

The Effects of Smokeless Tobacco Use on Hypnosis Induced by a Single Dose of Tiopental Sodium in Mice

FARELERDE DUMANSIZ TÛTÛN KULLANIMININ TEK DOZ TİOPENTAL SODYUM İLE İNDÜKLENEN HİPNOZA ETKİLERİ

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Summary

In this study, we investigated the effects of a widely used smokeless tobacco in South-East region of Turkey, named Maras Powder, on hypnosis induced by 25 mg/kg tiopental sodium (TS) injection intraperitoneally. Aqueous extract of Maras Powder (MP) was administered orally in 0.5 ml volume and 25, 50 and 100 mg/kg doses. Mean scores of the groups were found to be 30.43 ± 1.34 for TS, 32.0 ± 2.93 (t:0.49) for 25 mg/kg MP, 33.3 ± 2.08 (t: 1.15) for 50 mg/kg MP ($p > 0.05$ for both), respectively. On the other hand, 100 mg/kg MP prolonged the TS induced hypnosis period obviously in mice. The mean score was found to be 81.0 ± 2.46 minutes in this group (t: 18.05 pO.OOO1). This represents 2.7 fold increase in respect to control scores.

Key Words: Nicotine, Smokeless tobacco, Hypnosis, Anesthesia, Tiopental sodium, Mice

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The pharmacological effects of nicotine on several systems have been widely studied. Some forms of smokeless tobacco are used in some countries. An interesting type of smokeless tobacco is widely used in lieu of cigarettes in the South East

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Özet

Bu çalışmada 25 mg/kg dozda tiopental sodyum (TS) intraperitoneal enjeksiyonu ile indüklenen hipnoza, Güneydoğu Anadolu bölgesinde çok yaygın kullanılan ve dumansız tütün özelliğindeki Maraş otu'nun (MP) etkilerini inceledik. MP'nin sulu ekstresi oral yoldan 0.5 ml hacimde ve 25, 50 ve 100 mg/kg dozlarında kullanıldı. Grupların ortalamaları; TS için 30.43 ± 1.34 , 25 mg/kg MP için 32.0 ± 2.93 (t:0.49), 50 mg/kg MP için ise 33.3 ± 2.08 (t:1.15) olarak bulunmuştur (her iki MP dozu için $p > 0.05$). Diğer taraftan, 100 mg/kg MP, farelerde TS ile indüklenen hipnoz periyodunu açık bir şekilde uzatmıştır. Bu grubun ortalaması; 81.0 ± 2.46 dakika olup (t: 18.05 pO.OOO1) bu değer kontrol grubuna göre 2.7 kez artışı ifade etmektedir.

Anahtar Kelimeler: Nikotin, Dumansız tütün, Hipnoz, Anestezi, Tiopental sodyum, Fare

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region of Turkey. It is prepared from *Nicotiana rustica* L. and wood ash (Maras Powder). The leaves of the plant are powdered and this powder is mixed with the wine wood ash (Approximately 50% of total content). A pinch of this mixture is applied to the mucosa of the lower lip for 4-5 minutes. This procedure is repeated many times during the day (1). Pharmacological studies have shown that this type of smokeless tobacco is a form of buccal nicotine use and its effects are not different from those of standard nicotine use in cigarettes (4). The con-

tent of nicotine in *Nicotiana rustica* L. was searched and contradicted results were obtained. Saitoh F, et al, conducted a study on sixty *Nicotiana* species and found that there was no remarkable difference in nicotine content of *N. tabacum* L. (Tobacco of ordinary cigarettes) and *N. rustica* L. (2). On the other hand, Shmuk A A, was found that the nicotine content of *Nicotiana rustica* L. is 6-10 times higher than *Nicotiana tabacum* L. (3).

It was reported that Maras Powder use has increased the incidence of epithelial abnormalities and buccal carcinoma which are related to the length of use especially after 15 or more years of exposure (5). This powder has also been shown to exhibit a sister chromatid exchange (SCE) inducing effect on human T-lymphocyte chromosomes. However, this effect was significantly lower than that found in smokers (1). The incidence of micronuclei increased in the buccal mucosa cells of smokeless tobacco users (6). In addition, leukoplakia, tooth abrasion, periodontal bone destruction and gingival recession have an increased incidence in smokeless tobacco users (7-10). Nicotine limits the physical performance (11), causes tachycardia, rises blood pressure, causes vasoconstriction (12-14) and has antinociceptive (15) and local anesthetic (16) effects. Additionally, the effects on the pain reception (15,17), leucomotor activity and many other system effects were widely studied and well known (18).

Although *Nicotiana rustica* L. also includes some other alkaloids in very small quantities (3), it contains large amount of nicotine (5-6 times more than *Nicotiana tabacum* L.). Preclinical studies have shown that the effect of Maras Powder is similar to that of pure nicotine (4).

In the present study, we investigated the effects of aqueous extract of Maras Powder on hypnosis induced by 25 mg/kg tiopental sodium injection intraperitoneally in mice.

Materials and Methods

In this study, 28 male mice, weighing 35-40 g and nourished under normal conditions at the Atatiirk University Experimental Animal Laboratory, were used. Prior to the experiment, animals were divided into four groups and seven mice in each group housed together. They were given rat

chow and tap water ad libidum.

Tiopental Sodium (Abbott-İstanbul) was obtained from Anesthesiology Department of Atatiirk University Medical Faculty and Maras Powder (MP) was purchased from Kahramanmaraş province of Turkey. MP was dissolved in distilled water. »

Mice in all groups were injected tiopental sodium (TS) 25 mg/kg, intraperitoneally in 0.5 ml volume. 60 minutes before TS injection, distilled water to first, 25 mg/kg MP to second, 50 mg/kg MP to third and 100 mg/kg MP to fourth groups in 0.5 ml volumes were administered orally. Hypnosis period was determined by a simple chronometer.

For statistical analysis, One-way ANOVA and Independent sample t-test were used and data are expressed as mean±SEM. When p-values were smaller than 0.05, the difference was considered to be statistically significant.

Results

TS (25 mg/kg) induced hypnosis period was found as 30.43±3.34 minutes. Mean scores of the groups were found to be 32.0±2.93 (t:0.49) for 25 mg/kg MP and 33.3±2.08 (t: 1.15) for 50 mg/kg MP (p>0.05 for both), respectively. On the other hand, 100 mg/kg MP prolonged the TS induced hypnosis period obviously in mice. The mean score was found to be 81.0±2.46 minutes in this group (t: 18.05 pO.0001). This represents a 2.7 fold increase with respect to control scores (Figure 1).

Discussion

Nicotine is a widely used addictive compound and its harmful effects are well known. The effects of it on anesthesia induction and hypnosis are not studied enough. In the present study, we investigated the effects of aqueous extract of smokeless tobacco which has a very high nicotine content (4), on the hypnosis period induced by 25 mg/kg TS injection, intraperitoneally in mice.

Nicotine is absorbed in substantial quantities from smokeless tobacco (19). As well as nicotine, nitroso-compounds and reactive oxygen species derived from tobacco, could also play a role in the etiology of the effects of it (20). Nicotine markedly stimulates the central nervous system, produces

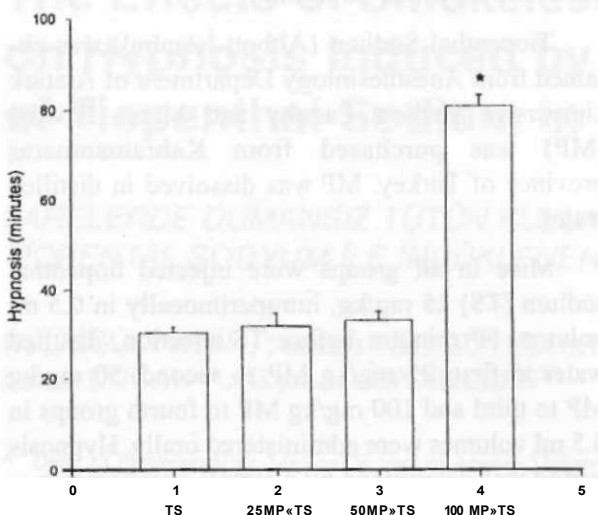


Figure 1. The effects of Maras Powder (MP) in hypnosis period induced by Tiopenthal Sodium (TS), 25 mg/kg. * $p < 0.0001$.

tremors and convulsions. Stimulation of the central nervous system is followed by depression and central paralysis (21). Additionally, it has been shown that nicotine increases pain threshold and reduces pain in mice (22,23). It has been suggested that the analgesic action of nicotine is due to an increase of beta endorphin release and endogenous opioid activity. According to our results, MP may exert its hypnosis potentiating effect via interfering with endogenous opioid receptors.

It was also reported that MP has a local anesthetic action (16). Mechanism of action of the local anesthetics are well known. They exert their action via sodium channel blockade (24). In the present study, MP probably exerted its effect by blocking sodium channels which are located on the neuronal membrane and this effect could be potentiated the effect of TS.

It has been reported that aqueous extract of smokeless tobacco exerts its effect partly by mediating bradykinin B_2 receptors (25). Quinines have an ability to disrupt the blood brain barrier and allow increased central nervous system penetration (26). In our model, high dose of MP probably facilitated the penetration of TS from blood brain barrier via affecting the bradykinin pathway.

Despite it is very crucial to have some information about the effects of nicotine addiction on tiopenthal sodium induced anesthesia and hypnosis, there is limited information and need further preclinical and clinical studies on this topic.

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