Clinical chemistry values in elderly Korean people: single institutional study

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Introduction

The population older than 65 years of the Korea was about 11.3% of the total population last year [1], and is expected to reach 24.3% and 38.2% in the year 2030 and 2050, respectively [2]. The proportion of elderly people to visit the hospital is increasing and laboratory tests are performed to screen them for many pathological conditions. The chemistry tests can be very important in diagnosis, especially for elderly people, in

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aboratory values change with age and interpreting laboratory results from elderly people using the reference intervals for younger adults may not be appropriate. The authors investigated the distribution patterns of routine chemistry values from elderly people to determine whether current reference intervals are also valid for elderly people. A total of 1,215 persons older than 65 years and 1,827 healthy adults below 65 years of age were evaluated. Blood samples were collected after an overnight fast and analyzed for chemistry tests. Computing the central 95th percentile showed that the total protein, albumin, ALP, LD, creatinine, uric acid, triglyceride, HDL-cholesterol, and electrolytes of elderly people were within the standard reference intervals used in our laboratory. For AST and ALT, the upper range of the central 95th percentile in the elderly population was found to be outside the common reference interval. However, the central 90th percentile values of AST and ALT were compatible with the common reference intervals. GGT, BUN, total cholesterol, LDL-cholesterol, and glucose showed higher values than the upper limits of the reference intervals. For common clinical chemistry tests, the common reference values in general should be applicable to elderly people, even though some parameters showed wider distributions in the elderly.

Keywords: Clinical chemistry tests; Reference values; Aged
Whom clinical symptoms and signs are not typical or often absent even during an acute event. Common reference intervals are needed for adequate interpretation of these tests. Since many chemistry markers change with aging and the current reference intervals are mostly based on a population in the age range from 20 to 50 years, however, interpreting laboratory results from elderly people by the reference intervals for younger adults may not be appropriate [3-5]. Defining a ‘healthy’ elderly population and collecting data from them are difficult because diabetes, cancer, cardiovascular diseases, and some types of medication are common in older people. Therefore, reports of laboratory reference values for elderly people are sparse in Korea.

In this study, authors compared the distribution patterns of routine chemistry values from elderly people to younger adults to investigate if chemistry values change with aging and if present reference intervals are also valid to elderly people.

### Materials and methods

#### 1. Populations

From January, 2009 till June, 2011, The 2,604 Korean individuals above 65 years of age were selected from the people attending general health check-ups at Kyungpook National University Hospital. They were screened by using a health questionnaire that contained questions about medical history, present illness, and present medication and excluded from the final diagnosis of cancer, hyperlipidemia, diabetes, cardiovascular disease, viral hepatitis, and any past history of confirmed disease such as stroke. And some subjects were also excluded because of strong suspicion of disease from their laboratory data [3,6]: C reactive protein >200 mg/dL, blood urea nitrogen (BUN) >42 mg/dL, creatinine >2.6 mg/dL, total proteins >90 g/dL, glucose >180 mg/dL. Finally, 1,215 elderly people (group I) then consisted of 1,003 persons (551 males and 452 females) for 65 to 74 years (group Ia) and 212 persons (110 males and 102 females) older than 75 years (group Ib). 1,827 younger healthy adults (982 males and 845 females) below 65 years of age (mean age, 52.8 years; range, 21 to 64 years) (group II) were also evaluated as a comparing group. The study was

| Test item          | Method                                                | Unit     |
|--------------------|-------------------------------------------------------|----------|
| Total protein      | Biuret method                                         | g/dL     |
| Albumin            | Dye (BCG) binding method                              | g/dL     |
| AST                | IFCC without pyridoxal phosphate without sample blank | U/L      |
| ALT                | IFCC without pyridoxal phosphate without sample blank | U/L      |
| ALP                | PNPP/AMP buffer/IFCC                                   | U/L      |
| LD                 | UV method (pyruvate → lactate)                         | U/L      |
| GGT                | Szasz (γ-glutamyltransferase)                          | U/L      |
| BUN                | Urease with GLDH (coupledenzyme)                       | mg/dL    |
| Creatinine         | Jaffe method, kinetic colorimetric assay (ID–GC/MS, traceable) | mg/dL    |
| Uric acid          | Uricase method                                         | mg/dL    |
| Sodium             | Ion selective electrode                                | mmol/L   |
| Potassium          | Ion selective electrode                                | mmol/L   |
| Chloride           | Ion selective electrode                                | mmol/L   |
| Total cholesterol  | Enzymatic colorimetric assay                           | mg/dL    |
| Triglyceride       | Enzymatic colorimetric assay                           | mg/dL    |
| HDL-cholesterol    | Homogenous enzymatic colorimetric assay                | mg/dL    |
| LDL-cholesterol    | Homogenous enzymatic colorimetric assay                | mg/dL    |

BCG, bromocresol green; AST, aspartate transaminase; IFCC, International Federation of Clinical Chemistry; ALT, alanine transaminase; ALP, alkaline phosphatase; PNPP/AMP, p-nitrophenylphosphate/amino-methyl-propanol; LD, lactate dehydrogenase; UV, ultraviolet; GGT, gamma-glutamyl transpeptidase; BUN, blood urea nitrogen; GLDH, glutamate dehydrogenase; ID-GC/MS, isotope dilution gas chromatography–mass spectrometry; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
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Table 2. Comparison of clinical chemistry values in elderly people (group I) and young adults (group II)

| Variable            | Unit     | Group I | Group II | P-value |
|---------------------|----------|---------|----------|---------|
|                     | n        | Mean    | SE       | n        | Mean    | SE       |         |
| Total protein       | g/dL     | 1,216   | 752      | 0.01    | 1,827   | 751      | 0.01    | 0.661   |
| Albumin             | g/dL     | 1,216   | 4.47     | 0.01    | 1,827   | 4.47     | 0.01    | 0.722   |
| AST                 | U/L      | 1,215   | 23.68    | 0.23    | 1,825   | 22.25    | 0.17    | <0.0001 |
| ALT                 | U/L      | 1,214   | 20.35    | 0.3     | 1,752   | 20.01    | 0.28    | 0.014   |
| ALP                 | U/L      | 1,216   | 73.25    | 0.63    | 1,827   | 66.84    | 0.44    | <0.0001 |
| GGT                 | U/L      | 1,216   | 28.49    | 0.75    | 1,809   | 30.99    | 0.69    | 0.024   |
| LD                  | U/L      | 217     | 3872     | 4.08    | 1,192   | 355.56   | 1.74    | <0.0001 |
| Total cholesterol   | mg/dL    | 1,138   | 189.85   | 0.87    | 1,753   | 187.42   | 0.7     | 0.021   |
| HDL-cholesterol     | mg/dL    | 1,216   | 53.64    | 0.38    | 1,827   | 54.61    | 0.32    | 0.038   |
| LDL-cholesterol     | mg/dL    | 1,106   | 111.62   | 0.77    | 1,648   | 113.29   | 0.61    | 0.155   |
| Triglyceride        | mg/dL    | 1,158   | 118.95   | 1.39    | 1,723   | 113.77   | 1.19    | 0.001   |
| Total amylase       | U/L      | 458     | 60.32    | 0.98    | 1,333   | 58.66    | 0.47    | 0.412   |
| BUN                 | mg/dL    | 217     | 16.08    | 0.28    | 1,193   | 14.17    | 0.11    | <0.0001 |
| Creatinine          | mg/dL    | 1,207   | 1        | 0       | 1,826   | 1        | 0       | 0.099   |
| Uric acid           | mg/dL    | 1,216   | 4.87     | 0.04    | 1,826   | 4.9      | 0.03    | 0.778   |
| Serum glucose       | mg/dL    | 1,116   | 97.03    | 0.32    | 1,740   | 95.32    | 0.25    | <0.0001 |
| Sodium              | mmol/L   | 1,211   | 142.22   | 0.07    | 1,825   | 141.52   | 0.05    | <0.0001 |
| Potassium           | mmol/L   | 1,211   | 4.23     | 0.01    | 1,825   | 4.31     | 0.01    | <0.0001 |
| Chloride            | mmol/L   | 1,211   | 104.55   | 0.08    | 1,825   | 105.16   | 0.06    | <0.0001 |

SE, standard error; AST, aspartate transaminase; ALT, alanine transaminase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; LD, lactate dehydrogenase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BUN, blood urea nitrogen.

approved by the institutional review board of Kyungpook National University Hospital and all the study participants gave written informed consent.

2. Methods

Blood samples were collected in BD Vacutainer SST (Becton Dickinson, San Jose, CA, USA) from a median cubital vein after an overnight fasting. Chemistry tests were performed on Modular Analytics (Roche Diagnostics, Mannheim, Germany). The analytic method and the reference range in our laboratory was presented (Table 1).

3. Statistics

PASW Statistics 18 ver. 18.0.0 (SPSS Inc., Chicago, IL, USA) was used for analysis. The distribution pattern was assessed using Kolmogorov-Smirnova test. Comparisons between groups were evaluated with Mann-Whitney test and Kruskal-Wallis test. Mean values, as well as the central 90th and 95th percentile, were calculated for all measurements in each group. The significance level was set at $P, 0.05$.

Results

Compared with young adults (group II), elderly
people (group I) showed significant increases in aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), lactate dehydrogenase (LD), BUN, total cholesterol, triglyceride, and glucose, and significant decrease in high-density lipoprotein (HDL)-cholesterol (Table 2). Especially, AST, ALT, LD, total cholesterol, triglyceride, and glucose were increased with age when comparing group Ia with group Ib (Table 3). In spite of these significant differences between group I and group II, computing the central 95th percentile of group I showed that total protein, albumin, ALP, LD, creatinine, uric acid, triglyceride, HDL-cholesterol, and electrolytes were within the common reference intervals which we generally use in our laboratory. For AST and ALT, the central 90th percentile values were compatible with the common reference intervals (Figure 1). GGT, BUN, total cholesterol, low-density lipoprotein (LDL)-cholesterol, and glucose showed higher upper 97.5th and even 95th percentile values than the upper limits of the common reference intervals (Figure 2).

### Discussion

Selection of an ideal reference population for the
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age in this study was 65 years or older. As an argue could be present that the subjects analyzed in this study were not representative of an healthy elderly population, authors tried to reduce the deviation by excluding those with present illness and of strong suspicion of disease from their laboratory data mentioned above. Thus there is a need to establish certain criteria to define "healthy elderly population" before conducting a future research by increasing the number of object groups in liaison with a number of laboratories.

In this study, compared with young adults, elderly people had significant increases in AST, ALT, ALP, GGT, LD, BUN, total cholesterol, triglyceride, and glucose. However, the values of most of the parameters in elderly people were similar to the common reference intervals currently used. Yet, the limitation of this study is that the 12-hour fast of the subjects was not identified in the case of triglyceride.

For most liver enzymes, the significant increases were observed in the elderly people. This finding agrees with those reported by several investigators [8,10,11]. Tietz et al. [8], however, reported higher values in 60- to 90-year-old population than younger people and then decrease after 90 years old. Fulop et al. [12] found no changes of AST. In spite of some variations, their results obtained in elderly population were

elderly people is difficult, because first, the exact definition of age for "elderly" is not clear, second, their characteristics are very heterogenous in terms of nutrition, physical activity, and medication, and third, the morbidity rates increase with age as the prevalence of cardiovascular disease, stroke, or malignancy is too high [3,6-9]. In general, "elderly" is taken to mean over 65 years of age, thus, the inclusion criterium of

Figure 1. Central 95th percentile of clinical chemistry values in elderly people. ALP, alkaline phosphatase; RI, common reference interval; LD, lactate dehydrogenase; HDL, high-density lipoprotein. "2.5 to 97.5 percentile in the age group I (65 years or above) of the research subjects. The upper and lower limits of the box are the 97.5 and 2.5 percentile and the horizontal bar is the median value (n=1,215).
in good agreement with their reference values [8,10-13]. GGT values in this study showed modest increase by age in both men and women, and were needed to be compromised.

We found an increase in glucose values with age, and this finding was also observed in other reports [8,10,14]. Although the distribution patterns of glucose values for elderly people were much higher than the usual reference intervals, the value of 97.5 percentile in elderly population was still lower than the cutoff value for a diagnosis of diabetes. As we know the high prevalence of diabetes in elderly population, a careful monitoring will be needed.

There was an increase of urea nitrogen with age. This finding agreed with most studies [6,8,14] from the aspect of decreased renal function with age. On the other hand, creatinine values showed no remarkable changes in this study, and were also very variable according to researchers [8,14]. The reason was thought that decrease in renal creatinine excretion was compensated with the low production by decreased renal mass in elderly person.

Lower albumin values in elderly people reported by other authors [8,10,12,15] suggested that it was attributed to either aging process alone or decreased state of health of these individuals. Serum iron values were also lower than those in young adults and confirmed by most [8,16,17] but not all studies.

Fraser et al. [18] brought up a question that biological variabilities should increase with age because of the compromised homeostasis, however, they confirmed that within-subject variations in elderly people were similar to those in younger subjects. Biological variations in elderly people were not investigated in this study. It was thought to be important aspect in geriatrics laboratory and needed further evaluation.

**Conclusion**

For routine clinical chemistry tests these results
suggest that the common reference values in general are applicable to elderly people, even though some parameters showed wider distributions in elderly. However, when interpreting chemistry test results in elderly people, one should take the age-related alterations into deep consideration. For further attempts to define the reference values for various laboratory tests in the elderly population, this study will provide a meaningful information.

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REFERENCES

1. Statistics Korea. Summary of census population [Internet]. Daejeon: Statistics Korea [cited 2013 May 21]. Available from: http://kosis.kr/gen_etl/start.jsp?orgId=101&tblId=DT_1IN1003 &conn_path=i2&path.

2. Statistics Korea. Population projections for Korea [Internet]. Daejeon: Statistics Korea [cited 2013 May 21]. Available from: http://kosis.kr/gen_etl/start.jsp?orgId=101&tblId=DT_1B01001 &conn_path=i2&path.

3. Carlsson L, Lind L, Larsson A. Reference values for 27 clinical chemistry tests in 70-year-old males and females. Gerontology 2010;56:259-265.

4. Melillo KD. Interpretation of laboratory values in older adults. Nurse Pract 1993;18:59-67.

5. Hammerman-Rozenberg R, Cohen A, Ginsberg G, Maaravi Y, Ebstein RP, Stessman J. Laboratory reference values for the 70 year olds. Isr J Med Sci 1996;32:611-620.

6. Boulou O, Krieg MA, Janin B, Burckhardt P, Francioli P, Bachmann C. Clinical chemistry variables in normal elderly and healthy ambulatory populations: comparison with reference values. Clin Chim Acta 1998;272:127-135.

7. Bourdel-Marchasson I, Lakir H, Puget E. Interpreting routine biochemistry in those aged over 65 years: a time for change. Maturitas 2010;66:39-45.

8. Tietz NW, Shuey DF, Wekstein DR. Laboratory values in fit aging individuals: sexagenarians through centenarians. Clin Chem 1992;38:1167-1185.

9. Willcox DC, Willcox BJ, Wang NC, He Q, Rosenbaum M, Suzuki M. Life at the extreme limit: phenotypic characteristics of supercentenarians in Okinawa. J Gerontol A Biol Sci Med Sci 2008;63:1201-1208.

10. Dietrich T. Geriatrics lacks reference values. Clin Chem News 1983;(Jun):19-20.

11. Garry PJ, Hunt WC, VanderJagt DJ, Rhyne RL. Clinical chemistry reference intervals for healthy elderly subjects. Am J Clin Nutr 1989;50(5 Suppl):1219-1230.

12. Fulop T Jr, Worum I, Varga P, Foris G, Bars L, Mudri K, Leovey A. Blood laboratory parameters of carefully selected healthy elderly people. Arch Gerontol Geriatr 1989;8:151-163.

13. Huber KR, Mostafaie N, Stangl G, Worofka B, Kittl E, Hofmann J, Heijtmann M, Michael R, Weissgram S, Leitha T, Jungwirth S, Fischer P, Tragl KH, Bauer K. Clinical chemistry reference values for 75-year-old apparently healthy persons. Clin Chem Lab Med 2006;44:1355-1360.

14. Landahl S, Jagenburg R, Svanborg A. Blood components in a 70-year-old population. Clin Chim Acta 1981;112:301-314.

15. Greenblatt DJ. Reduced serum albumin concentration in the elderly: a report from the Boston Collaborative Drug Surveillance Program. J Am Geriatr Soc 1979;27:20-22.

16. Zauber NP, Zauber AG. Hematologic data of healthy very old people. JAMA 1987;257:2181-2184.

17. Lipschitz DA, Udupa KB, Milton KY, Thompson CO. Effect of age on hematopoiesis in man. Blood 1984;63:502-509.

18. Fraser CG, Cummings ST, Wilkinson SP, Nevile RG, Knox JD, Ho O, MacWalter RS. Biological variability of 26 clinical chemistry analytes in elderly people. Clin Chem 1989;35:783-786.
요약

노인의 경우 질병에 이환되어도 임상증상이 없거나 비전형적일 수 있으므로 진단의학검사결과의 올바른 해석은 질병의 진단과 경과관찰에 매우 중요하다. 진단의학검사는 종종에 따라 영향에 영향을 받는 것이 있으며 젊은 성인에 대한 참고 구간을 기준으로 노인에서 검사결과의 해석을 하는 것은 적합하지 않을 수 있다. 저자들은 통상적으로 사용하고 있는 참고 구간이 노인에게도 그대로 적용할 수 있는지 알기 위해 노인인구를 대상으로 임상 화학 검사결과의 분포 양상을 조사하였다. 경북대학교병원 건강증진센터를 방문한 65세 이상의 노인 2,604명 가운데 설문조사, 검사결과, 진료기록 등을 기준으로 건강한 노인 1,215명을 선정하였고 그룹 I, 65세 미만의 건강한 성인 1,827명을 대조군으로 그룹 II 비교하였다. 헬름바 공복상태후의 혈액 샘플을 채취하여 임상화학검사를 시행하였다. PASW 프로그램을 이용, Kolmogorov-Smirnov test로 결과 값의 분포양상을 보고 Mann-Whitney test와 Kruskal-Wallis test로 그룹별 결과를 비교 평가하였다. 노인의 중앙 95 백분위 수를 계산하면, 총 단백질, 일부분, alkaline phosphatase, lactate dehydrogenase, 크레아티닌, 요산, 트리글리세라이드, high-density lipoprotein-콜레스테롤, 그리고 천혈질은 통상 사용하는 참고구간 내에 있었다. Aspartate transaminase와 alanine transaminase의 경우는, 노인에서 중앙 95 백분위 수 값은 참고구간을 벗어났으나, 중앙 90 백분위 수 값은 일반적인 참고구간과 호환되었다. 반면에 gamma-glutamyl transpeptidase, blood urea nitrogen, 총 콜레스테롤, low-density lipoprotein-콜레스테롤, 그리고 포도당의 중앙 90 백분위 수 값의 하한은 참고구간의 하한을 벗어나지 않았으나 상한의 경우 상한보다 높은 값을 보여 주었다. 통상적인 임상화학검사의 경우, 비록 일부 검사종목의 값이 노인에서 더 넓은 분포양상을 보였으나, 일반적으로 사용되는 참고범위는 노인에게 적용될 수가 있을 것으로 보인다.

핵심요인: 임상화학검사: 참고범위: 노인

Peer Reviewers Commentary

우리나라 혈액화학검사 결과의 참고구간은 주로 정상 성인을 기준으로 작성된 것이고 혼히 교과서나 제조사가 제시한 참고구간을 소수의 자료로 검증하여 사용하는 경우가 많는데 본 연구는 65세 이상 1,215명의 건강인과 65세 미만 1,827명의 비교적 대수의 수검자들 대상으로 비교 분석하여 유용한 자료가 될 것이다. 아직 표준화되지 않은 종목이 많아 타 검사 기관과의 검사결과 결과의 절대값 비교는 허물지만 65세 미만의 결과와 65세 이상의 결과와의 비교는 가능하며 검사 결과의 해석이 도움이 된다. 즉, 대부분의 종목이 두 군간 차이가 없었으나 일부 종목은 65세 이상에서 더 넓은 분포를 보여 비정상 결과로 오인될 수 있는데 비해 본 연구의 결과를 참고하여 볼필요한 추가 진료를 막을 수 있을 것이다.

[정리: 편집위원회]