REVIEW ARTICLE

Effect of Smoking Habit in the Serotonin Level and *5-HTTLPR* Gene Polymorphism

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ABSTRACT

This study deals with the effect of smoking in the serotonin level and *5-HTTLPR* gene polymorphism. It included smoker and nonsmoker individuals, and blood samples were collected to an estimated serotonin level and DNA isolation for genotyping detection. The results reveal that smoking causes non-significant decreased in serotonin level ($p < 0.605$), and non-significant differences were observed with age and BMI. Among three genotypes LL, SS and LS, the LS were more observed in the non-smoker group while SS is more frequent in smoker group in non-significant differences ($p < 0.764$, 0.453), respectively. LL was a lower percentage in both groups. The allele frequency was detected by Hardy-Weinberg equation, where S allele was more observed in smoker (0.66) and non-smoker (0.58), respectively in non-significant differences ($p < 0.2445$). The serotonin level was decreased in LS and LL, respectively with significant changes in the smoker group ($p < 0.032$) while non-significant in non-smoker group ($p < 0.466$).

Conclusions: the present study concluded that the smoker may affect in the *5-HTTLRP* gene polymorphism that leads to changes in serotonin level.

Keywords: *5-HTTLPR* gene polymorphism, Serotonin level, Smoking habit.

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INTRODUCTION

The smoking habit still the harmful behavior pattern in the wild world and causes about six million deaths every year. The investigators predicted that smokers will lead to more than eight million deaths annually by 2030, also smoker die 10 years earlier than nonsmokers.[1,2] The Cotinine is a metabolite of nicotine.[3] Serotonin is a member of neurotransmitter involvement in different body functions, for instance mood and behavior changes, depression events and sleeping ability, the appetite level, body temperature direction; moreover its contributed in regulation of some endocrine and muscle contraction.[4,5] The association between serotonin and cotinine still contradict and several studies found that the smoker stimulated serotonin generations and serotonin production was exhausted by smokers.[6] On the other hand the nicotine has been found to be blocked serotonin receptors.[7]

The trans membrane transporter serotonin that responsible to reuptake of SER in synapse is encoded by serotonin transporter gene (*5-HTT*). Also these receptors regulates the magnitude and duration of serotonergic signaling.[8-10] The serotonin transporter gene-linked polymorphic region (*5-HTTLPR*) is functional polymorphism in the promoter region of the *5-HTT* gene.[11,12] The association between smoking and candidate gene polymorphisms well studied, but there were variations among populations and some findings remain somewhat equivocal.[13] The present study aims to study the impact of smoker in serotonin level and *5-HTTLPR gene variation*.

METHODOLOGY

Sampling and Data Collection

The collected of samples and data implemented during (May-July), all participants were approving for enrolled in the present study, blood samples were collected to DNA extraction and serotonin detection by ELIZA.

DNA Extraction and Amplification Conditions

DNA was extracted using favor gene extraction kit, the *5-HTTLRP* amplified by f: 5-GCCAGCACCTAACCCCTAAT-3 r: 5 GTAGGGTGCAAGGAGAATGC-3 amplification sizes

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were 366 bp for the L allele and 322 bp for the S allele. Electrophoresis conducted by agaros1% 70V, 0.5TBE buffer for 40 minutes with ethidum bromide staining.

Data Analysis

The data clarified as mean ± stander error, independent t test, and ANOVA one way for statistical analysis at *p-value* <0.05, the genetic analysis implemented by odd ratio, CI95%, and allele frequency by hardy-Weinberg analysis.

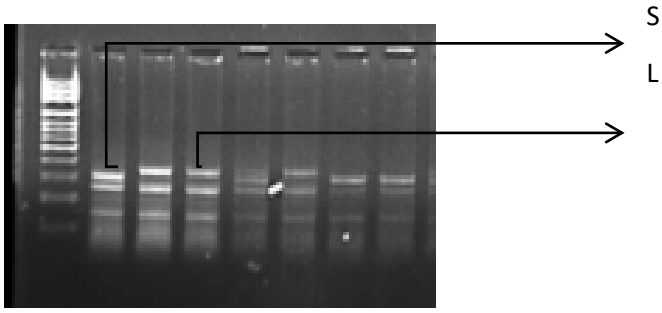

Figure 1: The genotyping of *5-HTTLRP* in study groups, LL, LS and SS genotypes, the electrophoresis conditions 1% agaros and 70 V for 40 minutes

Table 1: Mean differences of Age, BMI and serotonin level in smoker and non-smoker group

Smoking habit	*Age*	*BMI*	*Serotonin ng/mL*
Non-smoker	26.95 ± 0.911	24.63 ± 0.781	171.58 ± 8.249
Smoker	26.00 ± 1.879	23.95 ± 1.536	162.66 ± 7.078
Sig	0.644	0.698	0.605

Table 2: Genotypes distribution and allele frequency of *5-HTTLPR* in smoker and non-smoker group.

Genotypes	*Smoker%*	*Non-smoker%*	*Odd ratio (CI%)*	*Sig*
SS	50	33.33	0.5000 0.0817 - 3.0597	0.4533
LS	33.33	50	1.5000 0.105 - 21.3130	0.7646
LL	16.66	16	RG	
L	0.33	0.41	1.4057 0.7922 - 2.4943	0.2445
S	0.66	0.58		

RG, references group, CI%, confidence interval %

Table 3: Impact of *5-HTTLRP* genotyping in serotonin levels in study groups

Genotypes	*Smoker*	*Non-smoker*
SS	175.66 ± 8.45248a	185.37 ± 18.19236
LS	151.00 ± 5.00b	168.25 ± 9.22786
LL	147.00 ± 0b	154.00 ± 20.21551
Sig	0.032	0.466

Duncan test, different letter refer to significant differences among groups at p<0.05

RESULTS AND DISCUSSION

Present output exhibits those non-significant differences in age and body mass index (BMI) (p <0.644, 0.698), respectively. The serotonin level was not affected by smoking habit and found slightly decreased in smokers' group (162.66 ± 7.078) than non-smoker group (171.58 ± 8.249) (Table 1).

The serotonin has a main function in the human body and affected by several factors.[14] Smoker can be impacted in serotonin level, although of fluctuated results of numerous studies, present study shows a decrease in serotonin level in smoker in non-significant differences. This deals with results by Ghada *et al*., finding an inverse significant correlation between serotonin and Cotinine.[15] Others found elevations in serotonin level in smoker, this belongs to the blocking of serotonin receptors by smoking.[6,7]

The *5-HTTLPR* gene polymorphism was detected by allele specific PCR, and the results represented by short allele and long allele three genotyping were observed for LL, LS, and SS (Figure 1). The LS was more observed in non-smoker group while SS is more frequent in the smoker group in non-significant differences (p <0.764, 0.453), respectively. LL was a low percentage in both groups. The allele frequency was detected by Hardy-Weinberg equation, and S allele was more observed in smoker (0.66) and non-smoker (0.58), respectively in non-significant differences (p <0.2445) (Table 2).

The 5-HTT gene is a high polymorphic segment, one of these polymorphisms is dependent in present study, which is located at the promoter region, polymorphic represent by insertion/deletion of about 44 bp at the 1,000 bp from the transcription initiation site. This polymorphism was effective in serotonin activity. The short (S) allele is associated with lowering the transcriptional activity in compared with the long (L) allele.[9] In present study there wasn't association observed between *5-HTTLRP* and smoker and this deal with Sieminska *et al*. as no significant differences in the rates of *S* allele carriers in ever smokers and never smokers. Another study found that the individuals having L allele were more inclined to smoke.[16,17] However, there were other affecting factors in this association like population heterogeneity, stratification, age, gender, personality and environmental factors.[18]

The effect of *5-HTTLRP* in the serotonin level was clarified in Table 3. The serotonin level was decreased in LS and LL, respectively, significant changes in smoker group (p <0.032) while non-significant in the non-smoker group (p <0.466), Earlier Little et al., found that the S allele cells have been shown to take up less serotonin from the medium than LL genotype cells in postmortem brain.[19] The Preclinical research was reported that the S allele is associated with lower binding potential to the 5-HT_{1A} receptor implicated in nicotine-induced behavioral sensitization.[20] The present study concluded that the serotonin may be effected by the smoker, and the *5-HTTLRP* polymorphisms didn't related to smoking, but the polymorphisms cause significant differences in serotonin level in smoker. This lead to say that the slightly serotonin decreasing in smokers may be affected by other factors and other polymorphisms of genes.

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