Title: LIPID PEROXIDATION IN CRITICALLY-ILL PATIENTS.

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INTRODUCTION. Peroxidation of polyunsaturated fatty acids (PUFA), which are mainly found in biomembranes, takes place by the attack of oxygen radicals, and the peroxidized lipids then cause denaturation of proteins and inactivation of enzymes of sulfhydryl group. In the clinical settings, peroxidized lipids, which are detected as thiobarbituric acid reactant substance (TBARS), are reported to increase in patients with atherosclerosis, cerebrovascular disease, and liver disease. On the other hand, antioxidant systems such as α-tocopherol (VE) are present in vivo, and protects us from peroxidation. In this study, we determined the TBARS and VE in plasma of critically-ill patients and evaluated the significance in terms of disseminated intravascular coagulation (DIC).

METHODS. Twenty-four critically-ill patients (male 13, mean age 55±16) who were treated at the Intensive Care Unit were studied. Fifteen preoperative, ASA risk 1 patients (male 7, age 33±18), who subsequently underwent elective orthopedic or gynecologic surgery were studied as controls. Critically-ill patients consisted of sepsis 7, pneumonia 6, neurosurgical 5, and post-cardiac surgical 6. They were maintained on total parenteral hyperalimentation (TPN) and VE was supplemented 15 IU/day. Blood was drawn into a heparinized syringe and plasma was obtained by centrifugation at 3000g. Plasma samples were stored at -20°C until determination. In critically-ill patients, blood was obtained every two days throughout the stay in ICU. In control patients, blood was drawn prior to induction of anesthesia after overnight fasting. A 0.1ml of plasma was mixed with 7% sodium dodecylsulfate, 0.1N hydrochloric acid, 10% phosphotungstic acid, and 0.5% thiobarbituric acid, and incubated at 95°C for 60 min. TBARS was determined fluorometrically after extraction with n-butanol. 1,1,3,3-tetraethoxypropane was used as a standard of malondialdehyde (MDA). VE was determined fluorometrically[1].

Informed consent was obtained either from patients or family. The protocol was approved by the institution.

RESULTS. Table shows the results of determination. VE was 1.00±0.13 mg/dl (mean±S.D.) in control patients. It decreased significantly in critically-ill patients (0.64±0.25 mg/dl, $p<0.001$). TBARS was 7.67±1.86 nmolesMDA/ml in control group. It increased significantly in critically-ill group (9.69±2.87 nmolesMDA/ml, $p<0.01$). Among the critically-ill patients, septic and post-cardiac surgical patients showed significantly increased values of TBARS compared with the control ($p<0.01$). Eight patients developed DIC, and in those patients, the TBARS values during DIC were significantly increased compared with pre-DIC values (10.32±2.93 vs. 13.77±5.19 nmolesMDA/ml, $p<0.05$)(Figure). Three of the 8 patients recovered from DIC and their TBARS values subsequently decreased.

DOSCUSSION. Little is known of the significance of increased TBARS in plasma of critically-ill patients. It might reflect severe organ damage, especially of the lung or the liver. Because the former is often exposed to high concentration of oxygen, particularly in patients with acute respiratory failure, and both organs are rich in antioxidant systems. We have shown that the TBARS was significantly increased in plasma of critically-ill patients, especially in those with sepsis and post-cardiac surgical low cardiac output syndromes. It is interesting that the TBARS increased with the development of DIC and decreased when DIC subsided. The TBARS is known to inhibit $PGI_2$ synthesis[2], and the increased level of TBARS might further deteriorate DIC. α-Tocopherol level was also significantly decreased in those patients. Plasma α-tocopherol was reported to be within normal range in patients with short-gut syndrome who were maintained on TPN with 15 IU/day of VE supplementation, and the observed results in critically-ill patients might indicate that peroxidative process was in progress in those patients.

REFERENCES.

1. Abe K, Katsui G: Fluorometric determination of tocopherol in serum. Nutr Food 28:277-280, 1975
2. Moncada S, Gryglewski RJ, Bunting S, et al: A lipid peroxide inhibits the enzyme in blood vessel microsomes that generates from prostaglandin endoperoxides the substance which prevents paltelet aggregation. Prostaglandins 12:715, 1976

TABLE.

| | N | TBARS nmolesMDA/ml | α-Tocopherol mg/dl |
|---|---|---|---|
| CONTROL | 15 | 7.67±1.86 | 1.00±0.13 |
| CRITICALLY-ILL | 24 | 9.69±2.87* | 0.64±0.25* |
| sepsis | 7 | 10.60±2.30* | 0.65±0.29* |
| pneumonia | 6 | 8.67±3.45 | 0.49±0.30* |
| cardiac | 6 | 10.53±2.11* | 0.72±0.10* |
| CNS | 5 | 8.62±3.68 | 0.67±0.21* |

*P<0.01, compared with control value
cardiac: post-cardiac surgery
CNS : neurosurgery

FIGURE.