UNIVERSITY OF MEDICINE AND FARMACY OF CRAIOVA

DOCTORAL SCHOOL

DOCTORAL THESIS

ABSTRACT

EFFECTS OF PROPOFOL ON REDOX BALANCE IN SURGICAL PATIENTS, IN PERIOPERATIVE PERIOD

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Contents

I. General Considerations

1. The interaction between surgical stress and oxidative stress-basic element for selecting the complete postoperative therapy.

1.1. Characteristics of surgical stress.

Waldron's vision (1985) states that the surgical act is defined as a "benign violence" (an appropriate term to highlight the creation of a plague, even when the goal is to avoid sickness).

The body does not make any difference between the benefic traumatic injury and the spontaneous one, perceiving only the existence of an intense physical stress.

1.2. Preoperative period.

Virtually all diseases that require surgery, including traumatic injury, force an oxidative treatment of tissues.

The early role of oxidants is clearly seen in the inflammatory response and involves damage to the affected tissues.

1.3. Peroperative period. (intraoperative).

Among the medicines administered intraoperatively, some of them are oxidizing and others stimulate the inflammatory and immune responses (especially for the respiratory tract directly exposed to inhalation anesthetics). The anaesthesiologists' concern is to minimize the oxidizing effects of the administered substances and to select those that have a protective effect against the Sox.

When the blood flow is restored in the ischemic areas, the reperfusion injury occurs, in which high levels of O_2 cause oxidative deterioration and the extraction of toxins from tissues mobilized into the general circulation. Oxidising molecules produce the lipoperoxidation of cell membranes. The oxidant attack determine the stimulation of the inflammatory reactions and the release of cytokines, which trigger the evolution towards oxidative injury enhanced by inflammatory cells. Although the inflammatory reaction is necessary and predicts a good healing, the exaggerating of the inflammatory response contributes as a local and systematic stressor impairing favorable development.

1.4. Postoperative period, postoperative healing.

The most important mechanisms, recognized as favorable wound healing are aiming for a relationship between tissue recovery (growth), inflammation reduction and the elimination of the infection. Moderate inflammatory reaction is extremely important due to the release of cytokines and other inflammatory mediators, which are needed to stimulate the production and release of growth factors for the vascular endothelium, needed to ensure the blood supply to the new tissues. The O_2 additional intake is important for postoperative therapy. However, O_2 in excess can increase the formation SRO, so the judicious combination of O2 intake and the intake of nutritional supplements is essential for wound healing.

2. Oxidative stress- pathophysiological and clinical definition.

2.1. Pre- and postcondiţionarea.

Reducing the flow of O_2 is before the normoxic reperfusion is called post conditioning and protects against ischemia-reperfusion (I / R), as a result of preventing the occurrence of peroxides and glutathione depletion in the mitochondria. It was concluded that reperfusion injury is due to the release of free O_2 radicals in the ischemic tissue. Observed alterations may be reversible or irreversible, depending on the severity and duration of the ischemic period. Ischemic preconditioning (PCI) was introduced to assure cardioprotection against ischemia-reperfusion injury. This method showed a reduction of the post ischemic arrhythmias incidence and a recovery of cardiac function and infarct size reduction after global ischemia.

2.2 Oxidative stress sources (S.ox)

a. The endogenous intracellular sources

b. The endogenous extracellular plasmatic sources.

c. Exogenous sources

2.3. Antioxidants (AO)

The classification of the antioxidants which have therapeutic effects:

1 Natural, physiological, present in body AO

2.Pharmacological AO (synthetic)

2.4. The oxidative stress-injury evolution, cell level oxidative aggression.

The reduction of blood flow (FS) in peripheral tissues, overwhelms the defense mechanisms of the organism (antioxidant) and generates ischemic injury.

During reperfusion and re-oxygenation, the rises of several species of free radicals degrade cell membranes and capillaries. It is postulated that O_2-, OH and free lipid radicals may be formed by the action of XO and / or by the release from neutrophils, which are activated by leukotriene.

Re-oxygenation replenishes the ATP levels, enabling the uptake of calcium by mitochondria, which increases the calcium overload and the destruction of mitochondria.

3. Propofol- anesthetic that influences redox balance

The Propofol is the most widely used intravenous anesthetic today.

The Propofol is primarily a hypnotic. The mechanism of action is not fully understood, however, evidence suggests that an important part of the hypnotic action is mediated by gamma-aminobutyric acid.

As a chemical formula, Propofol is diisopropylphenol, so it is made up of a phenolic ring that binds at positions 2 and 6 two isopropyl groups, resulting in a substance with low water solubility and high liposolubility. This is the reason why the creation of propofol is done in present in the form of an oil-in-water emulsion with soya bean oil (10%), purified egg phosphatide (egg lecithin) and glycerol.

Propofol has antioxidant effects which are due to its chemical formula similar to vitamin E and its free radical scavenger activity. Propofol inhibits the phagocytosis and decreases the growth of pro-inflammatory mediators triggered by surgery or other factors.

II. Personal contributions

Introduction.

The incision and surgical techniques of clamping / declamping of blood vessels (hemostasis) induce an unbalanced redox balance due to the growth of oxidants that cause the installation of oxidative stress to the operated patients. If the oxidative excess produced by the increase in the production and reactivity of ROS exceeds their compensation value by endogenous antioxidants, there will be redox imbalance evolving toward the installation of oxidative stress, of injury and even oxidative aggression, when the oxidant toxic byproducts disseminate in circulation.

The maintenance of redox balance, involves the production and consumption in equivalent amounts of both oxidants and antioxidants. In case of oxidant excess, antioxidants are consumed, allowing the increase of oxidizing tasks, phenomenon that characterizes the manifestation of oxidative stress.

Anesthesia uses substances that act in both directions (oxidant-antioxidant), the antioxidant effect being performed by the action of ROS scavenger. The potentiation of the antioxidant capacity of blood using exogenous antioxidants, among which you can find some anesthetics, may be beneficial for the postoperative evolution of the patient, whose oxidizing tasks were expected to grow in the intraoperative period.

Premise.

Highlighting the moment of the installation of oxidative stress associated with surgical stress at the operated patients, with the help of two biochemical indicative parameters: the organic hydroperoxide levels in the blood and the reduction capacity of serum iron.

Objectives:

-The characterization of umoral changes due to oxidative stress during surgery

-Estimating the correct obtained values, statistically providing them with high performance tests.

-Highlighting the antioxidant effects of propofol for patients

Material and method

The total loot of the study involved three groups of surgical patients, and were practiced two types of surgery, and we observed anesthetic effects of substances over redox balance. In this way we conducted three studies, three separate models of surgery and anesthesia.

The Measurement free radicals

We used ROS method to measure by chemiluminescence (CL). This method can monitor the formation of reactive oxygen metabolites including superoxide (O2.-), hydrogen peroxide (H_2O_2), OH, and HOCl.

The gas chromatography (GC) and mass spectrometry (MS) we used to measure lipid peroxides (aldehydes, izoprostans, peroxides cholesterol / cholesterol esters); peroxides are extracted, reduced to alcohols, separated through GC and identified by MS.

We use MDA like method of determination of lipid peroxidation.

Model 1

Working hypothesis:

Evaluation of the antioxidant properties of propofol in a surgical model of ischemia and reperfusion.

In the second place, ischemia-reperfusion model validation for another study with general anesthesia.

The use of the tourniquet commonly used in orthopedics, vascular and reconstructive surgery of the extremities for the benefit of providing a bloodless surgical field.

During ischemia, oxygen radicals are produced in unirrigated tissues. Loosening the tourniquet after hypo period (non) irrigation allowed the release of reactive oxygen species in the flow of reperfusion.

Method

We selected 34 patients from CF Clinical Hospital Craiova, proposed for orthopedic surgery: diagnostic and therapeutic arthroscopy, in which the tourniquet is used.

In our hospital diagnostic and therapeutic arthroscopy is performed under these conditions. We randomized patients in two grups.

Group D. We have achieved sedation with diazepam 10 mg, which was carried out after by subarachnoid anesthesia with 0.5% hyperbaric bupivacaine 12.5 mg.

Group P We assured sedation with propofol 0.5 mg / kg, followed by subarachnoid anesthesia with hyperbaric bupivacaine 0.5% 12.5 mg and continued with continuous infusion of propofol at a rate of 2 mg / kg / h.

We acquired blood for four determinations: before the start of anesthesia (T0), but after the finishing of preoperative infusion of Ringer solution, one minute (T1) before releasing compression pneumatic (1BTR), and at 5 and 30 min (T2, respectively T3) after releasing compression (ATR) for measuring ROS in plasma.

Results

Measurements have revealed that there were not statistically significant differences between the groups in terms of values of ROS before beginning anesthesia at T0 point.

Descriptive	**Group D**	**Group P**
n	17	17
Mean	6312.47	6214.18
Median	6345.00	6140.00
Standard Deviation	244.14	290.86
Standard Error	59.21	70.54

Table 1 Descriptive statistical analysis ROS- moment T0-sumarry- values in the two groups

Also, there were not significant statistical differences in point T1, one minute before compression release (1BTR) between groups. (4398 count 10 s group diazepam, 3735 numbered 10 and propofol group).

Applying comparative tests between the groups there were not revealed any significant differences at this time of the study.

However, in both groups ROS values were slightly lower than the values considered reference (baseline).

5 minutes after the release of compression (5 ATR) T2 in propofol group, the concentration of ROS (6617 count 10 s) remains low around the baseline (6214 count 10 s).

Diazepam group was a significant difference numbered 12773 on 10 compared to baseline (6312 numbered in the 10s).

At time T2, there was a significant difference between the groups.

30 minutes (T3) after the compression (30 ATR) there were detected statistically significant differences between the ROS between the two groups being a higher level in group D compared to group P, group D 15960 counts per 10 seconds as compared to 5383 counts per 10 in group P.

In group D, there were also significant differences compared to the BL group at this point (T3) - 6312 counts per 10 seconds from BL compared to 15960 counts per 10 seconds to 30 minutes ATR).

Compared two trends show that in Figure 1.

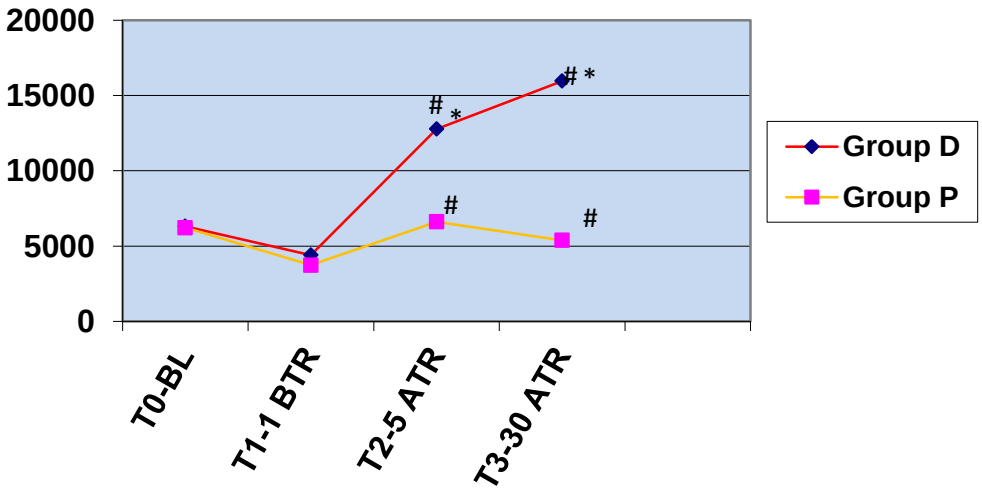

Figure 1 Graphical representation of average values of ROS during the study compared

* - P <0.05 BL differences (Group D)

- P <0.05 difference between groups

Discussion and conclusions

Although skeletal muscle is relatively resistant to ischemia, several studies have shown that oxygen free radicals cause damage to muscle during reperfusion.

Oxygen free radicals are produced during orthopedic surgery performed by applying a tourniquet ischemic.

Our study showed that propofol (Group P) did not produce significant differences within 30 minutes after reperfusion compared to the value considered to be the baseline at the beginning of anesthesia.

In contrast, at diazepam group in the same period, we observed a significant increase in levels of ROS, so it seems that from this point of view propofol is a better choice for sedation at patients who received regional anesthesia for orthopedic surgery that require ischemic tourniquet.

We have also found that the concentration of ROS in plasma in group D decreased slightly before reperfusion (BTR) compared to the baseline, which would have been the result of the effects of sedation, released of the stress in the operating room.

In Group P we've noticed a more prominent drop in plasma concentrations of ROS 1 BTR, but without statistical significance.

This may be due to both effects, both propofol that reduce oxidative stress by acting as a free radical scavenger and regional anesthetics, which reduces stress inducer hormones, such as adrenaline, noradrenaline and cortisol.

So, in our study propofol seems to be protective against oxidative stress in the case of peripheral ischemia-reperfusion.

This study demonstrates that sedation with propofol under regional anesthesia produces better antioxidant defense than sedation with diazepam against ischemic injury followed by reperfusion due to tourniquet's application in orthopedic surgery.

Model 2

To study the production of ROS, at the same model of ischemia-reperfusion devoted, we study the influence of two regimes of general anesthesia, over oxidative status, one of regimens being based on propofol.

Method

We investigated 34 patients from CF Clinical Hospital Craiova, which required knee arthroscopy, a technique that uses the tourniquet. Patients were divided into two groups: sevoflurane (Group S) and propofol group (group P), each with 17 patients.

The induction of anesthesia. Group S: thiopental 4mg / kg and fentanyl 4mcg / kg; Group P: propofol and rocuronium administered to facilitate insertion of laryngeal mask.

Maintaining anesthesia. Group S. sevoflurane inhalation (3.4%); Group P: propofol administered at a rate of 10 mg / kg / hr reduced from 8 mg / kg / hr, and 6 mg / kg / h to 10 minute interval, in accordance with the concepts of the current total intravenous anesthesia (TIVA) or / and balanced anesthesia.

We sampled venous blood to determine plasma levels of malondialdehyde in five periods of the surgical act:

- T0- before induction of general anesthesia to obtain the blank value, baseline (BL)
- T1- 1 minute before applying the tourniquet's
- T2- 1 min before compression release
- T3- 5 minutes after tourniquet release site
- T4- 30 minutes after tourniquet release site

Results

There were no significant differences between groups in terms of MDA values before the induction.(table 2)

Descriptive	Group P	Group S
n	17	17
Mean	2.87	3.07
Median	2.87	3.12
Standard Deviation	0.29	0.44
Standard Error	0.07	0.11

Table 2 Descriptive summary analysis- concentration of MDA in the two groups, at T0

However MDA values in both groups had lower values than the amount considered BL, but without statistical significance. (T1 vs T0)

5 minutes after the initiation of reperfusion (T3) in the propofol group, MDA concentration decreases compared to MDA concentration before initiating ischemia. (table 3).

Descriptive	T3	T0
Mean	2.38	2.87
Median	2.36	2.87
Standard Deviation	0.95	0.29
Standard Error	0.23	0.07

Table 3 Descriptive summary analysis of the concentration of MDA in group P at times T0 and T3

In the sevoflurane group at that time was a slight increase (3.42 micromol / liter vs 3.07 micromol / liter). (T3 vs T0)

Between the two groups at this time (T3) differences were significant.

The representation of the mean of the MDA concentration values for both groups in all 5 points is shown in figure 2.

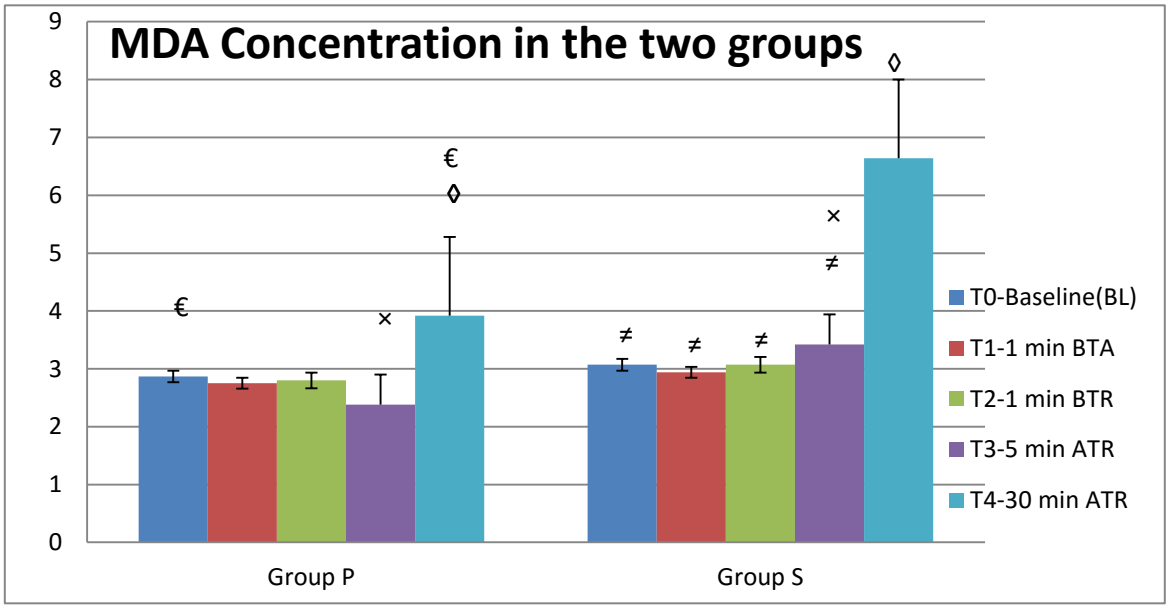

Figure 2 Average representation of the MDA concentration values for both groups in all 5 points. Concentration of malondialdehyde (MDA) in the plasma (micromol / l). Data is expressed as mean ± SD.

≠ - p <0.05 BL, 1 min BTA BTR 1 min, 5 min vs 30 min ATR ATR

◊ - p <0.05 vs Group P Group S, 30 min ATR

X - p <0.05 vs Group S Group P 5 minutes ATR

€ - p <0.05 vs 30 min ATR BL

Group P largest decrease in MDA was measured at 5 minutes ATR (2.38 ± 0.95 micromol / l) - (T3) compared to 1 min BTR (2.8 ± 1.45 micromol / l) - (T2) and 30 min ATR (3.92 ± 0.61 micromol / l) - (T4).

30 minutes after the reperfusion, there were observed significant differences between the two groups, MDA increase in group S was higher (3.92μmol / liter propofol group and 6.64 micromol / liter in the sevoflurane group).

In the group increased MDA levels were also statistically significantly (from 2.87 to 3.92 micromol / liter in the propofol group and from 3.07 to 6.64 micromol / liter in the sevoflurane group).

The results showed statistically that: there were not significant differences between groups in connection with MDA values before induction of anesthesia, but values in both groups were lower than the control value, BL, but without statistical significance. (T1 vs T0).

MDA decrease was obvious in group P at the time of 5 minutes ATR- T3 (2.38 micromol / l) compared to T0 (2.87 micromol / l), T2 1min BTR (2.8 micromol / l) and T4-30 min ATR (3.92 micromol / l).

30 min after the reperfusion, there were observed significant differences between the two groups, MDA increase in group S were higher (3.92 micromol / l vs 6.64 micromol / l).

Discussion and conclusions

In our study it was observed that propofol produces significant decrease in oxidative attack 30 minutes after reperfusion. In contrast, the sevoflurane group had an increase in MDA after the oxidative attack. As a result, propofol seems to be a good choice for this type of surgery member.

We noticed that the plasma levels of MDA decreased insignificantly in group S before reperfusion (BTR) compared to BL, and this might have been the result of sedative effects and the release of stress in operating room- general volatile anesthesia effect (group S).

Plasma concentration of MDA in Group S, 30 min ATR was significantly higher compared with group P at the same point of time.

In the same group P we noticed most prominent decrease in plasma levels of MDA, 5 min ATR. This reduction can be explained by the fact that the tissues that have been in ischemic injury were saturated with propofol prior to the initiation of ischemia.

In our study, propofol seems to be more protective against oxidative stress secondary to peripheral ischemia-reperfusion.

This study demonstrates that TIVA with propofol offers an antioxidant defense better than inhalation anesthesia with sevoflurane against injury reperfusion linked to the release of the tourniquet in orthopedic interventions. It takes more research to clarify this effect, but also to clarify the effects of sevoflurane on oxidative stress in peripheral tissues.

Model 3

We have selected another surgical model to highlight the effects of anesthetics on the balance redox substances, a frequent surgery in abdominal surgery.

Motivation.

Highlighting the installation of oxidative stress during abdominal surgery.

Objectives:

- The characterization of umoral changes due to oxidative stress during surgery associated with laparotomy for sigmoidectomy colectomy (a common gastrointestinal intervention).

- Investigation of antioxidant effects of propofol at patients undergoing surgery.

Method.

We divided into two groups of 21 patients each:

• Group S: surgical act performed under anesthesia with sevoflurane

• Group P: we use propofol as an anesthetic essential

The anesthesia was induced with sevoflurane 8% (group S), or 1.5-2.5 mg / kg propofol (group P), with the 0.003 mg / kg of fentanyl and 0.6 mg / kg rocuronium. Topical anesthesia of the larynx was performed with 4% lidocaine. Anesthesia was maintained with 2% -4% sevoflurane (group S), or 5-8 mg / kg / h propofol (group P), in the presence of 0.001 mg / kg h fentanyl and rocuronium 0.5 mg / kg / h.

We have taken two milliliters of blood from each patient three different times during the surgical anesthetic act:

• before induction of anesthesia (T0)

• At the beginning of surgery (T1)

• the removal of the colon (T2)

• at the end of surgery (T3)

• transfer into postanesthetic care unit (T4)

We determined the two elements of redox balance. organic hydroperoxides and reducing ability of plasma iron.

Results

21 patients in the group S and 21 patients in group P, were included in the study (Table 4).

	S Group	P Group
Number	21	21
Age (yr)	65±7.2	62±8.1
Weight (kg)	59±8	58±7.3
Time of surgery (min)	216±54.6	224±63.1
Diuresis (ml)	382±120.9	403±142.3
Cristaloids (ml)	2897±622.5	2874±644.3

Table 4 Patient characteristics

Circulated Hydroperoxide levels in the blood, as measured by the d-Roms, have not undergone any changes during surgery or intensive therapy in group S.

Hydroperoxide values measured by blood test d-ROMS during the procedure with sevoflurane anesthesia are shown in Table 5.

Descriptive	**T0**	**T1**	**T2**	**T3**	**T4**
Mean	401.24	413.14	393.19	389.86	408.86
Median	401.00	412.00	400.00	399.00	422.00
Standard Deviation	80.97	75.05	88.41	79.66	69.70
Standard Error	17.67	16.38	19.29	17.38	15.21

Table 5 Descriptive summary analysis of collected amounts d-Roms group S

Comparative analysis in the group S show that there were significant differences at any time during the study.

Group P-hydroperoxide levels were significantly lower at the end of surgery, compared with pre-anesthetic values (T4 vs T0) (296 ± 384 vs 89.56 ± 91.45 for UCarr).

Hydroperoxide values measured by blood test d-ROMS propofol anesthesia during the procedure are shown in Table 6.

Descriptive	T0	T1	T2	T3	T4
Mean	383.71	380.43	361.10	295.86	388.24
Median	383.00	377.00	373.00	254.00	396.00
Standard Deviation	91.45	69.52	64.09	89.56	95.24
Standard Error	19.96	15.17	13.99	19.54	20.78

Table 6 Descriptive summary analysis of values collected group P d-Roms

Comparative statistical analysis in the group was done with ANOVA and the emphasis regarding which difference is more significant by comparing two by two was shown using the Student t test , Friedman test and Wilcoxon Signed Rank test.

There were significant differences between hydroperoxides values measured at the end of surgery (T3) group P compared with preoperative values (T0).

The values determined at T3 in P group were also significantly lower compared to pre-anesthetic and end of the intervention in group S. (Figure 3)

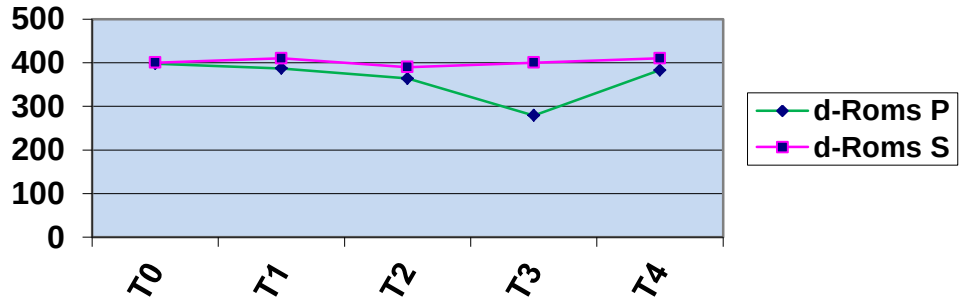

Figure 3 Hydroperoxide measured by blood levels of d-Roms test during the intervention in two groups

Reducing ability of plasma iron (PFRA) has not changed during the surgery group.

Also,a brief descriptive analysis of statistical parameters for group P, the variable of the reducing capacity of serum iron, the analysis performed automatically by EXSTAT is presented in Table 7

Descriptive	**T0**	**T1**	**T2**	**T3**	**T4**
Mean	210.67	204.19	188.71	200.76	204.48
Median	225.00	219.00	197.00	187.00	208.00
Standard Deviation	58.12	46.78	63.81	60.53	50.71
Standard Error	12.68	10.21	13.92	13.21	11.07

Table 7 Descriptive summary analysis of statistical parameters for reducing ability of plasma iron group P.

In group S, the value of reducing capacity in serum iron decreased significantly from 219.81 ± 40.05- amount of pre-anesthetic for this group to 82.57 ± 37.37 mmol / L at the end of surgery. (T3 vs T0) (table 8)

Descriptive	**T0**	**T1**	**T2**	**T3**	**T4**
Mean	219.81	191.19	155.81	82.57	219.62
Median	236.00	196.00	163.00	89.00	233.00
Standard Deviation	40.05	67.39	64.00	37.37	52.79
Standard Error	8.74	14.71	13.97	8.15	11.52

Table 8 Descriptive summary analysis of statistical parameters for the reducing ability of plasma iron group S

Statistical analysis revealed significant differences in group S (T3 vs T0).

Reducing ability of plasma iron (PFRA) during surgery for the S and P makes it easier to notice the difference between groups. (See figure4)

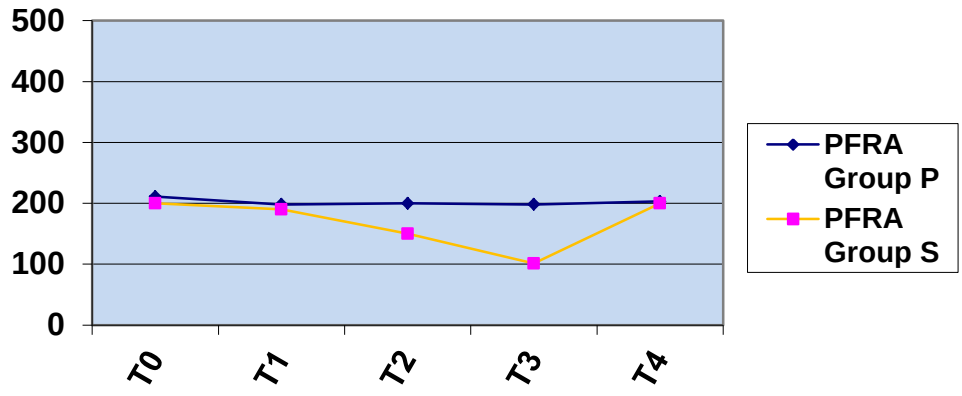

Figure 4 Iron reducing ability of plasma (PFRA) during surgery for the S and P

Hydroperoxide levels and reducing ability of plasma iron returned to their pre-anesthetic values in PACU in the two groups.

CONCLUSIONS

In sigmoidectomy at patients who received sevoflurane anesthesia the reducing ability of serum iron decreased during surgery, indicating a decrease in antioxidant potential. However, blood levels of hydroperoxides is not changed, indicating that the oxidative damage of biological component was at a very small scale. These conflicting results show that a certain quantity of ROS was generated, but most were quickly removed or detoxified by the action of antioxidants before affecting the surrounding biological components. This led to a temporary decrease in antioxidant potential.

Our results indicate that an increase in the oxidative stress at patients during sigmoidectomy is usual. However, oxidative toxicity is transient and is not so virulent.

It is quite interesting that propofol anesthesia not only maintains the reducing capacity of serum iron, but also decreases the hydroperoxides during the group P. Because propofol is a small amphipathic molecule,it is easily distributed in different environments, and It has a good affinity for both hydrophilic and lipophilic ROS. Therefore, it can eliminate any type of ROS in the early stages, possibly before starting the propagation reactions.

Although the importance of controlling intraoperative oxidative stress remains unclear, actual results may help us to develop better methods to improve postoperative recovery rates.

DISCUSSIONS

We measured two variables, which can assess oxidative stress produced in anesthetic-surgical act: hydroperoxides in blood and the antioxidant capacity of plasma at patients undergoing mild surgeries in order to highlight the antioxidant qualities of two anesthetics : sevoflurane (class inhaled) and propofol (class intravenous).

Recent data from oxidative stress research, assess that the molecular mechanisms of oxidative stress induction by the surgical act are related to neutrophil activation and / or dysfunction of mitochondria, which are the major sources of ROS in vivo. Hemodynamically, intraoperative, there occur phenomena of ischemia/reperfusion by clamping blood vessels and declamping.

Sevoflurane anesthesia is associated with the decrease of antioxidant capacity of plasma due to its antioxidant potential decrease, while the hydroperoxide remains unchanged, which underscores the effect of minor oxidation of biological components. This biochemical state would be due the amount of ROS rapidly degraded and / or eliminated, detoxifying being provided by endogenous antioxidants (compensatory mechanism, protective). Propofol appears to block the oxidant contact with biological components, so oxidative toxicity is imperceptible, being transient without altering cellular components.

ROS concentrations increase due to the development and propagation and reactivity reactions, often determine a widely studied phenomenon: the transforming the oxidant into antioxidant and reversing oxidants in antioxidants. Because of this mechanism, taking a therapeutic attitude of administration of antioxidants is difficult, having in view the idea of " doing no harm" by intensifying biological toxicity by administering an antioxidant, which will be quickly converted into oxidant.

If lowering the level of hydroperoxides with the administration of propofol in the surgical interventions where the surgical stress is minor, is obvious, this is hard to be observed when the surgical stress is high.

The evolution of the antioxidant capacity of plasma marks a slight decrease after the administration of propofol and an increase towards the end of surgery, compared to its level at T0. (preanesthetic).

The changes of the observed values in plasma (of the antioxidant capacity) were not statistically significant, but I have indicated in order to be resumed in any future studies.

As an antioxidant, propofol seemed to be better than sevoflurane (the inhaled anesthetic).

MDA values with signifying the degradation of cell membranes by lipoperoxidation under the action of the oxidative tasks, highlighted the role of both anesthetics,on influencing the redox balance thus: propofol-the oxidative attack 30 minutes after reperfusion does not change, sevoflurane: in it’s presence,the levels of MDA increase, which shows the lack of blocking the oxidative attack.

The results obtained by different authors are contradictory, so clinical study of redox homeostasis is extremely important, imposing infracelular penetration level research in order to solve the problem of inner (endogenous) -outer (exogenous) ratio and achieving optimal proportions of oxidants -antioxidants, in antioxidant therapy.

Numerous studies consider that sevoflurane and other halogenated anesthetics have protective effects on the myocardium. Sevoflurane is currently considered as one of the anesthetic substances valuable in inducing myocardial preconditioning, whom it induces increased resistance to hypoxia conditions.

Compared with sevoflurane, propofol has no protective effect on the myocardium, but is a good defender against ROS production, in the process of peripheral ischemia-reperfusion.

III. Final conclusions

1. In anesthesia with propofol ,the biochemical table of redox balance suggests the intervention of a mechanism for fast and prompt action of endogenous antioxidants, during surgical incision.

2. Propofol diffuses in the hydrous sectors of the body, exercising its scavenger action after attracting ROS lipophilic and hydrophilic and participates in their elimination in the early stages of the surgery, blocking undesirable propagation of oxidizing effect.

3. The preventive correction of the installation trends of the oxidative stress appears to be ensured with anesthesia with administered propofol at the start of the intervention.

4. The application of oxidative stress control methods from the start of surgery, may help maintain homeostasis, through the efficient delivery of mitochondrial respiration.

5. The current methods of investigation of the relationship redox intra/ extracellular are few and used only for research purposes, though two parameters; ROS dosing and plasma antioxidant capacity are indicative parameters, easily to explore, perform and use.

6.The statistical analysis of the obtained results revealed that some are borderline statistical significance, while others had no significant purpose, so changes can be regarded as seised comments or findings that could be studied in detail in the future.

7. The study of oxidative stress remains a key objective of the research, which requires knowledge to specific genes, the elements involved in regulating redox balance and expressing it using biochemical and clinics.

8. Our attempt to study a tiny part of the unfolding ratio oxidant / antioxidant capacity of plasma, used the results of actual research about ROS, which we implemented in anesthetic-surgical practice.

9. A fundamental factor for surgical wound healing is maintaining the oxidant / antioxidant ratio at a level corresponding to the cellular respiration.

10. Promoting aggressive administration of antioxidants in relation to healthy eating or cure any disease can not be negated by scientific studies, but provide conflicting results.

11. If our results are a little convincing, the courage to try actual theoretical knowledge in anesthesic-surgical practice and the popularizing of results can be useful and usable.

12. If applying the biochemical determinations proposed by us is possible,trying them could lead to a selection of appropriate therapies, depending on the topic, pathology.

13. Propofol favorably influences some parameters of oxidative status, but it's influence on the overall postoperative developments require more detailed studies and much larger batches.

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