Comparative Analysis of Antioxidant Defense During On-Pump and Off-Pump Cardiac Surgery

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Introduction and objectives. The transient myocardial ischemia that occurs during cardiac surgery leads to oxidative stress and the production of free radicals. The resulting damage can be reduced if cardiopulmonary bypass is avoided. We obtained indirect measures of the oxidative damage occurring during cardiac surgery by monitoring the glutathione system and we studied the influence of cardiopulmonary bypass.

Patients and method. The study included 19 patients undergoing cardiac surgery. Cardiopulmonary bypass was used in 9 (47.4%). Blood samples were obtained from each patient at different times during and after surgery. Total, oxidized and reduced glutathione levels were measured, as was the activity of related enzymes (i.e., glutathione peroxidase, glutathione reductase, and glutathione transferase).

Results. The total glutathione level decreased more in patients in whom cardiopulmonary bypass had been used. In addition, the oxidized glutathione level was reduced in these patients, which suggests that antioxidant defense was not fully effective. In contrast, the oxidized glutathione level tended to increase in patients in whom cardiopulmonary bypass had not been used. There was no significant difference in enzymatic activity between the two groups.

Conclusions. In this study, patients who underwent off-pump cardiac surgery had a better antioxidant profile. The implication could be that cardiac surgery without cardiopulmonary bypass has a less damaging effect on ischemic myocardium.

Key words: *Antioxidant defense. Cardiac surgery. Oxygen free radical. Glutathione. Ischemia-reperfusion. Oxidative stress.*

Análisis comparativo de la defensa antioxidante en cirugía cardíaca con y sin circulación extracorpórea

Introducción y objetivos. Durante la cirugía cardíaca se produce una isquemia miocárdica transitoria que implica el desarrollo de fenómenos de estrés oxidativo con liberación de radicales libres. El daño resultante puede ser menor si se obvia el *bypass* aortopulmonar. Se estudia el sistema antioxidante del glutatión como medida indirecta del daño oxidativo asociado con la cirugía cardíaca. Se analiza la influencia del empleo de circulación extracorpórea.

Pacientes y método. Se incluye a 19 pacientes en los que se realizó cirugía cardíaca, 9 de ellos con bomba (47,4%). De cada paciente se extrajeron muestras sanguíneas en diferentes momentos (intraoperatorios y postoperatorios) y en ellas se cuantificaron el glutatión (total, oxidado y reducido) plasmático e intraeritrocitario y se determinó la actividad enzimática implicada (glutatión-peroxidasa, glutatión-reductasa y glutatión-transferasa).

Resultados. El glutatión total disminuyó más en los pacientes operados con circulación extracorpórea. También se redujo el glutatión oxidado plasmático e intraeritrocitario, lo que expresa una defensa antioxidante ineficaz, mientras que en los casos sin bomba esta tendencia fue creciente. No hubo diferencias significativas en la actividad enzimática entre ambos grupos.

Conclusiones. En nuestra serie, los pacientes intervenidos sin circulación extracorpórea mostraron un mejor perfil antioxidante en relación con el sistema del glutatión. Esto puede traducirse en que la cirugía cardíaca sin bomba resulta menos agresiva para el miocardio.

Palabras clave: *Defensa antioxidante. Cirugía cardíaca. Estrés oxidativo. Glutatión. Isquemia-reperfusión. Radical libre.*

INTRODUCTION

In recent years, there is growing interest in the problems caused by oxidative stress in numerous medical procedures.[1-4] One such case, for example, is cardiac

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ABBREVIATIONS

CK-MB: MB (muscle/brain) isoenzyme of creatine kinase.
CPB: cardiopulmonary bypass.
GSH: reduced glutathione.
GSHpx: glutathione peroxidase.
GSHtf: glutathione transferase.
GSSG: oxidized glutathione.
GSSGrd: glutathione reductase.
TG: total glutathione.

surgery,[5] in which cardiopulmonary bypass can affect nearly all the organ systems, provoking lesions of varying degrees of severity. This injury is due, at least in part, to the phenomenon of "ischemia-reperfusion"; that is, both the interruption and the subsequent restoration of the blood flow that can have deleterious effects.[6-11]

Surgically induced myocardial ischemia, although transient, provokes the release of potentially toxic oxygen free radicals as part of a complex inflammatory cascade that progresses toward the site of the tissue injury,[5,12-17] triggering complications as it develops.[11,12] To combat the oxidizing or toxic effect of these free radicals, the organism launches a series of defensive (antioxidant) mechanisms that may or may not be effective or sufficient. Thus, the phenomena of oxidative stress are determined by the imbalance between oxidants and antioxidants, due either to an increase in the production of the former or to an inadequate neutralization on the part of the latter.[1,2,5,18,19]

On the other hand, improvements in anesthetic and surgical techniques are continually being introduced in the attempt to prevent or reduce the deleterious effects of the pump employed in cardiopulmonary bypass (CPB). In this context, cardiac surgery without CPB is becoming increasingly widespread, with very promising results in terms of morbidity and mortality,[20-22] probably because it is associated with lower levels of oxidative stress.[23] However, there are few studies comparing the two surgical techniques and providing a basis for this assumption.[15,16,22,24-28]

To estimate the damage associated with each type of cardiac surgery, the direct measurement of markers of oxidative stress (lipid peroxidation)[5,16,18,19,29] and the analysis of antioxidant defense[30-35] are equally valid approaches. This report deals with the comparative analysis of the phenomena involved in oxidative stress during cardiac surgery with and without CPB. For this purpose, we assessed an antioxidant system, the glutathione complex, which acts as an "interceptor," that is, it reacts directly with the free radicals to impede their action. The determination of glutathione concentrations provides information on its deposition in cells (erythrocytes) and plasma, as well as on the functional status of said system.

PATIENTS AND METHOD

Patients and Anesthetic Technique

In this study, we analyzed 19 cardiac operations performed in our hospital between October 2001 and September 2002. Cardiopulmonary bypass was employed in nine cases (47.4%) and all of the procedures were elective. Since the choice of the technique to be used was always made by the surgeon responsible for carrying it out, it was not possible to randomize the 2 groups; however, inclusion in the study was random (it is to be supposed that the number of operations during that period of time was much larger). The clinical characteristics of the patients are summarized in Table 1. All of them presented a contractility of more than 45% (mean ± standard deviation [SD], 61.5±8.6%) and stenosis of at least 2 coronary arteries. The antianginal therapy was the maximum tolerated by each patient and none of them presented comorbidity of interest.

The anesthetic technique always consisted of:

– Premedication with scopolamine and morphine in the hospital ward.
– Induction with etomidate, midazolam, and fentanyl.
– Maintenance on controlled mechanical ventilation with fentanyl, anesthetic gases (sevoflurane for off-pump procedures and isoflurane for on-pump surgery),

TABLE 1. **Clinical Profile of All the Patients Included in the Study***

	On-Pump	Off-Pump
Number of patients	9	10
Age, mean ± SD, years	63.67±14.14	63.50±0.71
Sex, men/total	5/9	6/10
Hypertension, n	5	6
Diabetes, n	3	3
Smoker, n	3	3
Previous myocardial infarction, n	3	6
Ejection fraction, mean ± SD	63.67±14.14	59.50±2.12
CPB time, mean ± SD, min	95.1±19.6	–
Ischemia time, mean ± SD, min	70.7±15.6	–
Combined surgery, n	6	1
Recovery room stay, median, days	3	4
Postoperative atrial fibrillation, n	1	3
Morbidity and mortality, n†	2	3
Heart failure, n	0	2
Myocardial ischemia, n	1	2
Infection, n	0	2
Mortality, n	0	1

*CPB indicates cardiopulmonary bypass; SD, standard deviation.
†Excluding atrial fibrillation.