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Original article

# PROCALCITONIN AS A NEW INFLAMMATORY MARKER IN ODONTOGENIC ABSCESSES OF HEAD AND NECK IN MALE POPULATION

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## ABSTRACT

**Introduction:** Procalcitonin (PCT) as a marker of inflammation has not been studied and analyzed in purulent inflammations of the head and neck of odontogenic origin, which is the aim of this original article.

**Materials and methods:** This retrospective study includes 31 men with odontogenic abscesses of the head and neck with a mean age of 42 years. As a control group, 31 healthy men are used. In all of them, leukocytes (WBC), neutrophils (Neu), C-reactive protein (CRP), and procalcitonin (PCT) are tested.

**Results:** The average values of the studied indicators in the patients are: CRP - 89.45±85.15 mg/l, WBC - 11.78±4.61x$10^3$/L, Neu - 8.79±4.58x$10^3$/L and PCT - 0.8±0.8 ng/ Jr. The average values of the same indicators in the control group are: CRP - 0.9±1.17 mg/l, WBC - 7.37±1.9x$10^3$/L, Neu - 4.13±1.43x$10^3$/L and PCT - 0.18±1.27 ng/ml. There is no positive correlation between PCT on the one hand and CRP, WBC and Neu on the other hand.

**Discussion:** The mean values of CRP, WBC, Neu and PCT are higher in men with odontogenic abscesses compared to the healthy controls, and this is statistically significant. Although PCT does not correspond to WBC, Neu and CRP, it has a number of advantages over them - it increases its concentration only in infections of bacterial origin, it increases its levels earlier and reaches its highest concentration earlier, it has a longer half-life, and its level declines more rapidly after infections.

**Conclusions:** All this suggests that PTC may soon become the most accurate marker in diagnosing, treating, and follow-up of patients with head and neck odontogenic abscesses.

**Keywords:** procalcitonin, inflammation, men, abscess, odontogenic, phlegmon, inflammatory marker, maxillofacial surgery,

## INTRODUCTION

According to data from our surgical medical practice, the most common emergency conditions in the head and neck area are inflammatory. Of these, the first in frequency are those where the cause of the inflammation is a diseased tooth, i.e. the so-called odontogenic inflammations. In them, the infectious agents, which in the case of abscesses and phlegmons are bacteria, enter the diseased tooth as the entrance door of the infection, most often through the root canals into the underlying bone of the upper or lower jaw. In the jaw, the bacteria spread initially in the subperiosteal space (subperiosteal abscess), then, lysing the periosteum, the purulent exudate passes between it and the mucosa of the jaw (submucosal abscess), and from there, along the path of least resistance, the pus passes into the adjacent soft tissue lodges (for example submandibular abscess in abscesses around the lower jaw or hard palate abscess in upper jaw abscesses) [1,2]. When two or more adjacent lodges are affected by the inflammation and the pus has spread over them, we speak of phlegmon [3]. The clinical picture in the latter is much more severe and varied, the course is longer, and the outcome of the disease, in many cases, is doubtful [4]. The more extensive the area and with more clinically severe symptoms of purulent inflammation, the more and longer the care for hospitalized patients is, and the treatment is more economically unprofitable [5]. This necessitates the use of such reliable and definitive diagnostic-therapeutic markers of inflammation as procalcitonin (PCT). Unfortunately, so far the latter has not been studied and analyzed in purulent inflammations of the head and neck of odontogenic origin, which is the purpose of the present original article. It compares it with already known and proven markers of inflammation such as C-reactive protein (CRP), leukocytes (WBC) and neutrophils (Neu) and discusses its advantages and disadvantages compared to them in the diagnostic-treatment process of sick men with odontogenic abscesses of the head and neck.

## MATERIALS AND METHODS

This retrospective study included 31 men with odontogenic abscesses of the head and neck who were hospitalized and operated on at the Clinic of Maxillofacial Surgery at the University General Hospital for active treatment "St. Marina" in the city of Varna, Bulgaria. Only men over the age of 18 with a history of a diseased tooth and a proven odontogenic abscess were included in the study. In all of them, the diagnosis was confirmed in three consecutive stages – first during the clinical examination by a maxillofacial surgeon, during which palpation data of a sharply painful infiltrate were established, then during the imaging study (ultrasound, nuclear magnetic resonance or computed tomography), in which the pus collection was seen, and finally during the operative treatment, in which a different amount of pus was evacuated. The mean age of the patients was 42 years, ranging between 18 and 79 years. The study did not include women, patients under the age of 18, patients with phlegmons and those in which there are reports of the presence of diseases and conditions in which it is possible to increase the level of PCT in the blood plasma and have false-increased results. Such diseases and conditions are cardiogenic shock, mycotic and parasitic infections, thyroid carcinoma, lung carcinoma, other neoplasias with paraneoplastic manifestations, taking drugs that stimulate the release of cytokines into the bloodstream, bronchial asthma, pneumonia and other diseases that lead to tissue hypoperfusion, pyrexia, burns, recent surgical manipulations and extensive trauma. The reason for excluding the patients with phlegmons of the head and neck of odontogenic origin is that the excessively high values of the investigated indicators of inflammation lead to excessively elevated average values of these indicators, which can lead to falsely very high values and disrupted data analysis. So, we prefer to let the group be more homogeneous. In all patients, preoperative venous blood was drawn for complete blood count, CRP, and PCT as a standard procedure.

As a control group, 31 healthy men, also with a mean age of 42 years, ranging between 19 and 81 years, who had venous blood drawn for complete blood count, CRP and PCT during preventive examinations in 2021 were retrospectively used. Inclusion criteria for the control group were that the men had no history of recent infection of any kind, were aged 18 years and over, and were male. Exclusion criteria are female gender, age under 18 years, and all the conditions and diseases described above that can lead to an increase in the blood concentration of PCT.

The blood of all patients with odontogenic abscesses and healthy male controls was processed at the Clinical Laboratory Clinic of the same hospital. PCT was investigated by latex-enhanced immunoturbidimetric analysis on a biochemical analyzer "ADVIA 1800" ("Siemens"); the reagent kit used was from "Diazyme Laboratories Inc.". CRP was examined on a biochemical analyzer, "COBAS 6000" ("Hoffmann la Roche"), using the immunoturbidimetric method with latex particles. Complete blood count, from which WBC and Neu's values were taken, was examined on an ADVIA 2120 (Siemens) hematology analyzer.

The information for all numerical values in this original article was processed on "Windows" 7.0 with the "SPSS" program. Data are presented as mean value ± standard deviation (SD). ANOVA analysis of variance was used to compare the differences in the four indicators studied, and Pearson's correlation analysis (r) was used to examine the relationship between them. The students' T-test was used to analyze the obtained numerical data. Those calculations where $p<0.05$ were considered significant.

## RESULTS

Table 1 shows the results of the investigated blood markers of inflammation in the studied 31 men with odontogenic abscesses of the head and neck, as well as their age.

**Table 1.** Values of CRP, WBC, Neu and PCT in the studied patients with odontogenic abscesses of the head and neck and their age

| Number by order | Age (years) | CRP (mg/l) | WBC ($x10^3$/L) | Neu ($x10^3$/L) | PCT (ng/ml) |
|---|---|---|---|---|---|
| 1 | 18 | 75.9 | 7.03 | 3.74 | 0.24 |
| 2 | 18 | 16.79 | 10.08 | 8.31 | 0.38 |
| 3 | 18 | 1.29 | 6.68 | 4.97 | 1.42 |
| 4 | 18 | 29.29 | 9.45 | 8.32 | 2.57 |
| 5 | 20 | 36.74 | 18.35 | 15.47 | 0.06 |
| 6 | 21 | 318.45 | 21.63 | 18.59 | 0.41 |
| 7 | 23 | 47.18 | 9.39 | 4.26 | 0.36 |
| 8 | 24 | 0.29 | 6.03 | 3.31 | 0.45 |
| 9 | 24 | 7.24 | 8.12 | 5.1 | 0.28 |
| 10 | 25 | 95.97 | 12.26 | 9.08 | 0.6 |
| 11 | 27 | 194.38 | 21.08 | 18.1 | 0.51 |
| 12 | 28 | 169 | 17.55 | 14.38 | 3.58 |
| 13 | 30 | 23.86 | 5.96 | 4.16 | 0.2 |

| | | | | | |
|---|---|---|---|---|---|
| 14 | 35 | 68.98 | 11.75 | 8.99 | 0.45 |
| 15 | 38 | 99.33 | 10.94 | 7.3 | 0.38 |
| 16 | 39 | 98.17 | 12.46 | 10.71 | 0.32 |
| 17 | 39 | 192.08 | 14.04 | 10.44 | 0.32 |
| 18 | 40 | 59.58 | 13.82 | 8.98 | 0.78 |
| 19 | 43 | 356.37 | 25.35 | 22.28 | 1.09 |
| 20 | 46 | 129.36 | 11.8 | 7.56 | 1.08 |
| 21 | 48 | 25.35 | 8.65 | 4.73 | 0.28 |
| 22 | 54 | 73.6 | 12.33 | 9.66 | 0.16 |
| 23 | 54 | 60.9 | 7.64 | 3.67 | 0.59 |
| 24 | 59 | 35.02 | 9 | 7.71 | 0.3 |
| 25 | 62 | 29.48 | 8.66 | 4.53 | 0.68 |
| 26 | 72 | 25.15 | 8.18 | 6.02 | 0.24 |
| 27 | 73 | 170.25 | 10.52 | 7.52 | 0.89 |
| 28 | 75 | 79.89 | 10.32 | 8.01 | 1.59 |
| 29 | 78 | 41 | 12.28 | 8.26 | 2.68 |
| 30 | 79 | 152.3 | 12.01 | 9.52 | 0.79 |
| 31 | 79 | 59.87 | 11.87 | 8.85 | 1.09 |

Table 2 shows the values of CRP, WBC, Neu and PCT in the healthy control men, as well as their ages.

**Table 2.** Values of CRP, WBC, Neu and PCT in the studied healthy men from the control group and their age.

| **Number by order** | **Age (years)** | **CRP (mg/l)** | **WBC (x10$^3$/L)** | **Neu (x10$^3$/L)** | **PCT (ng/ml)** |
|---|---|---|---|---|---|
| 1 | 19 | 0.2 | 8.2 | 4.2 | 0.1 |
| 2 | 24 | 0.3 | 7.72 | 3.86 | 0.2 |
| 3 | 26 | 0.5 | 4.87 | 2.49 | 0.22 |
| 4 | 26 | 0.2 | 6.1 | 3.62 | 0.06 |
| 5 | 27 | 2.5 | 8.28 | 4.74 | 0.38 |
| 6 | 27 | 3.1 | 9.36 | 4.73 | 0.42 |
| 7 | 29 | 0.2 | 10.23 | 6.07 | 0.08 |
| 8 | 31 | 0.2 | 5.62 | 3.2 | 0.05 |
| 9 | 32 | 0.5 | 12.51 | 8.21 | 0.12 |
| 10 | 32 | 4.1 | 5.07 | 2.93 | 0.42 |
| 11 | 35 | 0.4 | 5.13 | 2.8 | 0.1 |
| 12 | 37 | 0.5 | 8.12 | 4.4 | 0.2 |
| 13 | 37 | 0.3 | 9.41 | 4.68 | 0.11 |
| 14 | 38 | 0.8 | 7.4 | 3.53 | 0.11 |
| 15 | 40 | 1.9 | 6.43 | 2.84 | 0.39 |
| 16 | 41 | 2 | 7.44 | 4.04 | 0.33 |
| 17 | 42 | 0.9 | 7.37 | 4.13 | 0.17 |
| 18 | 42 | 0.2 | 10.54 | 6.81 | 0.01 |
| 19 | 44 | 0.7 | 4.9 | 2.9 | 0.19 |
| 20 | 45 | 0.4 | 10.07 | 7.92 | 0.18 |
| 21 | 46 | 0.3 | 7.5 | 3.5 | 0.14 |
| 22 | 47 | 0.7 | 8.45 | 4.34 | 0.07 |
| 23 | 49 | 0.4 | 8.52 | 4.57 | 0.11 |

| | | | | | |
|---|---|---|---|---|---|
| 24 | 51 | 0.3 | 6.46 | 3.04 | 0.06 |
| 25 | 53 | 0.2 | 7.4 | 4.2 | 0.06 |
| 26 | 53 | 0.3 | 6.71 | 3.8 | 0.06 |
| 27 | 55 | 0.2 | 6.4 | 3.9 | 0.15 |
| 28 | 65 | 4.8 | 6.16 | 4.54 | 0.63 |
| 29 | 65 | 0.2 | 6.38 | 3.04 | 0 |
| 30 | 67 | 0.2 | 4.04 | 1.72 | 0.07 |
| 31 | 81 | 0.5 | 5.56 | 3.2 | 0.3 |

Table 3 shows the mean, median, standard deviation, lowest measured value, and highest measured value of the studied CRP, WBC, Neu, and PCT in the studied men with odontogenic abscesses of the head and neck.

**Table 3.** Mean value, median, standard deviation, minimum value and maximum value of CRP, WBC, Neu and PCT in the studied group of men with odontogenic abscesses of head and neck

| Studied marker | Mean value | Median | Standard deviation | Minimum value | Maximum value |
|---|---|---|---|---|---|
| **CRP (mg/l)** | 89.45 | 60.9 | 85.15 | 0.29 | 356.37 |
| **WBC (x10$^3$/L)** | 11.78 | 10.94 | 4.61 | 5.96 | 25.35 |
| **Neu (x10$^3$/L)** | 8.79 | 8.26 | 4.58 | 3.31 | 22.28 |
| **PCT (ng/ml)** | 0.8 | 0.45 | 0.8 | 0.2 | 3.58 |

Table 4 shows the mean, median, standard deviation, lowest measured value, and highest measured value of the tested CRP, WBC, Neu and PCT in the tested healthy men from the control group.

**Table 4.** Mean value, median, standard deviation, minimum value and maximum value of CRP, WBC, Neu and PCT in the control group of healthy men

| Studied marker | Mean value | Median | Standard deviation | Minimum value | Maximum value |
|---|---|---|---|---|---|
| **CRP (mg/l)** | 0.9 | 0.4 | 1.17 | 0.2 | 4.8 |
| **WBC (x10$^3$/L)** | 7.37 | 7.4 | 1.9 | 12.51 | 4.04 |
| **Neu(x10$^3$/L)** | 4.13 | 3.9 | 1.43 | 8.21 | 1.72 |
| **PCT (ng/ml)** | 0.18 | 0.12 | 1.27 | 0 | 0.63 |

Reference values of CRP, WBC, Neu and PCT for men over 18 years of age are presented in Table 5.

**Table 5.** Reference values of CRP, WBC, Neu and PCT for men over 18 years of age

| Marker | Lower reference value | Upper reference value |
|---|---|---|
| **CRP (mg/l)** | 0 | 5 |
| **WBC (x10$^3$/L)** | 3.79 | 10.33 |
| **Neu (x10$^3$/L)** | 1.78 | 7 |
| **PCT (ng/ml)** | 0 | 0.5 |

Table 6 depicts the comparison of the numerical mean values of CRP, WBC, Neu and PCT between the studied male patients with odontogenic abscesses and the healthy male control group.

**Table 6.** Comparison of the studied group with odontogenic abscesses and the control group by numerical values of CRP, WBC, Neu and PCT

| | CRP (mg/l) | | WBC (x10$^3$/L) | | Neu (x10$^3$/L) | | PCT (ng/ml) | |
|---|---|---|---|---|---|---|---|---|
| | **Mean value** | **SD** | **Mean value** | **SD** | **Mean value** | **SD** | **Mean value** | **SD** |
| **Studied group** | 89.45 | 85.15 | 11.78 | 4.61 | 8.79 | 4.58 | 0.8 | 0.8 |
| **Control group** | 0.9 | 1.17 | 7.37 | 1.9 | 4.13 | 1.43 | 0.18 | 1.27 |
| **p-value** | p<0.0001 | | p<0.0001 | | p<0.0001 | | p<0.0001 | |

## DISCUSSION

PCT is proteinaceous in nature and is a precursor of calcitonin (CT) [6]. It was first described by Fernando Moya in 1975 [6]. In 1993, Assicot found that PCT increased its plasma concentration in patients with bacterial infections [7]. Since then, a number of studies have been carried out in which its blood concentration was investigated in many infectious diseases of bacterial origin such as sepsis and systemic inflammatory response syndrome (SIRS) [8,9], acute cardiovascular pathology [10], endocarditis [11], bacterial pneumonia and other acute respiratory infections [12], exacerbated chronic obstructive pulmonary disease (COPD) [13], exacerbated bronchial asthma [14], acute bacterial meningitis [15], acute appendicitis [16,17], acute necrosis of intestine [18], pyelonephritis [19] and acute and chronic hepatitis [20]. In all these diseases, the authors accept PCT reference values from 0.0 to 0.5 ng/ml.

In the absence of bacteria in the body, all the PCT that is produced by the parafollicular cells of the thyroid gland and the neuroendocrine cells of the intestines and lungs is converted to CT, and the plasma concentration of PCT in the body is 0.0 ng/ml. However, in the presence of a bacterial stimulus, these cells, as well as all parenchymal tissues and organs in the human body, such as adipocytes, kidneys, striated skeletal muscle and liver tissue, begin an enhanced synthesis of PCT and its plasma concentration rises [17].

It has been experimentally proven that PCT is synthesized only under bacterial stimulus, and viruses do not induce its synthesis [20]. There is evidence that its levels rise slightly in mycotic and parasitic infections, which is the reason why these are exclusion criteria in the present study [15].

When analyzing the data obtained from our study, it is found that the average measured values of the four investigated indicators (CRP, WBC, Neu and PCT) are within reference values in the control group of healthy men and are significantly higher than the upper reference limit in the studied men with odontogenic abscesses of the head and neck, and these differences were statistically significant (p<0.05) (Table 6).

Analyzing the four indicators in the study group and the control group, it was found that each one of them was significantly higher in sick men with odontogenic abscesses compared to healthy controls, and these differences were statistically significant (p<0.05). The mean measured value of CRP is almost one hundred times higher in men with odontogenic purulent infections compared to healthy controls (89.45±85.15 mg/l vs. 0.9±1.17 mg/l). The measured mean value of WBC is 1.6 times higher in the study group compared to the men of the control group (11.78±4.61x10$^3$/L vs. 7.37±1.9x10$^3$/L). The mean Neu value is more than twice as high in men with odontogenic abscesses compared to healthy control men (8.79±4.58x10$^3$/L vs. 4.13±1.43x10$^3$/L). The mean measured PCT value in men with odontogenic abscesses is 4.5 times higher than that in healthy controls (0.8±0.8 ng/ml vs. 0.18±1.27 ng/ml) (Table 6). Based on these numerical comparisons and the fact that they are statistically significant, we can conclude that PCT, as well as CRP, WBC and Neu, increases its numerical value in men with odontogenic abscesses of the head and neck.

The dependence of the relationship between the studied indicators and their influence on each other in the studied group of men was determined by correlation analysis using the Pearson method (r). The results show that a positive correlation only exists between the following parameters: extremely large between WBC and Neu (r=0.976; p<0.001) and significant between CRP and WBC (r=0.565; p<0.001) and between CRP and Neu (r =0.578; p<0.001). No correlations were found between PCT and the other investigated indicators (CRP, WBC and Neu), where p>0.05.

In addition, PCT has a number of advantages over the other three markers with which we compare it. WBC and Neu increase their concentration in the blood of infectious patients not only in bacterial infections but also in viral, mycotic and parasitic invasions [12]. PCT begins to increase its values in the blood plasma two to four hours after the presence of the bacterial microorganism in the human body and reaches a peak concentration between eight and twenty-four hours, while CRP begins to increase its blood levels 5-6 hours after the beginning of the bacterial action in the macroorganism and reaches its highest values between the thirty-sixth and fiftieth hour. On the other hand, the half-life of PCT is 24 hours, and that of CRP is 19 hours. Therefore, the plasma level of CRP declines more slowly than that of PCT when the infection resolves [13, 18].

All this gives reason to believe that PCT can not only be used in the diagnosis and treatment of inflammatory purulent infections of dental origin in men but also has a number of advantages over other proven markers of inflammation with which we compare it (WBC, Neu and CRP).

## CONCLUSION

Although PCT does not correlate with WBC, Neu and CRP, it emerges as an important indicator in the diagnosis and treatment of men with odontogenic abscesses of the head and neck because, like them, it increases its numerical values in patients with this pathology. Along with the advantages it has over other markers of inflammation in comparison, it is

emerging in the near future to be the most accurate test for monitoring the treatment and determining the prognosis of different inflammatory diseases. For the purpose of which it is necessary to carry out - in-depth research in this direction.

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