The effect of vitamin C on procalcitonin biomarker in community-acquired pneumonia

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Abstract

Introduction: Community acquired pneumonia (CAP) is a prevalent low respiratory infection. Diagnosis is based on clinical symptoms, radiologic evidence and culture. Biomarkers such as IL6, CRP and procalcitonin are helpful in diagnosis. Procalcitonin is a soluble biomarker in serum that increase in systemic inflammation and bacterial infections. People with normal procalcitonin have low risk to infect pneumonia. Patient with CAP have more oxidative stress than normal people. Studies show that receiving vitamin C can reduce incidence of pneumonia. The present study was designed to evaluate the effect of vitamin C supplement on procalcitonin biomarker in patient with CAP.

Methods: Patients with CAP who passed inclusion and exclusion criteria after obtaining informed consent, were assigned randomly in two groups of drug and placebo. The drug group received vitamin C (1000 mg/d) daily and medications that physician prescribed for treating CAP for 10 days and placebo group received placebo and medications that physician prescribed. The serum level of procalcitonin was measured at the beginning of the study and after 10 days of intervention.

Results: 35 patients finished the study. Serum level of procalcitonin on the first and tenth day did not show any significant difference between drug and placebo groups.

Conclusions: To clarify the relationship between the effects of vitamin C on procalcitonin in CAP, a larger sample size is required.

Keywords: Interlukin6, C-reactive protein, Procalcitonin, Community acquired pneumonia, Vitamin C
inflammatory factors production occurs in peripheral vessels [11]. Antioxidants reduce tissue oxidative damage and rapid inflammatory responses by affecting their activation genes [12]. Vitamin C is an antioxidant that significantly reduces the respiratory symptoms in most patients [13]. The evidence shows that ascorbic acid can probably have the anti-viral activity in vivo [14]. It is currently believed that people with low vitamin C levels are disposed to infection and oxidative stress [15]. According to the high cost of treatments with antibiotics and the harmful effects of increased number of patients and their treatment duration, using new methods for reduction of these items is necessary. Considering the effect of serum procalcitonin levels as a recovery indicator on antibiotic therapy duration and also the effect of vitamin C as an antioxidant on the recovery of pneumonia patients, the aim of this study was the determination of the exact relation between the effects of this supplement on PCT level in vitamin C and placebo receivers.

Material and method

At first, 40 CAP patients were included in this study and divided into two groups. Finally, 35 patients, 17 in vitamin C (1000 mg/d) receiver group and 18 in placebo receiver group, completed the study. 10 numbers of Vitamin C and placebo tablets were taken by patients in 10 days. On the first and tenth day, 2 CC of venous blood sample were taken from patients to measure the serum level of procalcitonin. Serum PCT level was evaluated by its specific kit using enzyme-linked fluorescence assay (ELFA) method.

Statistical analysis

Data were analysed by SPSS version 17.0 software. Statistical tests such as T-test, Chi-square and Fisher exact were used. Also, the Kolmogorov-Smirnov test was used for assessing data distribution. The PCT serum level data were not normally distributed, so mann-whitney u and Wilcoxon signed-rank test were used to examine the changes in the level of this factor. T-test and Paired-T tests were used for data that had normal distribution such as CRP, Erythrocyte sedimentation rate (ESR) and WBC serum level had no significant differences on first and tenth day of the study in both groups. PCT serum level was evaluated on the first and tenth day of the study in both groups. PCT serum level had no significant differences on first and tenth day. In both groups, the serum level of this biomarker decreased but these changes were not significant. However, Wilcoxon signed-rank test showed that ten-day-treatment for pneumonia with vitamin C or placebo made a significant change in procalcitonin serum level (Table 1).

There was no significant change in the ESR levels in both groups on the first and last day. In placebo receivers, unlike the vitamin C receivers, there was an increase in ESR level during the hospitalization. Paired-T test showed that pneumonia treatment in addition to vitamin C or placebo made no significant difference in ESR level (Table 2).

CRP level on the first and last day of hospitalization didn't significantly change and this biomarker decreased in both groups. According to the Paired-T test, treatment with prescription drugs in addition to vitamin C or placebo made a significant decrease in CRP level in both groups. But there was no significant relationship between the differences in the two groups (Table 3).

According to the p-values, WBC levels had no significant differences in two groups during the hospitalization and there was a decrease in two groups. Paired-T test showed that pneumonia treatment in addition to vitamin C made a significant decrease in WBC level but in placebo receivers, it didn't significantly decrease (Tables 4, 5).

Discussion

In the current study, PCT serum level was evaluated on the first and tenth day. This biomarker was significantly decreased in both groups but this decrease was not significant in vitamin C and placebo receivers. Therefore, vitamin C didn't affect the PCT level. Boussekey in his study assessed the value of PCT for CAP diagnosis and showed that PCT >2ng/ml had a relation with increased incidence of blood bacteria, sepsis shock, organs failure and death [16]. In Christ-Crain's study, it was shown that the use of PCT as a treatment guide decreased the antibiotic exposure and treatment duration compared with standard group [17]. Numerous studies show that low levels of vitamin C in plasma, white blood cells, and urine occurs during various infectious diseases, which is not only due to inadequate diet of this vitamin but also occurs under the influence of infection physiological changes. Alpha a Fowler et al. had a study on sepsis patients in 2014. The patients were divided into two groups: ascorbic acid receivers and placebo receivers (5% dextrose serum). PCT and CRP serum levels were evaluated in both groups. No
Fig. 1 Flowchart of patients who entered the study

Table 1 Wilcoxon signed-rank test showing the PCT level variation

| Vitamin C receiver | Placebo receiver |
|--------------------|-----------------|
| PCT                |                 |
| Average            | 0.8303          | 0.7947          |
| Standard deviation | 2.275           | 2.267           |
| Z                  | -3.214          | -3.386          |
| Sig                | 0.001           | 0.001           |

Table 2 Paired-T test showing the ESR level variation

| Vitamin C receiver | Placebo receiver |
|--------------------|-----------------|
| ESR                |                 |
| Average            | 38.7647         | 33.800          |
| Standard deviation | 23.0828         | 27.7699         |
| T                  | -0.92           | -0.447          |
| Sig                | 0.37            | 0.662           |

Table 3 Paired-T test showing the ESR level variation

| Vitamin C receiver | Placebo receiver |
|--------------------|-----------------|
| CRP                |                 |
| Average            | 53.933          | 59.1429         |
| Standard deviation | 29.2708         | 23.4300         |
| T                  | -2.873          | -3.046          |
| Sig                | 0.014           | 0.009           |

Table 4 Paired-T test showing the WBC level variation

| Vitamin C receiver | Placebo receiver |
|--------------------|-----------------|
| WBC                |                 |
| Average            | 8.3341          | 7.0867          |
| Standard deviation | 2.8563          | 2.3079          |
| T                  | -2.180          | -2.047          |
| Sig                | 0.047           | 0.061           |
adverse events were observed in ascorbic acid receivers. CRP level was significantly reduced in ascorbic acid receivers compared to the initial value and placebo group. Also, PCT level in placebo receivers increased in the first 24 h and it was significantly reduced in vitamin C receivers compared to its initial value in the first 48 hours. This study showed that ascorbic acid receiving can lead to a rapid decrease of inflammatory biomarkers in severe sepsis [18]. Another inflammatory biomarker is CRP. In the current study CRP, ESR, and WBC levels were evaluated on the first and tenth day. Changes of these biomarkers during the hospitalization had no significant relationship between the two groups. A study in 2007 indicated that daily evaluation of CRP can be useful for diagnosis of CAP patients. This biomarker had a better anticipating of patient status compared with other common markers like body temperature and leukocyte level evaluation. This study proved that rapid CRP decrease in patients led to a shorter duration of antibiotic therapy with the same effect and less toxicity. Therefore CRP measurement in emergency cases led to the treatment costs decrease [19].

Conclusions
According to the Wilcoxon signed-rank test, ten-day-treatment with vitamin C or placebo made a significant change in PCT serum level in both groups but this change between two groups was not significant. For more certainty, further studies in a larger community are needed.

Table 5 The average of PCT, CRP, ESR, and WBC levels on the first and tenth day

| Variables        | Average       | Standard deviation | P-value |
|------------------|---------------|--------------------|---------|
| PCT (first day)  | Vitamin C receiver 0.8303 | 2.27549 | 0.93 |
|                  | Placebo receiver 0.0772 | 0.07805 |           |
| PCT (tenth day)  | Vitamin C receiver 0.7947 | 2.26754 | 0.98 |
|                  | Placebo receiver 0.0430 | 0.05738 |           |
| ESR (first day)  | Vitamin C receiver 38.7647 | 23.08281 | 0.685 |
|                  | Placebo receiver 35.6250 | 20.81306 |           |
| ESR (tenth day)  | Vitamin C receiver 33.800 | 27.7699 | 0.730 |
|                  | Placebo receiver 37.2143 | 24.70185 |           |
| CRP (first day)  | Vitamin C receiver 53.933 | 29.2708 | 0.5 |
|                  | Placebo receiver 46.4312 | 31.9452 |           |
| CRP (tenth day)  | Vitamin C receiver 29.1429 | 26.7491 | 0.63 |
|                  | Placebo receiver 24.8571 | 19.2181 |           |
| WBC (first day)  | Vitamin C receiver 8.3341 | 2.85633 | 0.57 |
|                  | Placebo receiver 7.7833 | 2.88245 |           |
| WBC (tenth day)  | Vitamin C receiver 7.0867 | 2.30799 | 0.92 |
|                  | Placebo receiver 7.1743 | 2.77657 |           |

Abbreviations
CAP: Community acquired pneumonia; PCT: Procalcitonin; WBC: white blood cell; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

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Authors’ contributions
All the authors participated in the study design. MN, MS and HRB collected and documented the data and assisted in preliminary data analysis. MHW and MN wrote the initial draft. HHK participated in draft revision, data analysis and editing of the final draft. All authors read and approved the final manuscript.

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The dataset used in this study is available with the authors and can be made available upon request.

Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments.

Consent for publication
Not applicable.

Competing interests
The authors declared that they have no competing interests.

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