Influences of Sex and Age on Serum Ascorbic Acid

Rikuro Sasaki, Tadashi Kurokawa, Teiji Kobayasi and Shozo Tero-Kubota*

College of Medical Sciences, Tohoku University, Sendai 980
and * Chemical Research Institute of Non-Aqueous Solutions, Tohoku University, Sendai 980

Sasaki, R., Kurokawa, T., Kobayasi, T. and Tero-Kubota, S. Influences of Sex and Age on Serum Ascorbic Acid. Tohoku J. exp. Med., 1983, 140 (1), 97-104 — The concentrations of total ascorbic acid, reduced and oxidized forms of ascorbic acid, the ESR intensity of ascorbate radical, and the ratio of oxidized form of ascorbic acid to total ascorbic acid (DAsA/AsA) were estimated on 217 healthy controls, whose ages ranged from 12 to 96 years, in order to examine influences of sex and age. The concentration of total ascorbic acid was higher in females than in males throughout all age classes, but the oxidized form did not show a sex difference. Then it was found that the reduced form was higher in females than in males throughout all age classes. The concentrations of total ascorbic acid and reduced and oxidized forms of ascorbic acid, and the ESR intensity declined with age, but the DAsA/AsA ratio increased with age.

There has been considerable evidence that ascorbic acid functions as a defense against active oxygen radicals in addition to superoxide dismutase (Nishikimi 1975; Fessenden and Verma 1978; Bodaness and Chan 1979). The authors previously examined the nature of serum ascorbate radical and reported that both the ESR intensity of ascorbate radical and the concentrations of total and oxidized form of ascorbic acid in human serum declined with age, and that the decline in the level of ascorbic acid as well as ascorbate radical would indicate the decline in the defense mechanism with advancing age (Sasaki et al. 1982, 1983). From this standpoint, it is of great interest to examine whether or not there is a sex difference in the concentration of ascorbic acid in serum.

There are not many papers which refer to the sex difference in the level of ascorbic acid in human blood. Morgan et al. (1955), Brook and Grimshaw (1968), Burr et al. (1974), Pelletier (1975), Attwood et al. (1978) and Bates et al. (1979) have reported that the value of vitamin C in plasma and leukocytes is higher in females than in males, and the difference persists into old age. Loh and Wilson (1971) have shown that below the age of 60, the females have higher ascorbic acid values than the males, but after this age, the male concentrations exceed those in females. On the other hand, Baker et al. (1979) studied vitamin profiles of two

Received for publication, August 31, 1982.
elderly groups and ruled out sex as an influencing factor. Schorah (1981) has also mentioned that the difference between males and females disappears as plasma levels fall.

This paper is a report of studies on influences of sex and age on the concentrations of total ascorbic acid and reduced and oxidized forms of ascorbic acid, on the ESR intensity of ascorbate radical, and on the DAsA/AsA ratio in human serum.

**MATERIALS AND METHODS**

Subjects examined consisted of 95 males and 122 females, whose ages ranged from 12 to 96 years. None were taking vitamin supplementation at the time of examination. Blood was drawn early in the morning before breakfast.

Methods of chemical determination of the concentrations of total and oxidized form of ascorbic acid and methods to obtain the ESR intensity were described elsewhere (Sasaki et al. 1982, 1983). The concentration of reduced form was calculated by subtracting the concentration of oxidized form from that of total ascorbic acid.

The concentrations of total ascorbic acid and the reduced and oxidized forms of ascorbic acid, the ESR intensity, and the DAsA/AsA ratio were correlated to age in 95 males and 122 females, respectively, and the sex differences between the mean values were statistically examined.

**RESULTS**

Correlations between the total ascorbic acid and age in both sexes are shown in Fig. 1. Closed circles are for males and open ones for females. The solid line is the regression line for males and the dotted one for females. It is remarkable that both lines are parallel since the gradient of the regression line is almost identical. Furthermore, a marked decline in the distribution was observed in the older group, particularly in females. On the other hand, correlations between the

![Fig. 1. Correlations between the concentration of total ascorbic acid and age. Male (●, —), r = −0.453 (p < 0.001), y = 8.169 − 0.0649x. Female (○, ---): r = −0.526 (p < 0.001), y = 11.480 − 0.0719x.](image)
oxidized form of ascorbic acid and age showed approximately the same regression lines (Fig. 2). Correlations between the reduced form of ascorbic acid and age are shown in Fig. 3. There were a considerable number of subjects showing very low concentrations of reduced form, particularly in young males and elderly females. The regression lines were almost parallel. Correlations between the ESR intensity and age are shown in Fig. 4. Approximated gradients resulted in parallel regression lines. These results indicate that the concentrations of total ascorbic acid,
reduced form and ESR intensity are higher in females than in males throughout all age classes, while the concentration of oxidized form does not show a definite sex difference.
Correlations between the DAsA/AsA ratio and age are shown in Fig. 5. Although there was no significant correlation in overall male cases, a significant correlation was noted in overall female cases and the regression line was shown by the solid line (F). There were a fair number of subjects showing very high DAsA/AsA ratios in young males and old females. From this distribution, this ratio appears to be an inverse index of the reduced form.

Correlation coefficients between the concentrations of total ascorbic acid, reduced and oxidized form, ESR intensity and DAsA/AsA ratio and age are tabulated in Table 1. In both males and females, the concentrations of total ascorbic acid, and reduced and oxidized forms of ascorbic acid, and the ESR intensity declined significantly in proportion to age, but the DAsA/AsA ratio increased, particularly in females.

The mean values of the concentrations of total ascorbic acid, reduced and oxidized form, ESR intensity and DAsA/AsA ratio, standard deviations and “Student” t between both sexes are tabulated in Table 2. The sex difference was statistically very significant in the total ascorbic acid, reduced form and DAsA/AsA ratio, and significant in the ESR intensity. No significant difference was noted in the oxidized form.

**TABLE 1. Correlation coefficients in relation to age**

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>AsA</td>
<td>-0.453;</td>
<td>-0.526;</td>
</tr>
<tr>
<td>DAsA</td>
<td>-0.225*</td>
<td>-0.304;</td>
</tr>
<tr>
<td>RAsA</td>
<td>-0.388;</td>
<td>-0.461;</td>
</tr>
<tr>
<td>ESR</td>
<td>-0.383;</td>
<td>-0.448;</td>
</tr>
<tr>
<td>DAsA/AsA</td>
<td>0.190</td>
<td>0.260†</td>
</tr>
</tbody>
</table>

AsA, total ascorbic acid; DAsA, oxidized form of ascorbic acid; RAsA, reduced form of ascorbic acid; ESR, ESR intensity of ascorbate radical.

* p<0.05, † p<0.01, ‡ p<0.001.

**TABLE 2. Mean values, standard deviations and “Student” t**

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>AsA</td>
<td>6.01±2.82</td>
<td>7.98±3.25</td>
<td>4.69†</td>
</tr>
<tr>
<td>DAsA</td>
<td>3.14±1.41</td>
<td>2.95±1.37</td>
<td>0.42</td>
</tr>
<tr>
<td>RAsA</td>
<td>2.87±2.41</td>
<td>5.03±2.80</td>
<td>5.98†</td>
</tr>
<tr>
<td>ESR</td>
<td>0.41±0.13</td>
<td>0.52±0.15</td>
<td>2.36*</td>
</tr>
<tr>
<td>DAsA/AsA</td>
<td>0.58±0.25</td>
<td>0.41±0.20</td>
<td>5.57†</td>
</tr>
</tbody>
</table>

* p<0.05, † p<0.001.

**DISCUSSION**

This study indicates several interesting points: (1) The concentration of total ascorbic acid is higher in females than in males throughout all age classes. (2) The concentration of oxidized form does not show a definite sex difference. (3) The
concentration of reduced form is similarly higher in females than in males throughout all age classes. (4) There are a considerable number of young male subjects showing very low concentrations of reduced form. (5) The changes in ESR intensity are in parallel to those of total ascorbic acid and reduced form. (6) The concentrations of total ascorbic acid, reduced and oxidized forms and ESR intensity decline with age. (7) The DAsA/AsA ratio shows a significant increase with age in females.

As already mentioned, a majority of opinions agreed that the ascorbic acid is higher in females than in males and it declines with age (Morgan et al. 1955; Brook and Grimshaw 1968; Loh and Wilson 1971; Burr et al. 1974; Pelletier 1975; Attwood et al. 1978; Bates et al. 1979). There are, however, subtle differences between their findings. The results in this study seem to be consistent with most of these previous investigators, except for findings of no fall-off (Attwood et al. 1978) or conversion of vitamin C concentration of males over females with advancing age (Loh and Wilson 1971).

The blood ascorbic acid level is influenced by dietary intake. Schorah (1981) has stated that almost all evidence currently available points to intake as the main influencing age changes in vitamin C reserves. The difference in dietary habits between the young and elderly should be considered for the decline in vitamin C concentration with age. Burr et al. (1974) and Pelletier (1975) have found that differences between males and females exist where subjects have been matched for dietary intake. Morgan et al. (1955) have observed that females maintained higher serum levels of vitamin C on lower intakes than males. In addition, Brook and Grimshaw (1968) and Attwood et al. (1978) have also pointed out that the lower vitamin C concentration found in the plasma or leukocytes of the males as compared with that of the females are not solely due to dietary variations. A definite sex difference in the level of serum ascorbic acid appears to exist regardless of dietary habits. As to the possible cause for influences of sex in vitamin C status, Morgan et al. (1955), Loh and Wilson (1971), and Schorah (1981) have suggested that there is a difference in the metabolism of ascorbic acid between males and females. Brook and Grimshaw (1968), however, have stated it is not attributable to ovarian hormone activity, since the sex difference in vitamin C status persists in old age. Schorah (1981) has presented that the differences between males and females disappear as plasma levels fall. And he has mentioned when other factors such as markedly reduced dietary intake effect a decrease in blood vitamin C levels, metabolic differences between males and females can no longer be maintained.

In previous papers, only the concentration of total ascorbic acid has been estimated and this was regarded as vitamin C. Under the circumstance where a direct method to determine the reduced form is not used widely, it is no wonder that the total ascorbic acid is a matter of concern in relation to vitamin C. The chemical determination of total ascorbic acid and reduced form used in this study has been well established. The determination of fractionated ascorbic acids made it
possible to calculate the reduced form of ascorbic acid. The fractional determination seems to throw light on functions of ascorbic acid in the living body. This study discloses that the total ascorbic acid is higher in females than in males, although the oxidized form does not show a definite difference. Subsequently it is clear that the reduced form is higher in females than in males. It is of interest that there are a considerable number of young male subjects showing very low concentrations of the reduced form. This fact can be disclosed only by the fractional determination. This result may be due to dietary habit or smoking in this group, and may support that males are more influenced from aging process than females. At any rate there is no doubt that the difference in the reduced form is of great importance, since it is related to functions of vitamin C and ascorbate radical.

The authors previously reported on the significance of serum ascorbic acid, ESR intensity of ascorbate radical and DAsA/AsA ratio in relation to aging (Sasaki et al. 1983). From the viewpoint that the ascorbic acid functions as a defense against free radicals and the ESR intensity is an indicator or radical scavenger, distinct sex differences in the concentrations of total serum ascorbic acid, reduced form and the ESR intensity appear to be very important since they correspond to the difference in life span between males and females.

References