Association between the level of Bradykinin and viral infection in patient suffering from respiratory infection, renal transplant, and renal failure

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Abstract

**Background & Objectives:** The study was conducted to find out the relationship between viral infection and bradykinin level in sera of human suffering from virally infected, respiratory, renal transplant or renal failure diseases. Therefore, this study includes the evaluation of the immune status in the sera of patient suffering from renal failure, renal transplant and respiratory infected whose were virally infected with healthy subjects.

**Methods:** The immune response was evaluated by means of ELISA test for bradykinin level in the sera of 80 specimens included in this study: eight renal transplant, twenty renal failure, thirty-seven respiratory infected, and fifteen healthy subjects’ that were collected during the period extending from October 2018 to March 2019. Data about individuals were collected aseptically in sterile containers, after getting all data in special formula including, name, gender, age, disease.

**Results:** The results of the present study showed that there were very high significant difference of bradykinin level in sera of patients with a healthy group at p<0.05.

**Conclusions:** It could be concluded that Bradykinin secretion inhibited in viral diseases.

**Keywords:** bradykinin, viral infection, respiratory infection, renal transplant, renal failure

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**Introduction**

It is well documented that bradykinin is one of acute pain stimulator arising from tissue damage. There are two glycoprotein receptors mediate its direct effect, the first B1 related to injury or inflammation and second B2 constitutively expressed and secreted \textsuperscript{[1]}. A scientist suggested an essential role for B2 receptors in primary inflammatory processes of edema and acute inflammatory
pain, while B1 receptors appear to be involved in chronic responsive inflammatory conditions such as continual hyperalgesia. This give an indication B2 involved in normal conditions, whereas B1 attract researchers’ attention in altered function of visceral inflammation processes [2].

Bradykinin as a peptide originated from kininogens precursor through plasma or tissue peptides. It can be generated from tissue degradation and several chemical affects which results in the bradykinin expression on mucosal surfaces of various system. It has the ability to cause vasodilatation, leukocyte activation, and exudate accumulation from affected tissue due to its direct effect of acute or chronic inflammatory processes [3].

Acidification of the airways, allergen, inhalation of dry air as well as gram negative bacterial infection and viral infection initiate inflammation of lungs and airways results in filtration of polymorphnuclear cells with involvement of Kinins secretion [4-6]. As a result of this inflammatory processes and defense mechanisms bronchospasm, exudate accumulation and dilatation of micro blood capillaries of the airways, mucus secretion and evoke of plasma exudate after parental administration of bradykinin were noticed to be primarily mediated by activation B2 receptor [7]. The involvement of B1 receptor effect in respiratory disease was involved, but few effect or no relationships between B1 receptors and Bradykinin. Bradykinin are working under control of restriction of metabolizing enzymes, including angiotensin-converting enzyme, neutral endopeptidase as well as rapid desensitization of B2 receptors [8].

Bradykinin causes coughing when inhaled by humans [9]. This metabolizing enzymes as a peptide may also associate with cough when attach inhibitors of angiotensin-converting enzyme [10]. Cough induction by Bradykinin can likely be result from its direct effects on bronchial and pulmonary C fibers [13]. So that activation of B2 receptors indirectly, may contribute to cough initiation [12].

It is believed that bradykinin protecting kidney damage resultly from diabetes. Contradictory as it is believed to participate in development of Diabetic nephritis (DN). B2 receptor associated with the mediation of bradykinin physiological action, which considered to be renal protective [13,14]. Furthermore, increase bradykinin 1 receptor (B1R) in diabetic patients ended with increased inflammatory processes and bad prognosis of renal tissue [15,14].

So that family of bradykinin peptides can successfully be used as indicator biomarkers of DN, possibly through detection of early DN mediated by B2R and fibrosis as a final pathological inflammatory response in advanced disease mediated by B1R. Bradykinin has a shorter half-life in circulation, less than 30 Sec. [16] and quickly metabolized to smaller related peptides with various relationships to B1R and B2R [17,18]. The current study aimed to find the association of between bradykinin with viral infection and measurement of their level in sera of human suffering from respiratory, renal transplant or renal failure diseases.

Material and Methods

Study design and Subjects

This study, carried out in the department of Pathological Analysis Techniques in Al-Mustaqbal University College, during the period extended from October 2018 to March 2019. A total of 80 blood samples, eight renal transplants, twenty renal failure, thirty-seven respiratory infected, and fifteen healthy subjects’ blood samples (Merjan Medical City in Babylon and Al Karama Educational Hospital in Baghdad/ Iraqi) were collected aseptically in sterile containers, after getting all data in special formula including, name, gender, age and disease.

Ethical Approval

The agreements of all subjects’ intended in this study obtained before taking the study specimens. Furthermore, the study design was approved by the research Ethical committee at Pathological Analysis Techniques in Al-Mustaqbal University College.

Sera Sample Preparation and Preservation

After collection of Blood samples from subjects included in this study using a 5ml sterile syringe for each. Blood samples of renal transplant, renal failure, and respiratory infected as well as healthy individuals collected in sterile 10ml capacity plain tubes and labeled. After blood clot formation at room temperature within 30minutes, clotted blood sample centrifuged after detached of clotted boundaries using sterile wooden sticks or pasture pipette avoiding any hemolysis by gentle treatment. The samples were
spinning at 3000 r.p.m. for 10 minutes. Separated sera sample were collected and distributed in 0.5ml quantities in sterile containers, labeled and stored at -20°C until used.

Serological Assay

Bradykinin detected by Competitive ELISA Kit, (Elabscience Biotechnology Co., Ltd, Wuhan, and P.R.C.). Parameters measured according to instruction of the manufacturing company. HIV, Hepatitis B and Hepatitis C virus infection assessed by real time PCR technique, using SACACETM HCV/HBV/HIV REAL-TM KIT, (Italy). Polyomavirus BK virus was identified using BK virus Real Time PCR Kit, (cosmos biomedical comp.). Detection of infection with influenza virus carried by rapid device test (rapid test influenza A+B card, Cer Test Biotechnology SL. Spain). Only positive were included in this study as separated respiratory infected, renal failure and renal transplant subjects groups with viral infection.

Statistical Analysis

These data were done in the present study by using statistical package for social sciences version 18 (SPSS, IBM Company, Chicago, USA), in which the researcher used analysis of one sample test. Set P value $\geq 0.05$ as significant (95%).

Results and Discussion

Competitive ELISA results reveal that there was differences in bradykinin level among the four tested groups, the 8 renal transplants (BK virus), 37 respiratory infected (influenza virus) and 20 renal failure subjects (2 HCV infected and 18 HBV infected) in comparison with 15 healthy subjects (p <0.05). Whose gave decreased level of bradykinin, which were, 128.107 ± 21.805 ng/ml, 198.346 ± 18.186 ng/ml and 200.269 ± 33.078 ng/ml, respectively, while healthy group, revealed 21.857 ± 0.317 ng/ml.

Table 1: Level of bradykinin among sera of respiratory infected, renal transplant, and renal failure virally infected subjects groups in comparison with healthy group.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Respiratory Infected Subjects</th>
<th>Renal Transplant Subjects</th>
<th>Renal Failure Subjects</th>
<th>Healthy Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of virus</strong></td>
<td>Influenza virus</td>
<td>BK virus</td>
<td>HBV / HCV</td>
<td>Non virus detected</td>
</tr>
<tr>
<td><strong>Specimens No.</strong></td>
<td>37</td>
<td>8</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td><strong>Mean ± SD ng/ml</strong></td>
<td>198.346 ± 18.186</td>
<td>128.107 ± 21.805</td>
<td>200.269 ± 33.078</td>
<td>21.857 ± 0.317</td>
</tr>
<tr>
<td><strong>P. value</strong></td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The current study results showed a very high significant difference among the patient groups and health group, (P value $\leq 0.05$). Where it noted that renal failure and renal transplant in addition to the respiratory subjects whose were virally infected had decreased levels of the bradykinin compared to healthy group, this was controversial to expected results, as previous study revealed that bradykinin works as an inflammatory mediator $^{[2]}$.

Also, Blair $^{[19]}$ stated that bradykinin cause inflammatory cell influx to respiratory passages, This indicates that the viral infections led to the inhibition of inflammatory response, that is agreement with documentation of $^{[20]}$ who showed that the influenza virus affects the respiratory system lead to Inhibition of inflammatory response, The results of present study also consistence with $^{[21-23]}$ it
was stated that latent Herpes virus, BK virus and TT virus infections cause inhibition of inflammatory response for subjects suffering from renal transplantation or renal failure.

**Conclusion**

We can conclude that Bradykinin secretion inhibited in viral diseases. Therefore, we recommended that large scale study of different human viral diseases in correlation with anti inflammatory drugs, influenza virus, coronavirus, respiratory syncytial virus, human metapneumovirus, BK virus, HBV, HCV, TT virus as well as HIV.

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**Conflicts of interest**

None of the authors have any conflicts of interest relevant to this research subject.

**References**


