ADVERSE EFFECTS OF NICOTINE GUM IN ORIENTAL MALAY MALE SMOKER

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Summary

Smokers in smoking cessation programmes are prescribed Nicotine replacement therapies (NRT) to help them control cravings and withdrawal symptoms. However the dosage of NRT prescribed should be sufficient to prevent withdrawal symptoms but avoid adverse reactions. This report describes a case of adverse reaction to nicotine gum in a male Oriental smoker who was categorised as having poor nicotine metabolic status, who developed nausea, severe vomiting and diarrhoea with raised blood pressure and pulse rate, following the administration of a piece of 2 mg nicotine gum. Based on this case report, clinicians prescribing nicotine gum should beware of the possibility of adverse reactions in those with poor nicotine metabolic rate. Further research on the use of nicotine gum in smoking cessation programmes is required, in particular investigating those with poor nicotine metabolic status.

Key words: nicotine gum, adverse reaction, poor metaboliser, nicotine metabolism.

Nicotine replacement therapies (NRT) assist smokers in smoking cessation treatments to stop smoking by replacing a proportion of the nicotine formerly obtained from cigarettes [1]. Thus, NRTs alleviate the withdrawal symptoms experienced by smokers. However when prescribing NRT, the dosage required should avoid adverse reactions.

Nicotine is metabolised to cotinine in the liver, and this conversion is mediated by the cytochrome P450 2A6 enzyme (CYP2A6) [2-4]. In recent years, there has been growing evidence on the variability of nicotine metabolism in different populations, and this variability is attributable to the genetic polymorphism of the CYP2A6 enzymes [5,6]. Some individuals were reported to have defective CYP2A6 genes, and had reduced CYP2A6 activity and categorised as poor metabolisers whereas some individuals were reported to have duplicate genes, had increased nicotine metabolic activity and were categorised as ultrarapid metabolisers [7]. Thus, it is possible that individuals with poor nicotine metabolic rate, when exposed to NRT, and due to poor nicotine metabolic status may be at risk of adverse reactions as they may be exposed to prolonged and higher nicotine concentrations in the body. Clinicians in smoking cessation programmes may not be aware of the possibility of adverse events with nicotine gum in certain populations.

Therefore, this case report describes an adverse reaction following administration of a piece of 2 mg nicotine gum in an Oriental Malay male smoker. Ethical approval was obtained from the Institutional Ethics Committee and informed consent was obtained from the patient.

Case report

Mr B, was a 32 year old Oriental Malay male current smoker, entered a study to investigate nicotine metabolism which involved the administration of a piece of 2 mg nicotine gum. He first started smoking aged 18 years and smoked up to 10 filtered cigarettes per day for the past 14 years. He was medium built (weight 64 kg) with Body Mass Index of 23, and was found to be not dependent on nicotine (Fagerstrom Test of Nicotine Dependence (FTND) score of 3) [8]. After an overnight smoking abstinence (12 hours), the subject came to the clinic where baseline measures (Blood Pressure (BP), Pulse Rate (PR) and Carbon Monoxide (CO)) including a blood (5 ml) sample for nicotine and cotinine analysis was taken (0 min). A piece of 2 mg nicotine gum was then administered and the subject was instructed to chew the gum for 30 min (chewing technique used was 10 seconds with 30 seconds rest interval). A repeat measurement of BP, PR and CO and blood sample (5 ml) was taken at 120 min.

Prior to the administration of nicotine gum, BP measurement was 95/65 mmHg, PR was 72 beats/min and CO was 8 ppm. At thirty minutes after the start of chewing the nicotine gum, the subject complained of feeling unwell. He felt nauseated, severe headache and sweated profusely. This was followed by vomiting and several bouts of diarrhoea. At that time, BP had increased to 150/95 mmHg and PR increased 125 beats/min. The subject was advised to rest and discard the nicotine gum. At 2 hours post nicotine gum administration, BP had fallen to pre nicotine gum level of 95/60 mmHg, PR had decreased to almost pre nicotine gum level of 76 beats/min and CO measurement was 6 ppm. The subject's nicotine metabolism (determined by calculating the ratio of plasma cotinine/nicotine 2 hours after the administration of nicotine gum), was 0.4, and thus he was categorised as a poor metaboliser of nicotine metabolism [9-11].

Discussion

In recent years, the literature has reported the presence of poor metabolisers of nicotine metabolism among some Oriental ethnic groups. The prevalence of CYP2A6 poor metabolisers were reported to be as high as 30% among Japanese and 15% among Chinese, but the prevalence was reported to be low in Caucasians [10,12]. Understanding the genetic variability in nicotine metabolism is an important factor in understanding interindividual differences in smoking behaviour. Individuals who have poor nicotine metabolic status were found to have high plasma nicotine concentrations as nicotine was converted to cotinine slowly, whereas those with ultrarapid nicotine metabolic status had low plasma nicotine concentrations [7,9-11]. This article reports a case of adverse reaction in an Oriental Malay male smoker who experienced an adverse reaction following chewing nicotine gum. The probable explanation of the adverse reaction experienced by the subject could be due to having poor nicotine metabolic status (ratio of plasma cotinine/nicotine at 2 hours after nicotine gum < 0.6) [11]. Among the reported method to measure phenotype for nicotine metabolic status was by measuring the ratio of plasma cotinine/plasma nicotine at 2 hours after chewing a piece of 2 mg nicotine gum [9-11]. It was shown that the plasma cotinine/nicotine

ratio at 2 hours after chewing a piece of 2 mg nicotine gum significantly correlated with the area under curve (AUC) from 0 to 24 hours values. Using this method, those with plasma cotinine/nicotine ratio <0.6 were categorised as poor metabolisers [9-11]. Thus far, the author is not aware of any report linking the ethnicity of poor metabolisers of nicotine metabolism and adverse reaction to nicotine gum. Having poor nicotine metabolic status would suggests that nicotine from NRTs may remain longer in the body, thus making the smoker at risk of adverse effects. The adverse reactions reported by this subject is similar to those reported in the literature, where large doses of oral nicotine reportedly caused nausea and diarrhoea because of irritation of the gastrointestinal tract [13-14].

From this case report, clinicians who prescribe nicotine products in smoking cessation programmes should be aware of the possibility of adverse reaction in those of Oriental ethnicity, in particular those with poor nicotine metabolic rate. Knowledge regarding variation in nicotine metabolism and ethnicity could therefore be used to improve the efficacy of existing nicotine based smoking cessation products [15]. Further investigations are needed to address the different requirements of smokers with different nicotine metabolic status when prescribed nicotine based smoking cessation products. For example, this case report suggests that Poor Metabolisers of nicotine metabolism who have lower nicotine metabolic rate may be at risk of adverse reaction to a standard dose of nicotine replacement therapy.

Conclusion

Nicotine replacement therapy is commonly prescribed to smokers to aid smoking cessation. This case report suggests that individuals of oriental ethnicity with poor nicotine metabolic status may be at risk of adverse reactions when prescribed nicotine based smoking cessation products. Thus, clinicians working in smoking cessation programmes should be more aware of this possibility in those with oriental ethnicity and having poor nicotine metabolic status.

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