediate pleasurable sensation. In contrast, NRTs deliver low levels of nicotine with a blunted pleasurable sensation¹².

While there are a number of approved NRTs, a major drawback across all the products is that nicotine is not delivered in the same way, nor at the same rate and dose as cigarettes. Additionally, the sensory cues and rituals associated with cigarette smoking are not replicated by NRTs, thus impacting user acceptance. There are also concerns among users that NRTs may become addicting, and doubts about the effectiveness and safety of these products. As with several medical treatments, premature withdrawal has been reported with NRTs as well, which affects the efficacy of these products^{3,4,11}.

Discussion :

Do novel nicotine and tobacco products have potential to improve individual and public health and manage the overall harm caused by consumption of conventional cigarettes? What are the potential options for adopting THR in India?

Studies have indicated the introduction of non-combustible tobacco products has reduced the consumption of combustible tobacco products, and thus it can be inferred that these products are acceptable to the users. It is necessary to separately consider nicotine (which causes addiction) and harmful byproducts (which cause diseases). Therefore, THR products should play a role as cessation therapy. While no product would be completely safe, the focus should be on the outcome (reduction of harm, and lower risk of disease). The panelists unanimously agreed that THR products will be useful. Although medical treatment has been available in India, these treatments are expensive and require a long duration. Furthermore, varenicline which is commonly prescribed has adverse effects and is expensive. Therefore, there is a need for less harmful products, as medication is not the solution. *THR can be an alternative to reduce the harm caused by smoking tobacco. The options available in India are limited at the current time. There is therefore scope for expanding the portfolio of available options to lower the risk of disease among the population of smokers in India.*

NOVEL NICOTINE AND TOBACCO PRODUCTS

THR products which are associated with low risk of disease include electronic cigarettes (e-cigarettes) and other vapor products, snus and low-risk non-combustible nicotine or Heated Tobacco Products (HTPs)¹¹.

- Snus is an example of a successful THR product, as the use of snus has progressively replaced cigarette smoking in Sweden (58% of daily tobacco users use snus), with consequent low mortality rates (reduction in mortality from 26% in 1990-95 to 10% in 2002-07 among men). Snus has the advantage of not producing toxic combustion products and Tobacco-Specific Nitrosamines (TSNAs), as well as having lower risks of cancer, CVD and all-cause mortality compared with cigarette smoking¹¹.
- E-cigarettes or electronic nicotine delivery systems are a safer alternative to conventional smoking. These products are battery-powered and resemble a cigarette in appearance and in the need for repetitive hand-to-mouth movement, as well as the visual cue of smoke-like vapor. Unlike conventional cigarettes, combustion of tobacco does not occur.

Furthermore, e-cigarette vapor has substantially lower levels of potentially toxic compounds compared with conventional cigarettes. Maximum TSNA levels are 500-fold to 1,400-fold lower in e-cigarettes than conventional cigarettes. Formaldehyde, acetaldehyde, and acrolein (potentially toxic carbonyl compounds) have been detected in e-cigarette vapor in 12 brands of e-cigarettes but at levels substantially lower than in cigarette smoke¹¹.

- Comprehensive toxicological analysis of e-cigarette vapor indicates that the use of e-cigarettes may lead to lower exposure to harmful constituents, as well as lower cytotoxic and mutagenic effects¹³. In fact, the health risks are similar to those of smokeless tobacco, which has 1% of the mortality risk of smoking. Data indicates that current e-cigarette use does not increase the risk of Myocardial Infarction (MI). Rather, the association between e-cigarette use and MI depends on the history of conventional cigarette use¹⁴. Modeling studies have estimated that switching from conventional cigarettes to e-cigarettes for 10 years could lead to 6.6 million fewer premature deaths and 86.7 million fewer life-years lost due to cigarette use¹⁵. With respect to smoking cessation, the use of e-cigarettes is twice as effective as NRT in helping smokers quit¹⁶. Harnessing the potential of alternative products may be effective in achieving THR¹⁵. E-cigarettes are not associated with increase in serious health concerns and can be considered a much safer alternative to conventional smoking¹¹.
- Conventional cigarettes involve the combustion of tobacco, wherein the temperature at the tip is 700-950°C during puffs. The generation of toxic components occurs at 200-600°C. This gives rise to the concept that heating tobacco to lower temperatures could prevent the generation of toxic chemicals. Heated Tobacco Products (HTPs) utilize this concept and apply controlled heating to uniquely processed tobacco. HTPs heat tobacco to a maximum of 350°C⁹. Studies have reported that exposure to HTPs as opposed to conventional cigarettes leads to lower risk of lung cancer and CVD, and lower exposure to HPHCs. Beneficial changes have also been noted in lipid metabolism, endothelial dysfunction and cardiovascular risk factors among individuals who switch from conventional cigarettes to HTPs¹⁷. Furthermore, after the introduction of HTPs in Japan, there has been a significant reduction in hospitalizations due to COPD and ischemic heart disease (IHD)¹⁸.

Discussion :

Given the potential benefits of THR strategies, what measures can be taken to increase the awareness and understanding of harm reduction principles? Are any specific measures required to regulate the use of THR products among adolescents/youth, so as not to promote cigarette smoking, or use THR products as a stepping stone to cigarette smoking?

All forms of smoking cessation should be available in India as smoking is a lifelong disease that requires multiple treatment approaches. Smoking cessation strategies that are effective in other countries must be considered in India as well, so as not to deprive individuals of an effective solution. It is important to acknowledge the fact that cigarettes are the cause of addiction and life-threatening disease, while THR products reduce the risk of disease.

Although the use of e-cigarettes is banned in India, it may be necessary to re-consider this decision. The availability of a THR product on prescription as a smoking cessation aid has the potential of achieving the target of reduction of the risk of disease. As per the regulatory requirements in India, the e-cigarette is a "device" and thus it cannot be bought directly by customers. Appropriate regulatory procedures could be applied to ensure that the products meet the desired quality standards, and the availability and sale of these products occur only based on a prescription. The aim of introduction of THR products is to aid in smoking cessation and reduce the risk of disease in individuals exposed to tobacco. Simultaneously, awareness campaigns among youth to highlight that tobacco consumption in any form is harmful could be undertaken.

INDEPENDENT RISK ASSESSMENT OF HTPs

Several countries (USA, UK, Netherlands, Japan, Germany) have assessed the evidence and generally conclude that HTPs may be less harmful than cigarettes. In a ruling by the United States Food and Drug Administration (USFDA), they state "the proposed products, as actually used, reduces a user's exposure to Harmful and Potentially Harmful Constituents (HPHCs) if they switch completely from combusted cigarettes to the HTPs. A measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely in subsequent studies"²⁰. Authorities in the United Kingdom concluded that "The available evidence suggests that heated tobacco products may be considerably less harmful than tobacco cigarettes and more harmful than e-cigarettes"²¹. The National Institute for Public Health and the Environment, Ministry of Health, Welfare and Sport, The Netherlands in an evaluation of e-cigarettes

stated that "It may be concluded that the health risks associated with smoking conventional cigarettes are considerably higher than those associated with using e-cigarettes"²². There appears to be a general consensus that e-cigarettes and HTPs are less harmful than conventional cigarettes.

Discussion :

How can the evidence of evaluations from Government Agencies of other countries for HTPs be taken forward for developing regulatory strategies for THR in India? Based on the current ban on NNTPs in India, what are the important considerations for developing a policy-making document of THR? What measures can be taken to uplift the ban on NNTPs for THR?

It may be useful to conduct a detailed analysis of the conclusions of the agencies. Based on the findings, *the science of HTPs could be presented to regulatory authorities in India, for consideration as use as a smoking cessation therapy. In view of the lack of data from India, data from studies conducted in other countries could be presented.*

Is there a need for further studies demonstrating the reduced harm of HTPs or is the real problem a lack of awareness of the data? How can gaps in awareness be addressed?

There is information on the potential of HTPs from other countries, but studies from India are lacking, as these products are not available in the country. There is a need to test HTPs in India to understand the efficacy, safety, and viability of use in the Indian population. To successfully carry out a study, the product must be in sustained use for a prolonged period, to evaluate the effects on the users and the community. Furthermore, it is not ethically correct to carry out a randomized controlled trial. Nonetheless, if the manufacturer aims to conduct a trial in India, the relevant authorities must consider the dual outcome of aiding smoking cessation and reducing the risk of disease in individuals using tobacco. To achieve this dual outcome, the availability of effective, safe, and cost-effective products (whether pharmacological products or "devices" such as HTPs) that meet stringent quality standards and are available strictly under prescription for the purpose of smoking cessation, could benefit the community as a whole.

IMPACT OF NNTPs ON CIGARETTE SMOKING: EXPERIENCE FROM OTHER COUNTRIES

Japan is the largest consumer of HTPs, accounting for nearly 85% of the global market. The increasing market share of HTPs in Japan has led to a concomitant decline in annual cigarette sales, and a decline in aggregate consumption of tobacco products.

Nearly 70% of those who use HTPs in Japan have switched completely to HTPs, with dual use noted only in 9% of tobacco users. The introduction of HTPs led to a decline in cigarette smoking. Furthermore, usage among the youth remains low (0.1%). HTPs have a low impact on the use of tobacco by never-smokers (0.5%) and re-initiation by former smokers (<0.1%) in Japan. Similar data has emerged from UK as well¹⁹.

Discussion :

How can a balance be formed between heavily regulated nicotine pharmaceuticals and THR products, and unregulated tobacco products?

Cost is expected to be a major factor impacting the use of such alternative products. While the cost may initially be high, it is expected that a competitive market of HTPs may lead to reduction in costs. The HTPs would be available only on the prescription of a registered medical practitioner for the purpose of smoking cessation in an individual who aims to quit smoking. The products would be classified as “devices”, and hence would not be available for purchase without a prescription. It follows that the quality and composition of the product would be strictly regulated, unlike the tobacco products available in the open market.

SUMMARY

The road to smoking cessation is marred in controversy on the potential for misuse of smoking cessation therapies. While the panel acknowledges that the THR products in question carry the potential for misuse, the benefits of introduction of these products in India cannot be denied. In the context of cigarette smoking, the ideal is complete cessation, and the objective of harm reduction can be achieved with the use of multiple approaches. Towards this, several NRTs and other products have been developed over the years, with varying efficacy in achieving sustained cessation. The products must not only be effective, but also acceptable to the users, to ensure appropriate use for the desired duration, to achieve the required outcome. Novel nicotine and tobacco products such as electronic cigarettes have demonstrated considerable efficacy over NRTs and have a lower risk of disease. Several countries have adopted these products for the purpose of smoking cessation. In light of the evidence of reduction in disease and the toxicological studies, it would be useful to consider THR products for use in India. Given the burden of tobacco smoking and the consequent health effects, it is necessary to make available the most effective products as smoking cessation therapies. There is hope that the evidence on THR products can be reviewed objectively by the relevant

authorities, so that the individuals currently at increased risk of potentially life-threatening disease could benefit from a policy change that grants them an alternative smoking cessation aid that could improve the health of the individuals using it and the community.

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