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Fatoş ÖNEN[1]
Cansel TÜRKAY[1]
Ali MEYDAN[1]
H. Sebila DÖKMETAŞ[1]
Haldun SÜMER[2]
Lütfi HOCAOĞLU[1]
Serhat İÇAĞASIOĞLU[1]
M. Zahir BAKICI[3]

Prevalence of Rheumatoid Factor (RF) and Anti-native-DNA Antibodies (anti-n DNA) in Different Age Subpopulations

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[1]Departments of Internal Medicine, [2]Public Health, [3]Microbiology Faculty of Medicine, Cumhuriyet University, Sivas-Turkey

Abstract: In this study, we have evaluated the prevalence of RF and anti-n-DNA in different age subpopulations grouped according to their clinical status.

RF and anti-n-DNA were measured in the serum of 51 elderly people considered to be successfully aging (group 1), 65 chronically ill elderly (group 2), 65 chronically ill patients under 65 years (group 3) and 30 patients with rheumatoid arthritis (group 4). The results were compared to 100 healthy persons as a control group under 65 years.

The prevalences of RF in group 1, group 2 and group 3 were significantly higher than the healthy younger controls. Particularly the difference between group 2 and the control group was markedly significant ($p<0.001$). There was not any difference between group 1 and 2.

In multiple logistic regression analysis, we found significant relationship between RF positivity and chronic illness and also being elderly ($r=0.18$, $p<0.01$ and $r=0.14$ $p<0.05$). When being elderly factor was added to the analysis of relationship of RF and chronic illness, it was seen that the relation diminished but persisted ($r=0.11$, $p<0.05$). None of the patients in our study groups had antibodies to n-DNA.

In conclusion, we suggest that the prevalence of RF rises in both chronic illness and being elderly, but chronic illness is more effective on the RF positivity than being elderly.

Key Words: Rheumatoid factor, anti-native-DNA antibodies, elderly, chronic illness.

Introduction

Several autoantibodies have predictive diagnostic values for connective tissue diseases (CTD). Two of them, RF and anti-n DNA are often used in the practice of Rheumatology. RF is detected in 70 % of patients with rheumatoid arthritis (RA) (1). Anti-n DNA has high specificity for patients with SLE (2, 3).

It is known that the prevalence of RF is increased in elderly and is some diseases other than RA (1, 4-6). When the recent literature was reviewed, variable reporting of the prevalence of autoantibodies in aged populations were seen (3, 4, 7-12). The selection of subjects to be studied may be responsible for these variable reports.

To determine the effect of age and chronic illness on the prevalence of RF and anti- n DNA, we performed this study in individuals with different age and clinical status.

Materials and Methods

Five groups were studied:

Group 1 consisted of 51 "successfully aging elderly" (13) subjects (24 women and 27 men), in the range of 65 to 90 years (mean 72.06±1.04). They were from the rest home or were ambulatory volunteers who had no history of chronic illness, no regular medication intake and no clinical or laboratory evidence of acute and chronic illness.

Group 2 included 65 chronically ill patients (34 women and 31 men), in the age range of 65 to 93 years (mean 68.85±0.77). They had variable non-rheumatologic chronic illness such as diabetes mellitus, hypertension, coronary artery disease and chronic liver disease.

In group 3, there were 65 chronically ill patients (30 women and 35 men), in the range of 17 to 65 years (mean 42.25±0.77), who had variable chronic illness similar to those in group 2.

Group 4 consisted of 30 patients with RA (26

women and 6 men), in the range of 34 to 69 years (mean 55.23±2.11) and who fulfilled the criteria of the American Rheumatism Association (14).

The RF and anti-n DNA results of these groups were compared to 100 healthy younger controls (54 women and 46 men) in the range of 17 to 65 years (mean 32.55±0.95).

Sera from all subjects were analyzed in the same laboratory using the standardized techniques.

IgM RF was measured using a commercially available kit assay (RapiTex RF, Behring Diagnostic Inc., Westwood, USA). This was a rapid slide latex agglutination test for the qualitative and semiquantitative measurement of rheumatoid factor in human serum. A positive result was confirmed when agglutination occurred with RF latex reagent mixed with sera containing greater than 19 IU/ml of RF.

Anti-n-DNA Quick Test (Human Gesellschaft für Biochemica und Diagnostica mbH, Germany) was used to examine the presence of anti-n-DNA. This test is based on the following principle: Latex particles are bound with native deoxyribonucleic acid (n-DNA) by means of an intermediary albumin matrix. These coated latex particles combine with any antibodies to n-DNA in serum to give a visible agglutination. The test was considered as negative when no difference in agglutination was observed between specimen and negative control. The positive control and positive sera have shown distinct agglutination within 2 minutes.

Fisher's Exact Test and Multiple Logistic Regression Analysis were used for evaluation the statistical significance.

Results

The prevalence of RF in the successfully aging elderly (group 1), chronically ill elderly (group 2) and chronically ill aged under 65 (group 3) patients were found as 11.8 %, 21.5 % and 13.8 % respectively. These results were significantly higher than healthy younger controls (3 %). Particularly the difference between group 2 and the control group was markedly significant ($p<0.001$). There was not any difference between group 1 and 2 ($p>0.05$). The prevalence of RF in the chronically ill elderly patients was also higher than the chronically ill younger patients. Subjects with RA had a 76.7% prevalence of positive RF.

No individual in our study grups had anti-n DNA antibodies.

The prevalence of the RF and anti –n DNA in the four study groups and healthy young controls are presented in the table.

In the multiple logistic regression analysis, we found significant relationship between RF positivity and chronic illness and also elderly ($r=0.18$, $p<0.01$ and $r=0.14$, $p<0.05$ respectively). When elderly factor was added to the analysis of relationship of RF and chronic illness, it was seen that although the relation diminished it persisted ($r=0.11$, $p<0.05$).

Discussion

The prevalence of autoantibodies in elderly populations has been reported to be increased compared to that seen in younger populations (4, 5, 8, 10). This increase has been attributed to effect of progressive senescence of immune function (7) and it has been believed that serologic tests were not diagnostic because of false positive results were common in healthy elderly subjects (15). In contrast, it has been shown that prevalence of autoantibodies decresaed in elderly persons with rheumatological disease (11, 12, 16). Therefore the belief that aging in humans is accompanied by increased autoantibodies may not be always right. A review of the recent literature reveals variable reporting of the prevalence of autoantibodies in aged people (4, 7-12). In these studies, various clinical and laboratory criteria have been applied for patient selection. We must recognize that there is an important but often difficult distinction to be made between changes in all systems of human organism due to the normal process of senescence and those abnormal changes attributable, in part, to disease. And also it must be considered that significant heterogeneity of elderly populations are seen in different studies, so this may contribute to false results.

In 1984, the SENIEUR protocol was described as a method of selection of the subjects to be studied in immunogerontologic studies (17). In this protocol many non-specific disease-associated changes may be inappropriately attributed to the aging process.

Normal aging may be categorized into two groups: Usual and successful aging. In first of them, extrinsic factors heighten the effects of aging alone and in the second, extrinsic factors play a neutral or postive role (13). Previous studies have been usually performed only on chronically ill aged patients and have been excluded the healthy elderly people. In recent years, successfully aging subgroups were also studied in these

researches. Juby et al (9) reported that successfully aging individuals had a prevalence of RF and FANA which were not statistically significantly higher than a healthy young adult control group. They also found that patients with chronic illness had a markedly increased prevalence of RF which was statistically significant than both of the healthy elderly and the young control group.

Table RF and anti-n-DNA prevalence in the study groups and the control group

	n	RF(ê) (%)	Anti-n DNA(+)
Group 1	51*	6(11.8)	0
Group 2	65**	14(21.5)	0
Group 3	63*	9(13.8)	0
Group 4	30	23(76.7)	0
Controls	100	3(3)	0

* $p<0.05$ Group 1 or 3 v controls

** $p<0.001$ Group 2 v controls

We determined that the prevalence of RF in our successfully aging elderly group was significantly higher than the younger healthy controls, and the presence of chronic illness increased the prevalence of RF independent of age. Chronic illness was found to be more effective on the prevalence of RF than being elderly. Although successfully aging elderly had no history of chronic illness, no regular medication intake and no clinical or laboratory evidence of acute and chronic illness, they could have been exposed to an agent(s) which no longer exists today. Thus the higher titers among the elderly may not to be due to the aging per se but to a "cohort effect". The prevalence of RF in our RA patients was similar to those in other published reports (1).

Silvestris et al (7) had also shown that sera of elderly subjects contained statistically significantly higher amounts of IgM RF than young controls and the levels of anti-DNA were similar in both groups. In a cross-sectional study of 100 healthy elderly individuals, significant titers of IgM RF have been found in 10 %. Antibodies to single or double stranded DNA were not detected in any subjects (5). This paradoxical dissociation of the RF from the other levels of autoantibodies in elderly population could suggest a different significance of IgM RF which may be distinct from the anti-n DNA. In many healthy elderly people, the increased production of IgM RF may not be an expression of the general increase of autoimmune phenomena.

It has been found that the size of self-reactive B cell pool which synthezing RF increased with advancing age (6). This finding suggests that RF may play a physiologic role in the immune response.

There are variable reports about autoantibodies in the elderly with rheumatic disease as well as in healthy elderly (3, 11, 12, 16, 18).

We found that antibodies to n-DNA did not occur in any of our groups similar to Chakravarty et al (5). Some investigators reported that anti-double-stranded antibodies were found in healthy aged people (4, 8, 10), but this peculiar antibody differed from those found in patients with SLE with having low titers, belonging to the IgA class alone, negativity to Farr assay and no complement-fixing ability (4,10). Methodological differences may account for differences in reporting of prevalence of anti-n antibodies in elderly. We know that anti-n DNA has high specificity for patients with SLE (2, 3). We think that, as there were not any SLE patient in our study groups, all of them had negative anti-n DNA.

In conclusion, we suggested that the inclusion of subjects of successfully aging in the immunogerontologic studies is necessary for more correct results and this approach provides determining the clinical significance of autoantibodies in elderly people.

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