Effects of Ascorbic Acid on Lipid Peroxidation and Functional State of Neutrophils at the Early Period after Transurethral Resection of the Prostate

I. A. Volchegorskii and A. Yu. Vasil'kov

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 130, No. 11, pp. 516-518, November, 2000
Original article submitted April 5, 2000

Intravenous infusion of ascorbic acid in single doses of 500 and 1000 mg over 3 days after transurethral resection of the prostate elevated the content of lipid peroxidation products in the blood, increased the sensitivity of neutrophils to prodigiozan, and reduced the risk of infectious and inflammatory complications.

Key Words: *ascorbic acid; lipid peroxidation; phagocytosis; transurethral resection of the prostate gland; neutrophilic granulocytes*

Transurethral electroresection of the prostate (TUERP) is a highly efficient endosurgical treatment of benign prostate hyperplasia (BPH). Purulent and inflammatory complications are often found in the early period after TUERP [7]. Dysfunction of neutrophilic granulocytes (NG) plays an important role in the pathogenesis of purulent and destructive processes [5]. Laser irradiation of the blood activating lipid peroxidation (LPO) and stimulating bactericidal properties of NG is an effective approach to the therapy of functional disturbances in these cells [3]. Here we studied the effects of ascorbic acid (AA) in high doses on the content of circulating LPO products, functional state of blood NG, and the incidence of infectious and inflammatory complications in patients with BPH during the early period after TUERP.

MATERIALS AND METHODS

We examined 120 patients with BPH subjected to TUERP and divided into 3 groups (n=40). Group 1 and 2 patients were daily treated with AA (500 and 1000 mg, respectively) and received standard drug infusions. Group 3 patients received the same drug infusions without AA. Apparently healthy individuals with no signs of BPH served as the control (n=30).

Functional state of blood NG was determined by HCT test using standard kits (Reakompleks). Phagocytosis of polystyrene latex beads was assayed (phagocytic index). Apart from baseline (spontaneous) parameters, HCT test and phagocytic reaction under conditions of *in vitro* prodigiozan stimulation were performed.

The content of LPO products (conjugated dienes, CD) in blood serum was measured by extraction spectrophotometry [1]. The results were expressed in units of oxidation index (E_{232}/E_{200}). The concentration of the major plasma antioxidant ceruloplasmin [6,9] was estimated by the method of Revin [4] with modifications.

The blood was taken 1 day before and 6 days after surgery (48 h after the last intravenous infusion).

The results were analyzed by Student's t, Wilcoxon-Mann-Whitney, and Wald—Wolfowitz tests. The differences between the groups by the incidence of inflammatory complications were analyzed by Fisher's test.

RESULTS

During the preoperation period, functional state of NG in patients with BPH did not differ from the control (data not shown). Phagocytic activity of prodigiozan-

Chelyabinsk State Medical Academy

0007-4888/00/0011-1055$25.00

TABLE 1. Effects of Repeated Treatment with AA (3 Injections) on Functional State of Blood NG and Serum Content of LPO Products in Patients with BPH 6 Days after TUERP ($M\pm m$, n=40)

Parameter	Group		
	1 (without AA)	2 (AA, 500 mg/day)	3 (AA, 1000 mg/day)
Phagocytic activity, %	39±2	44±2*	46±2*
Phagocytic index	9.5±0.5	11.1±0.5*	10.7±0.4*
HCT test, activity (%)	54±4	64±4*	54±3
HCT test, intensity (arb. units)	0.64±0.06	0.76±0.05*	0.66±0.04
CD content			
heptane phase	1.37±0.06	1.40±0.07	1.50±0.06*
isopropanol phase	0.56±0.02	0.63±0.02*	0.62±0.02*
Incidence of infectious and inflammatory complications			
number of patients	12	3*	4*
% patients	30	7.5*	10*

Note. *p<0.05 compared to group 1.

stimulated NG from patients not treated with AA changed 6 days after TUERP: the phagocytic index in these patients (9.9±0.3) was lower than in the preoperation period (11.7±0.4, p<0.05) and healthy individuals (11.8±0.5, p<0.05). This shift reflects negative conditioning (inactivation) of blood NG during the postoperation period [5].

Postoperation inactivation of blood NG was accompanied by the development of inflammatory complications in 30% patients not treated with AA (urethroprostatitis, orchiepididymitis, and urosepsis, Table 1). It should be emphasized that 6 days after surgery, the concentration of circulating ceruloplasmin in patients with inflammatory complications (n=12, 38.2± 1.2 mg/dl) was higher than in patients without complications (34.6±1.2 mg/dl, p<0.05). The relative increase in ceruloplasmin content in patients with infectious and inflammatory complications was probably related to a more pronounced acute phase response [6,8]. This increase in the concentration of the major plasma antioxidant ceruloplasmin [6,9] was accompanied by a relative decrease in the content of circulating heptane-soluble LPO products. Six days after surgery, CD contents in patients with and without inflammatory complications were 1.24±0.07 and 1.49±0.13, respectively (p<0.05).

Postoperative treatment with AA dose-dependently increased blood content of LPO products (Table 1). AA in a dose of 500 mg promoted accumulation of only isopropanol-soluble lipid peroxides (3-fold), while in a dose of 1000 mg/kg this substance elevated the contents of both isopropanol- and heptane-soluble lipid peroxides. Our findings are consistent with published data that AA in high doses produces prooxidant effects, intensifies generation of semiquinone free radicals, and promotes LPO-stimulating activity of iron [2].

AA-induced LPO activation was accompanied by an increase in the sensitivity of NG to stimulation with prodigiozan *in vitro* (Table 1). At the same time, AA had no effect on spontaneous phagocytosis and HCT test (data not shown). It should be emphasized that 48 h after the last infusion of 1000 mg AA, phagocytic activity of prodigiozan-stimulated NG correlated with the content of heptane-soluble CD in blood serum (r=0.53, p<0.05). These results are consistent with published data on the conditioning (priming) effect of lipid peroxides on NG [3]. However, hyperactivation of LPO can lead to inactivation of NG. Infusion of AA in relatively low dose (500 mg) causes insignificant accumulation of LPO products in the blood, increases NG reactivity to prodigiozan (by phagocytic reaction and HCT test), and 4-fold decreases the incidence of inflammatory complications after TUERP. Repeated (for 3 times) administration of 1000 mg AA leads to a more pronounced activation of LPO, but primes NG only for phagocytic reaction and decreases the incidence of inflammatory complications by 3 times.

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