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A Trial for Smoking Cessation during Ten Days through using Antidepressant Imipramine 25 mg daily

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ABSTRACT

Purpose: This study explores the possible positive effect of imipramine on daily cigarettes smoking and if it may enforce stopping smoking during ten days by using 25 mg once at night orally.

Methods: Using placebo control study. In which adult smokers' volunteers were assigned to one of study groups; control (N=52) or Imipramine group (N=102). All volunteers take their medications as single daily dose at night and start to report number of cigarettes smoked daily for 10 days with reporting side effects appeared during the study.

Results: Imipramine group showed significant declining in number of cigarettes daily smoked as compared with day 1 of study and as compared with control group. 94.1% of volunteers reduced daily smoking also 11.8% of volunteers stop smoking at the end of study. Side effects reported in the study were drowsiness and headache and sleep disturbance.

Conclusions: Imipramine was effective to reduce number of daily cigarettes smoked and may help to stop this habit.

Keywords: Imipramine, Antidepressant, Tobacco, Cigarettes, Smoking

INTRODUTION

Smoking of Cigarettes consider one of global health problems, and one of leading causes of mortality in the world; this led to many smoke control campaigns and programs [1,2]. These programs offered help to stop smoking through forcing or encouraging cessation via behavioral therapy and/or by pharma cological means with variable degree of success [3-5]. This probably related to the complex effect of nicotine of cigarettes on CNS. Where Nicotine of cigarettes may affect release of many of neurotransmitters in various regions of brain; such neurotransmitters included dopamine, serotonin and glutamine [6,7]. Also; it leads to change in level of MAO-A activity in brain leading to mood change. In addition to addicting nature of nicotine presents in tobacco smoke [8,9]. These may be related to the variability in response to smoking cessation therapy.

Pharmacological therapy used for smoking cessation like bupropion, NRT, varenicline; Nortriptyline and cytisine have been shown to improve the chances of quitting. NRT or varenicline are equally effective as quitting aids. None of them was superior [10].

Stopping tobacco smoking may leads to depressive symptoms or causing a depressive episode that may be relieved by re smoking or its rationally could be ameliorated by using of antidepressants. Some antidepressants may affect some neural pathways already modulated by nicotine of cigarette [11,12]. Clinical trials found that antidepressants like nortriptyline and bupropion may improve depression associated with stop smoking and help a long-term smoking cessation; but with little number of serious adverse effects. Maintaining a long-term smoking cessation; may be independent of their antidepressant effect [12,13].

Imipramine (tofranil)® is one of efficient tricyclic antidepressants that has many clinical uses; specially in controlling depression, neuropathic pain and controlling enures is [14-16]. It binds and affects large number of receptors and transmitters in brain like serotonin, Norepinephrine, dopa mine acetylcholine and others, like histamine [17-22]. This complexity in mode of action made it of interest for investigation the possibility of forcing smoking cessation in adults' smoker. The Novelty of this study; is that; the potential effect of imipramine in dose 25 mg per day; at night on cigarettes smoking was not reported.

Aims of the study

Evaluate the potential positive effect of imipramine 25 mg single daily dose before sleep on number of cigarettes smoked during 10 days trial; and if it leads to stop smoking.

METHODS

Study design

The study was double blinded placebo control study.

Study groups

Apparently healthy Adult smoker volunteers (smoker for ≥ 1 years & age ≥ 18 years) are randomly assigned to one of the two groups of the study that include placebo control (N=51); study group (received imipramine 25 mg single tablet before sleep) (N=102).

The study continued for ten days. Each volunteer received data collection forma include name; telephone number, age, gender, type of cigarettes (trade name), quantity of nicotine and tar per cigarette and duration of smoking in years. Each volunteer received single daily dose of each drugs mentioned above as oral tablet; after signing of a written consent by each volunteer. Each volunteer was asked to report number of cigarettes smoked and appeared side effects at the end of each day of trial. Data collection forma received from each volunteer after completion of ten days.

Data analysis

Data analyzed using Medcalc® software V12. One way Anova and T test was performed to find significant differences ($p<0.05$) between groups in age; years of smoking; nicotine and tar contents of cigars number of cigarettes smoked. Chi square analysis was used to find the significant ($p<0.05$) differences in rate of smoking declining and percent of positive outcome between groups.

RESULTS

1. Age; smoking duration; Nicotine & Tar concentration per cigarettes

As in Table 1 there were no significant ($p<0.05$) differences in age (p value=0.923); average duration of smoking in years (p value=0.2312); Nicotine concentration per cigarettes (p value= 0.0507) and finally tar concentration (p value=0.6956).

Table 1: Age; smoking years; and average nicotine and tar concentration per cigarette; for groups of the study. Some of data expressed as Mean ± standard deviation

	Control Group	Imipramine	
	N=51	N=102	**P values**
Age (years)	30.5 ± 10.7	30.7 ± 11.5	
Age Range	20-56	16-73	0.923
Years of smoking	11 ± 6.5	9.4 ± 8.3	
Smoking duration range (years)	47178	12785	0.2312
Average nicotine (mg) per cigarette	0.26 ± 0.15	0.32 ± 0.24	0.0507
Average tar (mg) per cigarette	2.6 ± 1.55	2.7 ± 1.83	0.6956

2. Reported daily cigarettes smoking

As in Table 2, during the study, there was a significant ($p<0.05$) declining in number of daily cigarettes smoked by volunteers in Imipramine 25 mg group (p value<0.0001 for imipramine versus p value=0.593 for control group); this declining was significant as compared with control group. (p value<0.0001). The changes in daily cigarettes smoking is clear in Figure 1.

Table 2: Average daily cigarettes smoked during the study. Data expressed as Mean ± standard deviation

	Control Group	Imipramine	P values
	N=51	N=102	
Day1	22.76 ± 5.83	21.08 ± 10.47	<0.0001
Day2	24.27 ± 6.65	19.74 ± 9.87	
Day3	23.88 ± 7.03	18.5 ± 8.84	
Day4	24.24 ± 6.91	17.84 ± 8.39	
Day5	24.47 ± 6.32	16.73 ± 8.07	
Day6	22.94 ± 7.05	15.66 ± 8.5	
Day7	23.86 ± 7.2	14.48 ± 8.55	
Day8	23.55 ± 6.89	13.7 ± 8.56	
Day9	25.65 ± 6.39	13.45 ± 8.64	
Day10	23.1 ± 6.91	12.92 ± 8.3	
p- value	0.593	< 0.0001	

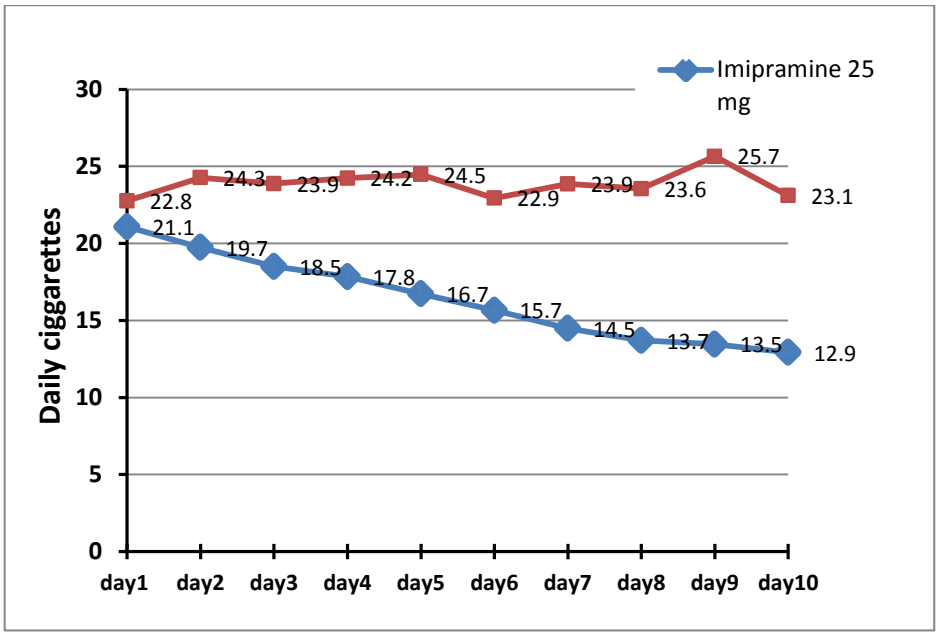

Figure 1: Shows changes in the reported daily number of smoked cigarettes in study groups. The declining was clear in imipramine group

At the 10th day of study there was significant ($p<0.05$) declining in number of cigarettes smoked as compared with day 1, in Imipramine group (p value<0.0001) and this declining was also highly significant as compared with control value in day 10 of study (p value<0.0001) as in Table 3 and Figure 2.

Table 3: Comparison between the reported numbers of cigarettes smoked in day 1 and day 10 of study. Data expressed as Mean ± standard deviation

	Number of cigarettes smoked		**P values**
	Control Group	**Imipramine**	
	N=51	N=102	
Day 1	22.76 ± 5.83	21.08 ± 10.47	0.2033
Day 10	23.1 ± 6.91	12.92 ± 8.3	<0.0001
P value	0.2936	<0.0001	
* Significant ($p<0.05$) as compared with day 1 values a Significant ($p<0.05$) as compared with control group			

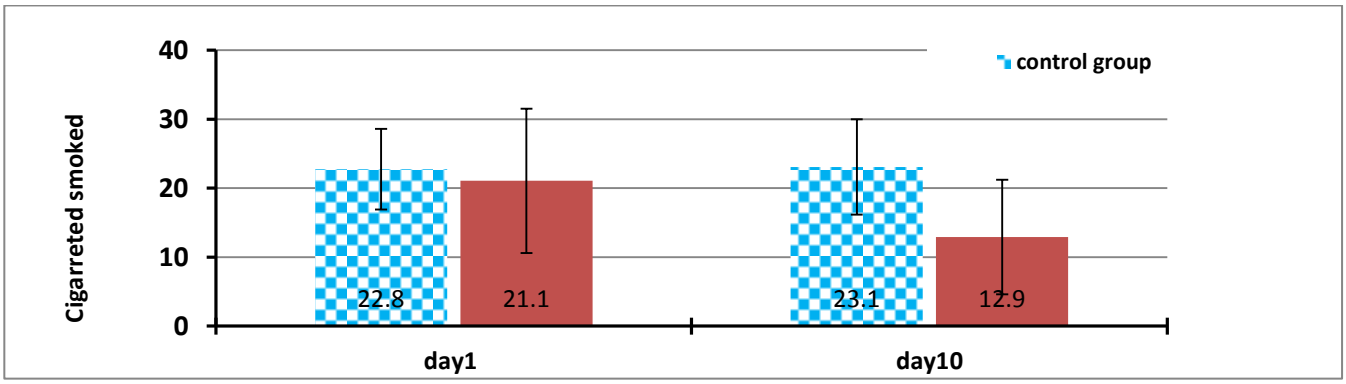

Figure 2: Shows difference between numbers of cigarettes smoked in 1st and 10th day in study groups. In which the declining was clear in Imipramine group

3. Percent change in cigarettes smoking

As in Table 4 The average percentage of declining in cigarettes smoking was significantly greater in Imipramine group at day 10 as compared with control value (-38 ± 35.1 *vs.* 5.87 ± 34.1 ; p value <0.0001). Also the total declining was significantly greater in imipramine group as compared with control (-20.95 ± 20.5 *vs.* 7.33 ± 16.3; P value <0.0001).

Table 4: Comparison between percent declines in cigarettes smoked measured in day 10 and as total change in study groups when compared with baseline values. Data expressed as Mean ± standard deviation

	Percent Declining		
	Control group	**Imipramine group**	
	N=51	N=102	**P values**
Day 10	5.87 ± 34.1	-38 ± 35.1	<0.0001
	95% CI -3.7 to 15.4	95% CI -44.8 to -31.1	
All over change	7.33 ± 16.3	-20.95 ± 20.5	<0.0001
	95% CI 2.7 to 11.9	95% CI -24.9 to -16.9	
95% CI =95% confidence interval for mean			

4. Percent of positive outcome

As in Table 5; significantly (p<0.0001) greater percentage of volunteers have positive outcome (measured as declining in number of cigarettes smoked) was in the imipramine group as compared with control group: where it was in day 10th (97.1% *vs.* 60.8% control) and when total change was measured (94.1% *vs.* 23.5% control).

11.8% of volunteers received imipramine have stopped smoking at the end of study; this ratio was significantly higher than control value (p value=0.0256). Odd ratio was high and favors imipramine group (Odd ratio=52; 95% CI 18.228 to 148.345 and P value<0.0001).

Table 5: Comparison between number & percentage of volunteers show positive outcome (declining in number of cigarettes smoked)

	Control group	Imipramine group	
	N=51	N=102	**P values**
Day 10	31 (60.8%)	99 (97.1%)	<0.0001
All over change	12 (23.5%)	96 (94.1%)	<0.0001
Complete abstinence	0 (0.0%)	12 (11.8%)	0.0256
Odd ratio	52	95% CI 18.228 to 148.345	<0.0001
Odd ratio >1 favor imipramine group			

5. The reported side effects

As in the Table 6; the most frequent reported side effects in the study was dizziness, sleepiness and headache. The incidence of these side effects was significantly ($p<0.05$) higher in Imipramine group. Sleep disturbances; nightmares, also occur more significantly ($p<0.05$) in imipramine group. While incidence of urinary retention and constipation were lower and imipramine group was not significant ($p<0.05$) different from that of control.

Table 6: Incidence of side effects reported by groups of volunteers during the study

	Control Group	Imipramine group	P values
	N=51	N=102	
Dizziness	18 (35.3%)	76 (74.1%)	<0.0001
Sleepy	20 (39.2%)	78 (76.5%)	<0.0001
Headache	13 (25.5%)	55 (53.9%)	0.0016
Sleep disturbance	3(5.9%)	40 (39.2%)	<0.0001
Nightmares	2 (3.9%)	23 (22.5%)	0.0068
Urinary retention	4 (7.8%)	22 (21.6%)	0.0571
Constipations	4 (7.8%)	17 (16.7%)	0.2128
Other side effects	1 (1.96%)	0(0%)	0.7228

DISCUSSION

Results of this study show clear gradual declining (Figure 1) in the reported number of cigarettes smoked after use of single daily dose of imipramine 25 mg at night; and there were about 11.8% of volunteers completely stopped smoking during and at the end of study. See Tables 1-5. These results may be related to ability of tricyclic antidepressant imipramine to affect various neurotransmitters in brain; the complexity of effects of imipramine may have some degree of similarity to that induced by nicotine present in tobacco smoke [23]. Imipramine relieves the depressed mood and may reduce the need for tobacco smoke. While nicotine does so probably through stimulating release of some mediators like serotonin and norepinephrine in various area of brain and causes relieving the depression and change in mood in smokers which happen prior to smoking cigarette [24]. Cigarettes abstinence ratio in this study was smaller than the reported by other antidepressants like nortriptyline and bupropion (nortriptyline 30.8% and

bupropion 41.5%) and imipramine 75 mg daily this may be related to short period of study (ten days *vs.* 6 months for other studies), but these results may be promising. [25]. Rates of reported side effects induced by imipramine in this study arranged in descending order were sleepiness, dizziness, headache, sleep disturbance, nightmare, urinary retention and constipation. These were comparable with the reported by F.M. Haggstra m et al. These side effects were well tolerated by volunteers and all they complete the study of ten days. These side effects were not different from the reported in the drug literature [26].

CONCLUSIONS

Imipramine (Tofranil®), in dose 25 mg given once at night may result in declining of number of daily cigarettes smoked, and may help in stop this habit.

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CONFLICT OF INTEREST

There is no conflict of interest; and the research is self-funded by researcher himself.

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