

Original Article

Comparison of the Effect of Propofol and Sodium Thiopental on Serum Levels of IL-23 and IL-17 after Electroconvulsive Therapy in Major Depression

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Abstract

Background: Major depression disorder (MDD) is related to changes in immune function. Electroconvulsive therapy (ECT) is used in patients with MDD and is performed under general anesthesia. This study aimed to compare the effect of propofol and sodium thiopental on serum levels of interleukin-23 (IL-23) and interleukin-17 (IL-17) after ECT in MDD.

Materials and Methods: This descriptive study was conducted on 62 patients with major depression treated with ECT. They were randomly divided into the propofol and sodium thiopental groups. The serum concentrations of IL-23 and IL-17 were measured using the ELISA method before ECT (T0), 30 min after ECT (T1), and 5 hours after ECT (T2). Data were analyzed using descriptive statistics and Chi-square tests, independent t-test, one-way ANOVA, and repeated measures.

Results: There were no significant differences between propofol and sodium thiopental groups regarding the serum levels of IL-23 and IL-17 ($p > 0.05$). The trend of serum levels of IL-17 and IL-23 was not significant over time ($p > 0.05$).

Conclusion: The choice of propofol or sodium thiopental for anesthesia in patients with MDD receiving ECT is not different regarding short-term effects on serum IL-23 and IL-17 levels.

Keywords: Electroconvulsive therapy, Propofol, Sodium thiopental, Interleukin-17, Interleukin-23, Major depressive disorder

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Introduction

Major depression is a chronic mood disorder that is common and recurrent (1, 2). Some studies have shown that major depressive disorder is associated with changes in immune function (3, 4). About three decades ago, major depression was associated with mild immune system suppression (5-7). However, after that, Levels of inflammatory mediators and immune

cell functions have been found to increase during the depression (8). A weak response to antidepressants and a chronic course of the disease has been indicated in patients with elevated inflammatory function (9). Liu et al. reported that low levels of IL-8 predict a better therapeutic response to antidepressant therapy (10). Kruse et al. also suggested that lower IL-8 levels might predict reduced depression severity following

antidepressant therapy (11). Nowadays, the reality that pro-inflammatory factors are included within the pathogenesis of depressive disorder has been broadly examined (8, 9).

IL-23 affects T-helper 17 (Th17) cells and stimulates these cells to produce IL-17 (12). Th17 cells have essential roles in various inflammatory diseases (13). The central cytokines released by Th17 cells are IL-22, IL-21, and IL-17, of which IL-17 is the most critical functional cytokine (14). IL-17 causes tissue damage, particularly in the central nervous system (15). There is evidence that IL-17 is a significant autoimmune regulator of the central nervous system (16). Th17 cells play an essential role in the pathophysiology of depressive disorder. Th17 cell count and IL-17A expression are upregulated in patients with MDD (17).

Electroconvulsive therapy (ECT) is a method for treating psychiatric diseases (18). Few studies are looking at the effect of ECT on immune system function (12, 19). ECT affects molecules in the brain, such as neurotransmitters and neuropeptides (20). The release of inflammatory cytokines may be considered a response to ECT (21).

Before ECT, general anesthesia creates patient comfort and reduces complications (22). Sodium thiopental and propofol are common intravenous anesthetics used to induce general anesthesia or sedation (23). The rapid onset and short duration of action of these drugs have made them the choice drugs in ECT. Sodium thiopental has been used for ECT anesthesia for a long time. However, propofol has become standard in the last decade due to its rapid recovery, lower incidence of postoperative nausea and vomiting, and lack of cumulative drug and bronchodilator effects (24).

In the study of Salo et al., the effect of sodium thiopental and propofol on Th1/Th2 balance was determined by measuring the serum levels of IFN- γ , interleukin-4, and interleukin-2. The results showed different effects of these drugs on the immune response. Unlike propofol, thiopental reduced IFN- γ and IL-4 concentrations without affecting IL-2 concentrations. High propofol infusion doses elevated the IFN- γ /IL-4 ratio. However, low-dose propofol did not alter the serum levels of cytokines (25). Studies on IL-17 and IL-23 and changes in their serum levels in

severe depressive disorder are limited. Since today the use of propofol instead of thiopental sodium is increasing, this study aimed to determine the effect of propofol and sodium thiopental on serum levels of IL-23 and IL-17 after ECT in major depression.

Methods

This descriptive study was performed on patients with MDD who were referred to the psychiatric ward of Moradi Hospital, the only psychiatric ward in Rafsanjan (Southeast Iran). The inclusion criteria were electroconvulsive therapy based on a psychiatrist's diagnosis, an age range of 20-60 years, no intracranial mass lesions, and no succinylcholine injection contraindications. The exclusion criteria include uncontrolled cardiovascular and pulmonary disease, infectious disease, corticosteroid medications, complex airway management, pregnancy, cardiac pacemakers, smoking, alcohol, drug abuse, and anesthesia-related problems. The sample size was calculated at 30 patients for each group based on Zincir et al. study and considering the following parameters (21).

$$\alpha = 0.05, \beta = 10\%, s_1 = 33.46, s_2 = 52.08, \mu_1 = 45.4, \mu_2 = 81.89.$$

The sample size for each group was 31 patients. The patients randomly selected one envelope out of 62 sealed envelopes (A= sodium thiopental, B= propofol) and were placed in one of the groups. The present study was approved by the Rafsanjan University of Medical Sciences (RUMS) Research Council and the University Ethics Committee (IR.RUMS.REC.1396.138). After providing the necessary explanations, written informed consent was obtained from all participants. Then, a standard Beck questionnaire (21 questions) was used to measure the severity of depression. The Beck depression inventory (BDI) is widely used for screening and measuring the severity of depression in different countries. Aaron Beck et al. introduced the questionnaire in 1961 and revised it several times. Cronbach's alpha coefficient was reported to be 0.89 (26). Each item of BDI is scored on a 4-point Likert scale ranging from zero to three, and the total score ranges from 0 to 63. Based on this scale, the severity of depression is divided as

follows: 0-9 without depression (healthy), 10-14 borderline depression, 15-20 mild, 21-30 moderate, 31-40 severe, and 41-63 very severe depression (26).

Before induction of general anesthesia for ECT, electrocardiogram monitoring and oximeter pulse probe are connected. Heart rate, systolic, and diastolic blood pressure were monitored and recorded. Demographic Information such as gender, age, weight, marital status, education, and history of treatment with ECT were also recorded to assess the similarity between the two groups.

Group A received 1.5-2 mg/kg sodium thiopental, and group B received 1-1.5 mg/kg propofol intravenously. Succinylcholine (0.5 mg/kg) was used to reduce ECT-induced contractions. Before ECT, the patients were hyperventilated using 100% oxygen to prevent hypercapnia.

Blood samples (4–5 ml) were taken before ECT (T0), 30 minutes (T1), and 5 hours after ECT (T2) to determine the levels of IL-17 and IL-23 (27). The serum levels of cytokines were determined using ELISA kits according to the manufacturer's instructions (Karmania Pars Gene, Iran). The ELISA reader at 450 nm read the final OD (optical density). The person who performed the laboratory tests was blinded to the grouping.

SPSS version 20 (SPSS Inc., Chicago, Illinois, USA) was used for data analysis. The normal distribution of the variables was examined using the Kolmogorov–Smirnov test. Differences between the groups were evaluated using descriptive statistics, Chi-square, independent t-test, one-way ANOVA, and repeated measure tests. A value of $p < 0.05$ was considered a statistically significant difference.

Results

The mean and standard deviation of participants' age and weight was 34.44 ± 8.02 years and 61.00 ± 14.28 kg, respectively. Thirty-four participants (54.84%) were male. Seventeen participants (27.42%) were single, and 74.2% ($n=46$) reported a history of treatment with ECT. The education level of 54.84% of the participants ($n=34$) was less than a diploma. The demographic characteristics of participants are compared in Table 1. The results indicated no significant difference between

the two groups.

According to Beck's questionnaire, the mean and standard deviation of the depression score in the propofol group was 26.82 ± 17.26 and in the sodium thiopental group 31.69 ± 17.27 . The Chi-square test did not show a significant difference in the severity of depression between the two groups ($P=0.520$). The severity of depression in the two groups is compared in Figure 1.

The mean and standard deviation of serum levels of IL-17 and IL-23 in the two groups are compared in Table 2. The Independent t-test results showed that the mean and standard deviation of serum levels of IL-17 and IL-23 at different times were not significantly different between the two groups. The repeated measures test showed that the changes in IL-17 and IL-23 serum levels over time were insignificant in either group (Table 2).

The mean and standard deviation of IL-23 and IL-17 serum levels before ECT, 30 minutes post-ECT, and 5 hours post-ECT were compared in the propofol and sodium thiopental groups according to demographic variables. No significant difference was observed in any groups ($p > 0.05$).

Discussion

It has been reported that patients with depression suffer from IL-23/IL-17 axis-related inflammatory responses, and increased serum levels of IL-17 are associated with an increased risk of depression (23, 24, 27, 28). These studies investigated the effect of propofol and sodium thiopental on serum levels of IL-23 and IL-17 after ECT in patients with major depression to determine which of these two drugs is less likely to interfere with the treatment of patients with depression and is safer. However, in previous studies, the comparison between the roles of propofol and sodium thiopental on the serum levels of IL-23 and IL-17A has not been investigated.

The results of the present study demonstrated that post ECT, the serum levels of IL-23 and IL-17 were not changed significantly in patients with major depression. Additionally, there were no differences between the groups regarding the serum levels of IL-23 and IL-17.

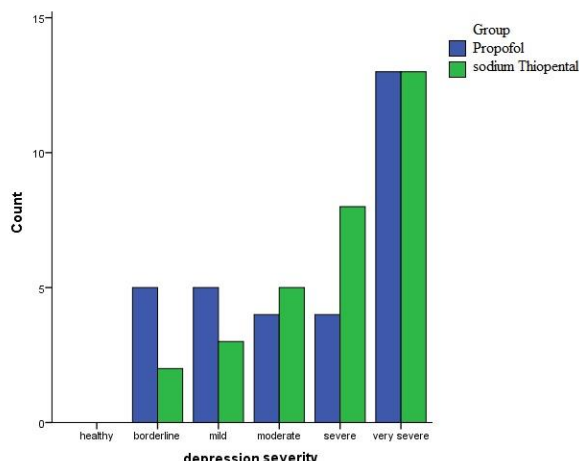


Figure 1. Comparison of depression severity between the propofol and sodium thiopental groups.

Table 1: Comparison of the demographic characteristics in patients with Major depressive disorder treated by ECT in propofol and sodium thiopental groups.

Variable	Sodium thiopental (n=31)	Propofol (n=31)	P	
Age (year) (Mean ± SD)	34.64 ± 9.14	32.54 ± 10.17	** 0.535	
Gender [N (%)]	Male	13 (41.93)	* 0.307	
	Female	18 (58.07)		12 (38.71)
Weight (kg) (Mean ± SD)	56.64 ± 11.83	63.77 ± 15.24	** 0.147	
Marital status [N (%)]	Single	11 (35.48)	* 0.637	
	Married	18 (58.06)		19 (61.29)
	Divorced	2 (6.46)		5 (16.13)
Education [N (%)]	Less than diploma	18 (58.07)	* 0.829	
	Diploma	9 (29.03)		12 (38.71)
	Bachelor	4 (12.90)		3 (9.68)
History of treatment with ECT[N (%)]	Yes	22 (70.97)	* 0.712	
	No	9 (29.03)		7 (22.58)

* Chi-Square * Fisher’s Exact Test ** Independent T-Test

Table 2: Comparison of the mean and standard deviation of IL-17 and IL-23 serum levels in patients with depression treated with ECT in propofol and sodium thiopental groups.

Variable	Sodium thiopental (n=31) (Mean ± SD)	Propofol (n=31) (Mean ± SD)	P	
IL-17 (pg/ml)	T0	11.69 ± 2.96	15.41 ± 9.02	0.195
	T1	12.26 ± 2.03	13.27 ± 2.64	0.397
	T2	11.50 ± 3.24	12.74 ± 2.03	0.206
p- value	> 0.05	> 0.05		
IL-23 (pg/ml)	T0	28.17 ± 7.18	25.15 ± 7.94	0.288
	T1	26.22 ± 4.48	26.20 ± 6.16	0.992
	T2	23.58 ± 9.08	25.41 ± 6.50	0.542
p- value	> 0.05	> 0.05		

T0= before ECT, T1= 30 min post ECT, T2= 5 hours post ECT.

P-value<0.05= significant difference

Lehtimaki et al. reported that ECT could induce immune cells to produce and release pro-inflammatory

cytokines (12). However, in this study, no significant difference was observed between serum levels of IL-17 and IL-23 before and after ECT following anesthesia with thiopental sodium or propofol. The effect of sodium thiopental, a rapidly induced intravenous anesthetic, on GABA-A receptors expressed in immune cells has been confirmed. The results of studies have revealed that sodium thiopental reduced T-helper and NK cells activity and increased T-inhibiting cell viability (28). Thiopental also can inhibit the expression of IL-1, IL-6, IL-8, and TNF- α and elevate the expression of IL-10 (23, 24, 28). Another investigation revealed that thiopental, compared to propofol, decreases the serum levels of IFN- γ and IL-4 without affecting the IL-2 serum level (28). Also, other studies have assessed the role of ketamine (29-31). Propofol also has anti-oxidant and anti-inflammatory properties (32). A study by Gonzalez-Correa et al. showed that propofol reduced IL-1, TNF- α , and IL-6 cytokines and, like thiopental, increased IL-10 (33).

Additionally, Jin et al. stated that a high dose of propofol increased the serum levels of IFN- γ , which is a pro-inflammatory Th1 cytokine. In contrast, its low dose did not alter the concentration (34). Therefore, high doses of the drugs show different effects on the immune system. A higher serum level of anti-inflammatory cytokines in patients receiving propofol demonstrates its anti-inflammatory properties (32-36). Contrary to what was mentioned, the present study showed that serum levels of IL-17 and IL-23 did not change significantly in the first 5 hours after ECT with sodium thiopental and propofol. It may be hypothesized that the patients suffering from severe depression may resist decreasing inflammation via IL-17/IL-23 axis.

Additionally, it may be related to ECT because it has been reported that ECT may act by modulating immunological mechanisms (37). Collectively, it may be hypothesized that ECT led to neutralizing the anti-inflammatory effects of sodium thiopental and propofol. In addition, the follow-up period in the present study may have been short, which means that the expression of IL-17 and IL-23 may be different in the two anesthesia groups with propofol or thiopental sodium. Still, the serum levels of these cytokines have not changed at the time of blood sampling in the

present study. Our findings showed that if blood sampling was performed at longer intervals (for example, 24 hours post-ECT), a significant difference in serum levels of IL-17 and IL-23 might be observed between the two groups. In this regard, in the study of Lehtimaki et al., it was also observed that IL-1 beta and IL-6 levels elevated sixth hours post ECT (12).

The study limitation is the low sample size, although it is similar or higher compared to similar studies. Another limitation is the short follow-up period after ECT. Given that propofol and sodium thiopental may affect the interleukin-17 and interleukin-23 gene expression, to achieve more accurate results, it is recommended to conduct studies with a more extended follow-up period post-ECT.

Conclusion

The present study showed that serum levels of IL-17 and IL-23 in patients with depression changed post Electroconvulsive therapy using propofol or sodium thiopental. However, there was no significant difference in serum levels of these interleukins between the two groups. Therefore, it can be concluded that changes in serum levels of these interleukins are related to the nature of ECT. Future studies with long-term follow-ups can provide more reliable results.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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