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Antioxidant effect of γ-tocopherol supplied by propofol preparations (Diprivan) during ischemia–reperfusion in experimental lung transplantation

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Abstract Free radicals are involved in ischemia-reperfusion injury and inflammatory processes. The commercial formulation of the anesthetic propofol contains γ-tocopherol and δ-tocopherol, which may exert antioxidant effects during transplantation. Animals were randomly assigned to a control group or experimental groups for lung transplantation after 3 and 24 h of ischemia. Individual tocopherols, malondialdehyde, biochemical indices, and hemodynamic, blood gas, and ventilatory parameters were determined during reperfusion. Results showed that administration of commercially available propofol provoked a time- and dose-dependent increment in serum γ-tocopherol and δ-tocopherol in control animals and in the group receiving lungs subjected to 3 h of ischemia, but not in the group with 24 h of ischemia. Malondialdehyde levels increased during reperfusion and did not differ significantly between the two experimental groups, which did not differ with respect to lung function either. γ-Tocopherol, supplied by the anesthetic, may act as an antioxidant that is consumed during reperfusion. This potential effect could be relevant to the choice of anesthetic agents in situations where free radical damage to tissues is expected.

Keywords Propofol · γ-Tocopherol · Ischemia-reperfusion injury · Lung transplantation

Introduction

Reactive oxygen species are implicated in the tissue damage associated with ischemia–reperfusion and other inflammatory processes [1, 2]. The potential targets of the oxygen-derived free radicals generated during the initial phases of reperfusion [3] include nucleic acids, proteins, and membrane lipids, lipid peroxidation being one of the major mechanisms involved in free radical-induced damage.

Propofol (PPF) is a rapid, short-acting general anesthetic that is widely employed in the induction and maintenance of anesthesia. Its phenolic chemical structure, similar to that of butylated hydroxytoluene and to that of α-tocopherol, confers a free radical scavenging capacity that has been demonstrated in vitro [4, 5, 6], especially against peroxynitrite [4], a potent inducer of lipid peroxidation, which is thought to play an important role in acute lung injury [4, 7]. In vivo, the protective effect of PPF is related to the decrease in

malondialdehyde (MDA) concentration observed after ischemia-reperfusion [8, 9]. However, although PPF has demonstrated antioxidant action at the doses utilized during anesthesia, there is no evidence that this action is relevant from a clinical point of view [4, 9, 10, 11]. In addition, in contrast to vitamin E, the effect of PPF is immediate [6, 12] and persists throughout the period of administration of the drug [13].

Due to its lipid solubility, commercially available PPF, or Diprivan (Zeneca), is formulated with its solvent, intralipid (IL). IL also has a dose-dependent antioxidant effect [11], and although in vitro it appears to inhibit the free radical scavenging activity of PPF [9], under certain experimental conditions its effect has been shown to be additive with that of the latter [11].

Among other compounds, IL contains soybean oil, with high concentrations in γ-tocopherol and δ-tocopherol, both with antioxidant activity [14, 15]. γ-Tocopherol is capable of scavenging reactive nitrogen species produced at the site of inflammation (i.e., peroxynitrite), leading to the formation of the less harmful nitric oxide and 5-nitro-γ-tocopherol, and may complement the scavenging of these species carried out by α-tocopherol [15]. In addition, γ-tocopherol can enhance nitric oxide generation and the expression of endothelial nitric oxide synthase, suggesting that this isomer may also be important in preventing vascular endothelial dysfunction [15, 16].

The objectives of this study were: (1) to assess the changes in endogenous serum retinol and α-tocopherol concentrations and the time- and dose-dependent distribution of γ-tocopherol and δ-tocopherol with Diprivan administration (control group); (2) to analyze the changes in the endogenous serum retinol and α-tocopherol concentrations and in the γ-tocopherol and δ-tocopherol concentrations supplied by Diprivan, associated with the ischemia-reperfusion syndrome produced by lung transplantation (experimental groups); and (3) to assess the potential effect of γ-tocopherol and δ-tocopherol administration during anesthesia on several clinical parameters of pulmonary function after lung transplantation.

Materials and methods

The study was approved by the Animal Welfare Committee and performed in accordance with the Principles of Laboratory Animal Care and the Spanish Law for the Protection of Animals. It was carried out in crossbred Landrace × Large White pigs weighing approximately 20 kg. The animals were randomly assigned to one of the following study groups.

Control group ($n=4$): injection of increasing doses of PPF. The animals were premedicated with a combination of ketamine (20 mg/kg body weight [bw]), diazepam (0.1 mg/kg bw), and atropine (0.02 mg/kg bw), injected i.m. Anesthesia was induced with 1.5–2% isoflurane and a 0.2 mg/kg bw i.v. bolus of pancuronium bromide to allow endotracheal intubation and connection to an Adult Star ventilator (Infrasonics), using 100% oxygen (fraction of inspired O_2, $FiO_2=1$). The ventilator settings were adjusted according to the body weight of the animal in such a way as to maintain a CO_2 value of 35–45 mmHg and a peak airway pressure of 15–20 cmH_2O; to achieve this, the tidal volume was set at 10–15 ml/kg bw, with a respiratory rate of 15 breaths/min, an end-inspiratory pause of 0.5 s, and an inspiratory flow calculated to achieve an inspiration-expiration ratio of 1:2. Anesthesia was maintained with 1.5% isoflurane and continuous i.v. infusion of midazolam (0.6 mg/kg bw per hour), fentanyl (5 μg/kg bw per hour), and pancuronium bromide (0.4 mg/kg bw per hour).

The jugular vein was isolated for injection of drugs and fluids and sample collection, and the carotid artery was used for monitoring of arterial blood pressure and sample collection. Median sternotomy and pericardiectomy were performed and the inferior pulmonary veins of both lungs were exposed; catheters were introduced into the latter and into the coronary sinus for sample collection.

Once baseline samples had been obtained from the jugular vein, carotid artery, right and left inferior pulmonary veins, and coronary sinus, the administration of isoflurane was discontinued and that of propofol was begun at doses of 6, 12, and 15 mg/kg bw per hour successively; blood samples were taken from the five sites 15, 30, and 60 min after the administration of each dose had commenced.

Experimental groups: lung transplantation after 3 h ($n=6$) or 24 h ($n=6$) of donor lung cold ischemia. Premedication was carried out as in the control group. Anesthesia was induced with a 2-mg/kg bw bolus of PPF, rather than isoflurane, and was maintained by continuous PPF infusion at a dose of 9 mg/kg bw per hour. The remaining anesthetics were administered at the same doses as in the controls. The surgical procedure was as follows: in donors, the venae cavae, aorta, pulmonary artery, and trachea were prepared through median sternotomy. After heparinization (3 mg/kg bw), the aorta was clamped and the heart arrested with a cardioplegic crystalloid solution. Then, the lungs were flushed retrogradely with cold (4°C) University of Wisconsin solution (UW) (60 ml/kg bw, under a perfusion pressure not exceeding 30 cmH_2O). Continuous ventilation was maintained and topical cooling was completed by irrigation of the chest cavity with cold saline solution. The heart-lung block was then extracted and the left lung was prepared for transplantation, including an atrial cuff with pulmonary veins outlet, and stored immersed in cold (4°C) saline solution up to transplantation. In recipients, transplantation was performed via left postero-lateral thoracotomy through the 4th intercostal space. The emiazygos vein was ligated and divided. After division of the pulmonary ligament, the pulmonary veins were ligated, and the left pulmonary artery and the left main bronchus were clamped and sectioned, extracting the recipient left lung. Bronchial anastomosis with donor lung was performed with a nonabsorbable 4–0 running suture; pulmonary artery and atrial cuff anastomosis were performed with nonabsorbable 5–0 running sutures, leaving the last one untied. After the clamp on the recipient bronchus was removed and ventilation of the transplanted lung was started, the arterial clamp was removed, allowing that the air was vented through the untied suture. The atrial clamp was then removed and the suture tied. Donor lung implantation took from 35 to 45 min.

Baseline blood samples were obtained from the left atrium; subsequent samples were collected from the inferior pulmonary vein of the transplanted lung 0, 60, and 120 min after reperfusion. At these times, hemodynamic parameters (systemic arterial, pulmonary arterial, and pulmonary capillary wedge pressures, cardiac output, and pulmonary vascular resistances) and blood gas and ventilatory parameters (PaO_2, PCO_2, arterial oxygen saturation, intrapulmonary shunt, alveolar-arterial oxygen difference, inspiratory and expiratory resistances, and static and dynamic compliance) were assessed.

Blood samples were collected and tubes were maintained at 4°C, protected from light, until serum separation (within 10–20 min) by centrifuging at 3000 rpm for 8 min. Hemoglobin (Hb) and albumin concentrations were determined in the blood samples using autoanalyzer methods routinely employed in humans. Total cholesterol and triglycerides were measured by enzymatic assays. MDA was measured as an index of lipid peroxidation in the animals subjected to lung transplantation by means of the thiobarbituric acid assay [17]. Retinol, α-tocopherol, γ-tocopherol, and δ-tocopherol were determined by HPLC as described elsewhere [18, 19].

Commercial preparations of propofol (Diprivan 2%, vial) used in the study were also extracted and analyzed to assess the individual tocopherol content, showing the following composition; 28 μg of δ-tocopherol (30%), 60 μg of γ-tocopherol (63%), and 6.5 μg of α-tocopherol (7%) per milliliter of emulsion.

Accuracy and precision of the analytical method used was evaluated periodically through our participation in the Fat-Soluble Vitamins Quality Assurance Program conducted by the National Institute of Standards and Technology (NIST; Gaithersburg, Md.). Accuracy was within 10% of assigned values, and within-day and between-day precision (blind duplicates from NIST) for the compounds of interest within the physiological range were < 5% and 10%, respectively, for all analytes evaluated.

Statistical analysis

The data are expressed as mean ± standard deviation. In the control group, the possible differences between the sampling sites after each dose and at every moment throughout the study were analyzed by ANOVA, followed by Tukey's multiple comparison test. When no such differences existed, the values obtained at each site were grouped together and two-factor repeated measures ANOVA was carried out using time and dose as the intrasubject and intersubject factors, respectively. In the experimental groups, to assess the intrasubject (time) and intersubject (group) differences, repeated measures ANOVA was used, followed by the Newman-Keuls multiple comparison test. A P value below 0.05 was considered to indicate a statistically significant difference in a two-tailed test. The results were analyzed using the SPSS statistical package (v.10.0).

Results

Control group

Under baseline conditions, retinol and α-tocopherol, but not γ-tocopherol or δ-tocopherol, were detected in blood and no differences were observed among the results at the five sites of blood collection. The retinol and α-tocopherol concentrations were not modified by the administration of Diprivan at any time throughout the study (Table 1), suggesting that these biochemical markers were not significantly affected by the surgical procedure.

When Diprivan was infused i.v., γ-tocopherol and δ-tocopherol were detected in serum samples, where the concentrations of both increased proportionately to the time elapsed and the dose administered (Table 1, Fig. 1). Again, at no time were there differences in the γ-tocopherol and δ-tocopherol concentrations measured

Table 1 Retinol and α-, γ-, and δ-tocopherol concentrations under basal conditions and after propofol (*PPF*) administration at progressively increasing doses

PPF (mg/kg per hour)		6 ↓			12 ↓			15 ↓		
	Basal	15 min	30 min	60 min	15 min	30 min	60 min	15 min	30 min	60 min
Retinol (μg/dl)	19.64 ± 6.44	21.23 ± 7.22	20.83 ± 4.74	20.48 ± 5.79	18.99 ± 4.85	17.61 ± 4.29	18.86 ± 5.11	19.62 ± 3.99	18.53 ± 4.17	18.00 ± 4.16
α-tocopherol (μg/dl)	103.51 ± 31.03	110.54 ± 34.19	111.31 ± 21.48	117.49 ± 35.21	98.16 ± 27.74	94.02 ± 23.88	101.92 ± 27.13	102.12 ± 19.99	97.01 ± 24.37	98.65 ± 24.46
γ-tocopherol (μg/dl)	0	4.59 ± 1.53*	8.74 ± 6.27†	12.14 ± 2.96*	14.37 ± 5.73	17.62 ± 6.25*	25.73 ± 9.70*	31.63 ± 14.54	33.16 ± 14.34	41.39 ± 16.16†
δ-tocopherol (μg/dl)	0	2.37 ± 1.52*	3.30 ± 1.81†	6.74 ± 6.40†	5.65 ± 2.56	5.84 ± 2.20†	8.93 ± 4.13†	10.44 ± 5.07	10.25 ± 5.37	13.20 ± 6.96*

*$P \leq 0.001$; †$P < 0.01$ (vs the preceding value)

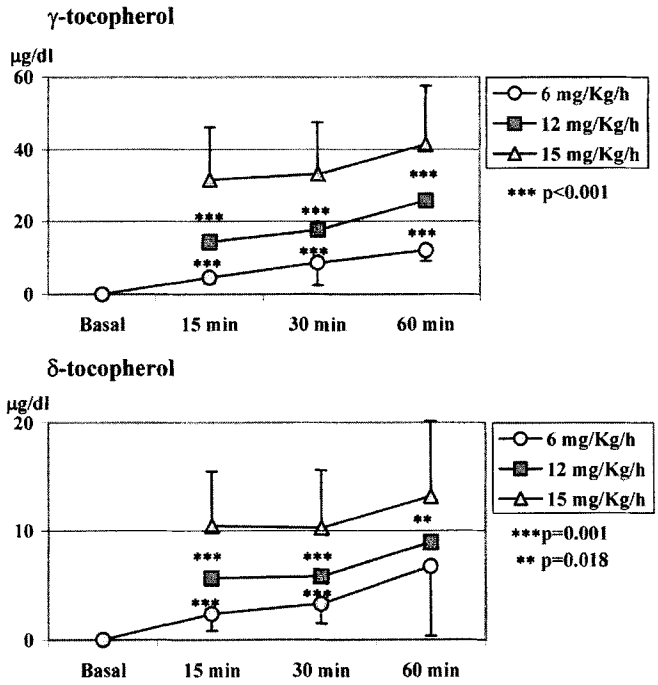

Fig. 1 Changes in γ-tocopherol and δ-tocopherol concentrations after injection of increasing doses of propofol (*PPF*). Statistically significant differences between adjacent curves are indicated

at the five sampling sites, a finding that agrees with the rapid distribution of the drug throughout the blood; thus, the five values obtained at each point and with each dose were grouped for statistical analysis.

Experimental groups

The retinol concentrations decreased in both groups at the start of reperfusion, while a significant decrease in the α-tocopherol level was observed only in the group corresponding to 24 h of ischemia when the values at the end of the study period were compared with the baseline measurements ($P < 0.05$). There were no differences between the experimental groups with respect to serum retinol and α-tocopherol concentrations, even when these values were adjusted for total lipids, albumin, and Hb to examine the possible effect that hemodilution might have on them (Table 2).

Similar to the findings in the control group, in the group corresponding to 3 h of ischemia, the γ-tocopherol and δ-tocopherol concentrations increased over time with the infusion of Diprivan, although the difference was significant only for γ-tocopherol. In contrast, in the 24-h ischemia group, neither the γ-tocopherol nor the δ-tocopherol levels rose, as would be expected with identical doses and times (Table 2, Fig. 2). The differences observed were not modified when the concentrations of these two tocopherols were adjusted for Hb, albumin, and total lipid levels.

The MDA concentrations increased in both groups, but this increase was significant only at the end of reperfusion in the 3-h ischemia group (120 min vs baseline, $P < 0.05$). At no time during the study were there significant differences between the groups that received lungs subjected to 3 h and to 24 h of ischemia (Fig. 3).

Table 2 Retinol and α-, γ-, and δ-tocopherol concentrations in groups receiving lung transplants (*LTx*) subjected to 3 and 24 h of ischemia (*PPF* propofol)

PPF (mg/kg per hour) ↓ 9	Basal	0 min	60 min	120 min
Retinol (μg/dl)				
LTx-3 h	18.7 ± 6.4	15.6 ± 6.3** ‡	14.6 ± 5.3 ‡	13.8 ± 4.4 ‡
LTx-24 h	18.5 ± 7.8	16.2 ± 6.4* †	15.0 ± 6.4 ‡	12.9 ± 6.1 ‡
Retinol/Hb (μg/g)				
LTx-3 h	1.96 ± 0.73	1.73 ± 0.65* †	1.55 ± 0.43 ‡	1.55 ± 0.42 ‡
LTx-24 h	2.01 ± 0.85	1.66 ± 0.68** ‡	1.50 ± 0.66 ‡	1.38 ± 0.67 ‡
α-tocopherol (μg/dl)				
LTx-3 h	129.8 ± 50.5	120.0 ± 56.3	119.1 ± 48.5	114.6 ± 41.9
LTx-24 h	107.1 ± 57.1	102.0 ± 48.9	98.4 ± 45.4	86.5 ± 43.0 †
α-tocopherol/total lipids (μg/mg)				
LTx-3 h	1.02 ± 0.39	1.06 ± 0.40	1.09 ± 0.35	1.10 ± 0.35
LTx-24 h	0.92 ± 0.50	0.89 ± 0.49	0.87 ± 0.50	0.92 ± 0.53
γ-tocopherol (μg/dl)				
LTx-3 h	35.1 ± 17.7	50.9 ± 31.5* †	63.1 ± 33.9* ‡	65.7 ± 33.9 ‡
LTx-24 h	23.4 ± 18.9	26.0 ± 10.5	33.1 ± 12.0	33.0 ± 8.6
δ-tocopherol (μg/dl)				
LTx-3 h	14.9 ± 6.9	18.1 ± 10.7	19.4 ± 13.6	19.5 ± 11.1
LTx-24 h	8.4 ± 4.3	8.9 ± 3.7	11.4 ± 4.6	9.7 ± 3.4

$^{**}P < 0.01$; $^{*}P < 0.05$ (vs the preceding value), $^{‡}P < 0.01$; $^{†}P < 0.05$ (vs baseline value)

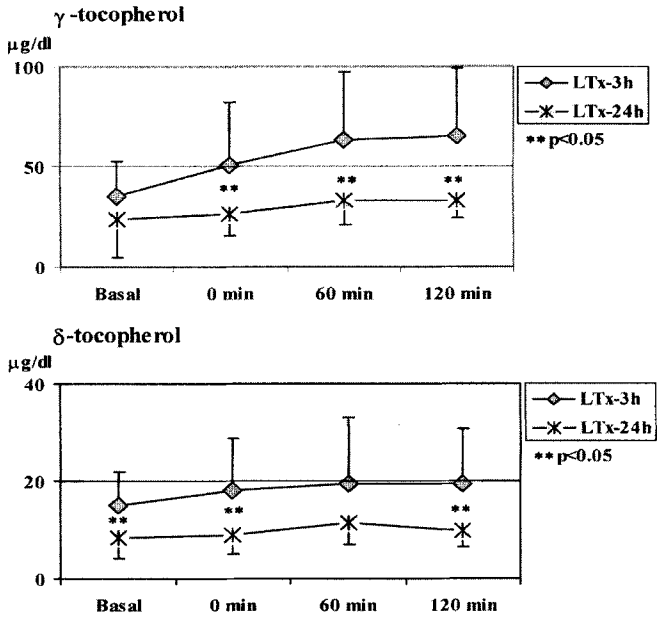

Fig. 2 Changes in γ-tocopherol and δ-tocopherol concentrations during propofol (*PPF*) anesthesia (9 mg/kg bw per hour) in lung transplantation (*LTx*) involving ischemic times of 3 and 24 h

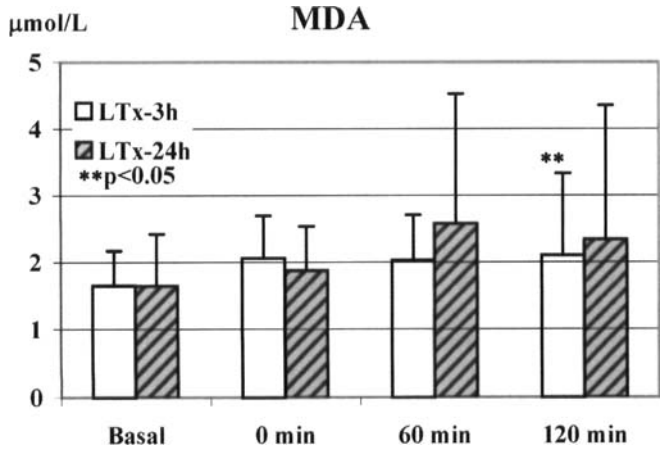

Fig. 3 Changes in malondialdehyde (*MDA*) concentrations in lung transplantation (*LTx*) involving ischemic times of 3 and 24 h. $^{**}P < 0.05$ vs the baseline value

The mean pulmonary artery pressure increased from the start of reperfusion in the transplants that had undergone 24 h of ischemia (baseline: 17 ± 6 mmHg; 0 min: 21 ± 8; 60 min: 22 ± 6; 120 min: 23 ± 8; 0 min vs baseline, $P < 0.05$; 60 min and 120 min vs baseline, $P < 0.01$), but there were no significant differences with respect to the lungs subjected to 3 h of ischemia. The pulmonary vascular resistances increased in both groups from the start of reperfusion, there being no differences between them (3 h: 207 ± 147, $299 \bullet 180$, 334 ± 157, and 366 ± 185 dyne per s/cm^{-5} at baseline, 0, 60, and 120 min, respectively; 0, 60, and 120 min vs baseline $P < 0.01$; 24 h: 261 ± 192, 378 ± 292, 648 ± 515, and 698 ± 513 dyne per s/cm^{-5} at baseline, 0, 60, and 120 min, respectively; 60 and 120 min vs baseline $P < 0.01$). PaO_2 remained within normal ranges, showing no differences between the two groups (3 h: 467 ± 50, 463 ± 71, 494 ± 49, 458 ± 65 mmHg; 24 h: 478 ± 41, 465 ± 68, 478 ± 50, 442 ± 37 mmHg at baseline, 0, 60, and 120 min, respectively). Static compliance was reduced in the two experimental groups from the start of reperfusion (3 h: 25 ± 3, 24 ± 3, 23 ± 2, 23 ± 4 ml/cmH_2O at baseline, 0, 60, and 120 min, respectively; 60 and 120 min vs baseline $P < 0.05$; 24 h: 27 ± 5, 23 ± 4, 21 ± 4, 20 ± 5 ml/cmH_2O at baseline, 0, 60, and 120 min, respectively; 0 min vs baseline $P < 0.05$; 60 and 120 min vs baseline $P < 0.01$), but there were no significant differences between them.

Discussion

The purpose of this study was to examine the changes in serum retinol and tocopherol concentrations during Diprivan (PPF + IL) infusion in a control group and in animals receiving lung transplants that had been subjected to ischemic times of 3 and 24 h. The quality control of the analytical method employed and the inclusion of the control group (with five blood sampling points among which there were no significant differences) render it improbable that the differences observed are due to bias related to the analytical approach or to sample collection; thus, these results seem to reflect changes caused by phenomenon associated with the effects of ischemia-reperfusion on the transplanted tissue, as observed at the venous effluent.

It is known that the formation of oxygen-derived free radicals continues up to 3 h after only 15 min of ischemia [9]. MDA levels have been widely used as a marker of lipid peroxidation because their measurement is simple and sensitive, although this approach has been criticized for its low specificity [17]. An increase in concentration of MDA in serum and/or tissues has been reported following ischemia and reperfusion and after unclamping in heart surgery [20, 21], and pre-treatment with PPF has been shown to reduce MDA production in experimental heart-lung transplantation, a decrease that is associated with antioxidant protection and improved cardiopulmonary function [20]. In addition, non-enzymatic antioxidants such as vitamin E are depleted during ischemia [20], and although these decreases have been partly attributed to hemodilution and to changes in plasma lipids, the oral or i.v. administration of α-tocopherol in humans has helped to reduce MDA production after tissue reperfusion, suggesting that α-tocopherol may be capable of impeding to some extent the oxidation of membrane fatty acids [21].

In view of the changes in γ-tocopherol and δ-tocopherol concentrations observed in the control group in our study, it would be expected that Diprivan infusion would produce an increase in both of these fractions in the experimental groups over time. However, an increment was observed only in the γ-tocopherol levels in the animals receiving lung transplants subjected to 3 h of ischemia, an increase that was not detected in lungs that had undergone 24 h of ischemia. Given that the protocol followed was identical in both cases, the lack of increase in this group suggests that, after prolonged ischemia, γ-tocopherol may act as an antioxidant, possibly being "consumed" as it traps free radicals (i.e., reactive nitrogen species) [14] generated during the inflammatory responses associated with lung transplantation.

On the other hand, if MDA production is related to the degree of injury inflicted on the organ by ischemia and reperfusion, higher concentrations would be expected in the group corresponding to 24 h of ischemia, a circumstance that was not observed. In this respect, the simultaneous absence of increases in γ-tocopherol and MDA concentrations in the cases subjected to 24-h ischemia could be indicative of an antioxidant effect of γ-tocopherol in the tissue, counteracting the production of MDA associated with free radical damage during reperfusion.

It could also be that, during i.v. infusion, the antioxidant action attributed to PPF [4, 5, 6] works synergistically with that of γ-tocopherol to reduce the oxidative damage produced during reperfusion, as has been reported under other experimental conditions [11]: both compounds are lipophilic and are not taken up by the cells, suggesting that they may exert their antioxidant activity in the extracellular medium and/or in the same phase (for example, the cell membrane), regenerating each other mutually. In fact, PPF and γ-tocopherol scavenge peroxynitrite, a radical that promotes lipid peroxidation and plays an important role in acute lung injury [7, 8, 9, 15]. In this sense, a possible limitation in the present study is that concentrations of PPF during the experiment were not measured. However, there are at least two reasons that this fact does not necessarily invalidate our results. First, it may be assumed that any effect attributable to the presence of PPF, under our study design, should have been similar in both experimental groups since the dose and timing of Diprivan infusion was exactly the same in animals subjected to 3 and 24 h of ischemia. Secondly, PPF concentrations may not reflect the behavior of tocopherols exactly, even when infused simultaneously, since both compounds have different physiological roles and, thus, may display different metabolic fates and/or disposal rates. In this context, given that the antioxidant effect of PPF appears to be immediate [6, 12, 13] and that its half-life in blood is much shorter than that of the tocopherols [22], the potential antioxidant effect of γ-tocopherol becomes more relevant during the later phases of reperfusion. This may explain the absence of an increase in serum γ-tocopherol levels in the group corresponding to 24 h of ischemia and the greater differences, with respect to the 3-h ischemia group, after 120 min of reperfusion.

Serum retinol concentrations are known to be altered during the acute phase response occurring after myocardial infarction, infection, and trauma [23]. In our study, their tendency to decrease could be related to a change in vitamin A metabolism during the acute phase response owing to surgical stress and/or hemodilution. However, in the control group, the concentrations remained stable and the adjustment of the values for different parameters did not modify the findings in any of the groups. Moreover, since retinol levels did not differ between the two experimental groups, the decrease in serum retinol levels seems to be directly related to the reperfusion process, regardless of ischemic time.

The decrease in α-tocopherol concentrations has been associated with free radical damage during reperfusion [20]. In our study, despite the adjustment for hemodilution, the concentrations remained stable in all three groups, albeit with a non-significant decrease in the 24-h ischemia group. Maintenance of α-tocopherol levels during reperfusion may be explained at least partly by the small amounts of this vitamin supplied by Diprivan, which help compensate for slight reductions, and/or the conservation of the antioxidant activity of endogenous α-tocopherol in the presence of that of propofol and/or γ-tocopherol (plus δ-tocopherol) supplied during anesthesia.

We are aware that an additional group for lung transplantation receiving another drug than Diprivan to maintain anesthesia and/or infused at different doses would have supported the antioxidant role of γ-tocopherol. However, the main reason for using our control group was to evaluate this widely used anesthetic regarding the time and dose distribution of tocopherols (supplied by Diprivan) as well as the fate and potential (antioxidant) effect of these tocopherols in relation to the ischemia-reperfusion syndrome associated with lung transplantation. Thus, under these conditions, we could directly relate changes in concentrations of these analytes with ischemia-reperfusion injury in lung transplantation, regardless of any change or effect derived from the surgical procedure. In this sense, our previous experience with animals subjected to heart transplantation (2 h of ischemia) maintained with inhalatory anesthesia (isoflurane) is consistent with the present results in the experimental group and data reported in the literature (unpublished observations). However, since inhalatory anesthesia is inadvisable in lung transplantation and because changes associated with ischemia-reperfusion

syndrome may also be related to tissue-specific mediators, comparisons with this (non-Diprivan) group may be misleading.

Finally, from a clinical point of view, the differences in change in serum γ-tocopherol concentrations observed between the experimental groups were not related to differences in pulmonary function. In our opinion, this finding is a consequence of the functional study performed simultaneously in both the recipient and donor lungs since, according to our experience, after 24 h of ischemia, the donor lung alone was incapable of maintaining adequate function. During the study period (120 min after reperfusion), the native lung was capable of maintaining oxygenation within normal range, despite structural and functional damage to the transplanted lung (elevated pulmonary vascular resistance and decreased compliance).

In conclusion, the γ-tocopherol and δ-tocopherol content of the commercial PPF preparation (Diprivan) may help to prevent or combat the oxidative damage induced by ischemia-reperfusion syndrome in experimental lung transplantation. This finding may be of interest in the choice of anesthetics for those situations, such as transplantation, in which free radical-induced tissue damage can be expected.

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