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EXPERIMENTAL STUDY

Effects of the general anaesthetic agent, propofol, on erythrocyte deformability

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Abstract: *Objectives:* Propofol is an anesthetic agent frequently used for sedation and general anesthesia. The purpose of our study was to investigate the effect of propofol, a general anesthetic, on erythrocyte deformability in rats.
Methodology: The study was performed on 20 male and 20 female rats, with 10 rats in each study group and 10 rats in each control group. The rats in the study group were administered propofol (150 $mg.kg^{-1}$) intraperitoneally, and the rats in the control group were administered SF. Erythrocyte packs were prepared using heparinized total blood samples. Deformability measurements were done by erythrocyte suspensions in PBS buffer. A constant flow filtrometer system was used to measure erythrocyte deformability, and the relative resistance was calculated.
Results: The use of propofol resulted in the increase in the relative resistance, which is an indicator for the erythrocyte deformability in both male and female rats (p=0.002, p=0.042, respectively).
Conclusion: A negative change in the erythrocyte deformability may cause a functional deterioration in blood flow and tissue perfusion *(Fig. 1, Ref. 23)*. Full Text (Free, PDF) *www.bmj.sk.*
Key words: erythrocyte deformability, propofol, rat.

General anesthesia agents are known to affect cardiovascular functions and microcirculation dynamics (1). However, whether these agents change the plasma reology and/or anesthesia may result in deterioration of tissue perfusion remains controversial. Changes in the plasma viscosity has been listed among the factors associated with anesthesia procedures responsible for deterioration of tissue and organ perfusion (2, 3). After surgical procedures performed using a general anesthesia, erythrocyte deformability and increased aggregation may be observed (3).

Hemoreological factors are sensitive to metabolic changes and may be affected by tissue perfusion due to cardiovascular problems. Disorders in the hemoreologic state may lead to an inadequate recovery in plasma viscosity (2). Erythrocyte deformability and plasma viscosity are important factors that affect organ and tissue perfusion (4). For migration of oxygen and vital molecules to the final organ, capillaries and clearance of metabolic wastes, erythrocytes must be able to extend and curve and have the capability to move in these areas. This capacity is termed as "deformability" (5).

Propofol (2,6-diisopropylphenol) is an intravenous anesthetic agent that is commonly used in daily clinical practice for sedation and general anaesthesia. Its cardiovascular side effects have been described in various studies. It can decrease the peripheral vascular resistance (6) decrease jugular venous oxygen saturation (7), induce haemolysis (8), and cause the so-called propofol infusion syndrome, an often fatal cardiac failure (9). Considering its hydrophobic properties, propofol has to be administered in an aqueous emulsion using soya oil. However, not only propofol but also soya oil may be responsible for these side effects. Thus, the pathophysiological mechanisms underlying the cardiovascular effects are not clearly described (10).

In earlier studies with various methodologies, propofol has been shown to cause OS, not to affect OS, or to have antioxidant effect (11–14). In *in vitro* studies, it has been shown to inhibit lipid peroxidation induced by oxidative stress in the liver microsomes, mitochondria, and brain synaptosomes (15). The products that arise due to lipid peroxidation associated with an increased oxidative stress, significantly affect the membrane permeability and microviscosity, thus diminishing the deformability capacity and survival of the erythrocytes (16).

We hypothesized that propofol and/or the emulsifier might do this through a direct action on the biophysical or functional properties of the blood constituents such as the red blood cell (RBC) deformability.

General anesthesia, either with inhalation or nonvolatile anesthetics, is known to affect the overall cardiovascular function as well as the microcirculatory hemodynamics. Alterations in the blood rheology under the influence of anesthesia have been observed and discussed among the responsible factors for the

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deterioration of tissue and organ perfusion related to anesthetic procedures. Propofol is one of the nonvolatile anesthetics which is widely used in surgery. In this study, the effects of propofol anesthesia on the red blood cell deformability of young male and female rats were evaluated.

Methodology

This study was conducted in the Physiology laboratory of the Kirikkale University upon the consent of the Experimental Animals Ethics Committee of the Kirikkale University.

In the study, 20 male and 20 female Wistar Albino rats (total number=40) of 175–350 gr in weight, raised under the same environmental conditions, were used. The rats were kept under 20–21 °C at cycles of 12-hour daylight and 12-hour darkness and had free access to food until 2 hours before the anesthesia procedure.

Four groups of ten rats were formed as the study and control groups for each gender (female rats=10 rats+10 rats; male rats =10 rats+10 rats). The study groups were administered propofol 150 $mg.kg^{-1}$ intraperitoneally and the control groups were given the same amount (150 $mg.kg^{-1}$) of SF.

Thirty minutes after propofol administration, all the rats were given ketamin 50 $mg.kg^{-1}$ intraperitoneally and intracardiac blood samples were obtained. Heparinized total blood samples were used to prepare erythrocyte packs. Deformability measurements were done by erythrocyte suspensions with 55 htc in PBS buffer.

The erythrocyte deformability was measured using a constant flow filtrometer system. The erythrocyte suspension delivered at 1 ml/min flow rate was passed through a nucleopor-polycarbonate filter of 5 um in diameter, and alterations in the filtration pressure corresponding to different flow rates were measured. The alterations in the pressure were transferred to computer medium with an MP 30 data equation system. The ratio of the values of filtration pressure for the cellular suspension and buffer were calculated, and the relative resistance was calculated.

Statistical analyses

The statistical analyses were performed with th SPSS 12.0 software program and $p<0.05$ was considered statistically significant. The findings were expressed as mean±standard deviation. The data were evaluated with the Kruskal-Wallis variance analysis. The variables with significance were evaluated with the Bonferroni corrected Mann-Whitney U test.

Results

The results of the study indicated that propofol increased the relative resistance, a marker of erythrocyte deformability in both male and female rats ($p<0.05$) (Fig. 1).

There were significant differences between the groups according to the comparisons with the Kruskal-Wallis test ($p=0.003$). The results obtained after the corrections with the Mann-Whitney U test were as follows: Comparisons of the male and female rat groups revealed similar results ($p=0.841$). The values of the male rats in the study group (propofol) were significantly higher than those of the male rats in the control group ($p=0.002$), and similarly, the values of the female rats in the study group (propofol) were significantly higher than those of the female rats in the control group ($p=0.042$). No statistically significant differences were found between the male and female rats that were given propofol ($p=0.052$).

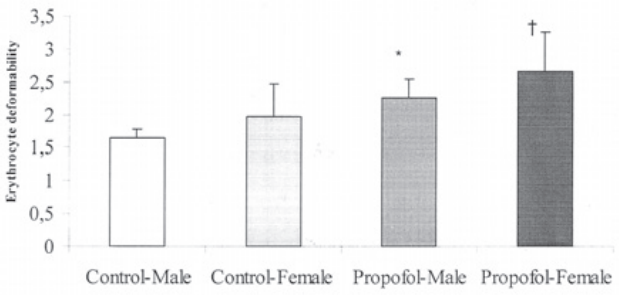

Fig. 1. The erythrocyte deformability values of the groups. * p< 0.05 compared to the control – Male, † p< 0.05 compared to the control – Female.

Conclusion

Hemoreologic factors may be directly or indirectly affected by anesthetic agents and their metabolites. Anesthetics alter the diameters of arterioles and venules and the response of these structures to stress. The effects of anesthetic agents on microcirculation are specific and dose dependent. The mechanisms that cause this interaction may be associated with oxidative disorders that occur during or after various anesthesia applications (17–19).

Alterations in the erythrocyte deformability may result in poor perfusion that can contribute to vascular complications of postanesthetic period that may arise in addition to other well-known mechanisms. This may lead to an inadequate recovery (18).

The erythrocyte deformability method used in this study is composed of hole of similar size to those in the capillary system, and thus, it is a reliable experimental model for microcirculation. An increase in the erythrocyte deformability index is a sign of reduced erythrocyte deformability. Erythrocytes with a low deformability index have a high capacity for deformability. They easily change forms while passing through the holes, and thereby, are filtered in a short time.

Inhalation and intravenous anesthetic agents are known to affect cardiovascular functions and microcirculation and ongoing studies re investigating the issue. Yesilkaya et al (20) have found that halothane and pentobarbital impair the erythrocyte deformability.

Dikmen et al (14) have reported that in clinical doses, propofol/remifentanil has no effect of the oxidative stress, and sevoflurane can protect erythrocytes against the oxidative stress.

Erdogan et al (1) have shown that midazolam does not impair the erythrocyte deformability index and does not affect the plasma viscosity.

Yerer et al (21) investigated the effects of desflurane on deformability and found that it impaired the deformability in young and old rats. Aydogan et al (22) showed the negative effects of sevoflurane on the deformability of the old rats.

Yerer et al (23), in their study on the effects of desflurane and sevoflurane on deformability, have determined that the erythrocyte deformability of female rats does not change with sevoflurane administration, while it is significantly increased with desflurane administration. The authors reported that contrarily, sevoflurane increased the erythrocyte deformability, which was attributed to the general protective effects of estrogen in female rats that may be reflected upon the erythrocyte deformability.

In our study, propofol was found to impair the erythrocyte deformability of both genders, but it was more pronounced in the male rats. This may be accounted for by general protective effects of estrogen in female rats.

In conclusion, it can be said that propofol, a general anesthetic agent, may lead to negative alterations in the erythrocyte deformability, which may result in functional disorders in blood flow and tissue perfusion. However, further detailed clinical and experimental studies are needed.

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