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Reply to Letter to the Editor

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Letter to the Editor

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Lipid emulsion and verapamil toxicity

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To the Editor,

I read the article "Therapeutic effects of intralipid and medialipid emulsions in a rat model of verapamil toxicity" written by Akgün Şahin et al. in the *Turkish Journal of Medical Sciences* with great interest (1). I think that this laboratory study, in which two lipid emulsions were equally effective in ameliorating the cardiovascular depression induced by a toxic dose of verapamil, is valuable (1). In addition, the two lipid emulsions have been reported as equally effective in reversing the effects of high-dose levobupivacaine-induced vasodilation in rat aortas (2). Recently, it was reported that lipid emulsion (intralipid) is effective in treating the cardiovascular collapse induced by intravenous toxic doses of verapamil (3,4). However, I noticed some issues while reviewing this article, which I would like to bring to your attention (1). First, statistical analysis regarding the difference in mean arterial pressure (MAP) among the three groups at each time point (for example: MAP_b, T_0, T_5, T_{10}, T_{15}, T_{30}, T_{40}, T_{50}, and T_{60}) was performed using a linear mixed model (1). However, I am not sure how Akgün Şahin et al. achieved a statistically significant MAP difference between two groups at each time point (see Table 1 in the original article) (1). For example, the MAP of the intralipid group at MAP_b and T_{10} was higher than that of the control and medialipid groups (Table 1) (1). As another example, the MAP of the intralipid group at T_{10}, T_{15}, T_{20}, T_{30}, T_{40}, T_{50}, and T_{60} was higher than that of the control (Table 1) (1). The detailed statistical analysis method (for example, the Bonferroni or Šídák test) regarding multiple comparisons of two specific groups (control versus intralipid, control versus medialipid, intralipid versus medialipid) at each time point should be described (5). Second, as the baseline MAP (MAP_b) was higher in the lipid emulsion (intralipid or medialipid) groups than in the control group (Table 1), even though the MAP of T_0 was not significantly different, it is natural that MAP at T_{15}, T_{20}, and T_{30} was higher in the lipid emulsion (intralipid or medialipid) groups than in the control group (1). In addition, the results obtained from the same statistical analysis method may be different depending on the absolute or relative value of MAP. Thus, data description using the percentage change of baseline MAP induced by verapamil infusion followed by lipid emulsion infusion may be more reasonable. Third, although according to Akgün Şahin et al. the rats were randomly assigned to one of three groups, MAP_b was higher in the lipid emulsion (intralipid and medialipid) groups than in the control group (Table 1) (1). Thus, if more careful randomization among the three groups were performed, the possibility of a difference in MAP_b between the control and lipid emulsion (intralipid or medialipid) groups would be reduced.

In conclusion, I think that this study contributes to data demonstrating lipid emulsion treatment as a nonspecific antidote to intractable cardiovascular collapse induced by a toxic dose of verapamil. However, if the above suggestions including a detailed description of the statistical method used for multiple comparisons following the linear mixed model, careful randomization, and percentage change of baseline MAP would be considered, this study would be improved and more informative for its readers.

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Reply to Letter to the Editor

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To the Editor,

We would like to thank Sohn for reading and evaluating our article entitled "Therapeutic effects of intralipid and medialipid emulsions in a rat model of verapamil toxicity", published in the *Turkish Journal of Medical Sciences*. We value the views regarding the statistical evaluation of our article. Although randomization was conducted in our study, the MAP_b value was found to be lower in the control group than in the other two study groups. In this case, if we had denoted the rate of change in MAP values in percentage, as suggested by Sohn, the degree of significance among the groups would have been determined better. Furthermore, when the MAP values' change in time is considered, it is observed that the values in the control group decrease in time and remain low and that MAP values in the intralipid and medialipid groups decrease down to T_5 and T_{10}, respectively, but in contrast to the control group, they increase (please see Table 1 in the original article).

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