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Flight hormones as therapeutic target for novel Coronavirus infectious disease

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Abstract. – Coronavirus Disease 2019 (COVID-19) pandemic has made more awful effect on wellbeing and economy worldwide on an extraordinary scale. Angiotensin I Converting Enzyme 2 (ACE2), the principal receptor of SARS-CoV2, has been found to be communicated with Dopa decarboxylase in unwinding the connection of catecholamines with COVID-19 infection. Cardiovascular (CV) sickness, diabetes, hypertension, and related conditions cause significant risks during the current situation and the affected people are under basic observation around the world. The hypertension and diabetes are related with alterations in the degrees of catecholamines associated with renal gland. The naive form of renal dopaminergic framework is related with the expanded reabsorption of sodium resulting in downregulation of the ACE2 expression. Catecholamine biosynthesis is managed by counter-controlling angiotensin type 1R (AT1R) and angiotensin type 2R (AT2R), incitement of AT2 lessens catecholamine biosynthesis by means of a diminishing in cGMP levels likewise incitement of AT1 initiate catecholamine biosynthesis. This audit sums up the conceivable contribution of catecholamines in intense COVID-19 contamination and furthermore featured possible restorative adequacy of catecholamine flagging pathways against the incessant SARS-CoV-2.

Key Words:
Catecholamines, Angiotensin I converting enzyme 2, Dopa decarboxylase, Renin-angiotensin system hypertension.

Introduction

Ever since from December 2019, the novel coronavirus disease (COVID-19) causes severe pneumonia which has spread over the world, bringing the WHO pronouncing it as a pandemic disease. While the pandemic is developing its course, scientists are working to test the wide assortment of medicines for the worldwide spread and battle against SARS-CoV-2 virus. The infection spread all around with high proficiency; in any case, its most hazardous impact exceptionally jeopardizes the matured, particularly those with diabetes mellitus, hypertension, and coronary illness. One of the most tested issues incorporates the utilization of medications endorsed for co-morbidities, for example, hypertension and diabetes mellitus, in patients who show the most elevated hazard for confusions with COVID-19[1]. The diabetic hypertensive individuals have more elevated levels of dopamine and norepinephrine when compared to healthy one. Consequently, the prominence of diabetes was related with lesser level of catecholamines[2]. The raised renal cortical catecholamines bring about hypertension and an expanded renal oxidative pressure prompts nephropathy. In such manner we recommended that dysregulation of catecholaminergic neurotransmission has been related with most noteworthy danger of COVID-19 disease. This review adds superior comprehension to the bidirectional relationship between catecholamines with that of renin-angiotensin framework for the treatment of COVID-19.

Catecholamine Signaling and Metabolism

Catecholamines are tyrosine based product containing a catechol ring (orthodihydroxyben-

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zene) and are artificially blended through a progression of enzymatic responses, starting with the translation of tyrosine to dihydroxyphenylalanine (L-DOPA) by tyrosine hydroxylase (TH). Norepinephrine has been derived from Dopamine by Dopamine β-hydroxylase and, when required, epinephrine will be derived from norepinephrine with the help of phenylethanolamine-N-methyltransferase (PNMT). Adrenergic or dopamine receptor, a member of G-protein coupled receptor super family is considered to be a related receptor for catecholamines. Mostly, dopamine receptors are arranged by means of two subcategories, including α and β, and are furthermore partitioned into α1 and α2 receptors, and β1, β2, and β3 receptors. The receptors are profound to possess clearly defined pharmacological activity, with the α1 and α2-receptors coupled to Gαq and Gαi respectively and restrict the production of cAMP while the β-adrenergic receptors couple to Gαs implicit the cAMP creation. Further, reports also shown that in certain conditions, β2-receptors possibly would couple with Gαi control cAMP creation which possibly intrude with the impact of other β-adrenergic receptors[3].

Regulatory Effect of Catecholamines During COVID-19 Infection

The kidney renal dopaminergic system along with renal renin angiotensin system (RAS) regulates the sodium balance. Dopamine, a hormone produced principally by the renal tubules causing natriuresis by the stimulation of release of renin release and also involves in inhibition of tubuloglomerular feedback[4]. The communication among the dopaminergic system along with renin-angiotensin system controls the sodium reabsorption in the renal system thereby regulating hypertension. Catecholamine signalling system plays a key role in counter-regulating these system through two major subtypes including Ang II receptor, angiotensin type 1 R (AT1) and angiotensin type 2R (AT2). The provocation of AT2 decreases catecholamine synthesis by means of reducing cGMP levels while the prompt of AT1 stimulation result in catecholamine biosynthesis by the activation of PKC. Consequently, the production of catecholamine in adrenal chromaffin cells has been associated with AT1 and AT2[5]. The Ang II synthesis is downregulated in higher concentration of salt conditions while intra renal dopamine fabrication is becoming higher likewise[6].

Based on the multi experiment matrix (MEM), there is an involvement of gene in significant coexpression link with ACE2 in the production of angiotensin and also the in the synthesis of serotonin and dopamine *via* DDC. In disparity with the presence of such link, a report has been shown that infusion of angiotensin in the hypothalamus of rat has been linked with increase in brain dopamine. With this manner, angiotensin was revealed to stimulate dopamine synthesis in renal gland[7]. Recent studies recommended that dopaminergic system will prompt AT2 receptor activation and also decrease the ROS which has been involved in additional therapeutic tactics. Further the signaling pathway followed by dopamine receptor family has been noted to retain normal blood pressure at least in part by delaying the activity of RAS along with ROS production still it has been regarded as a complex and interconnected network.

Viral Therapeutic Targets

While patients with COVID-19 may experience the ill effects of focal autonomic disappointment of respiratory capacities, it is essential to remember that ACE2 and DDC may coexpress and co-control in non-neuronal cell types. To be sure, in the middle of microarray datasets aggregated in MEM, the greatest noteworthy connection among DDC mRNA level and ACE2 is established while investigating colorectal adenocarcinoma tests. Affirming the perception, an overview of database "Human Protein Atlas" the present biggest protein expression chart book of ordinary human tissues, determined that ACE2 and DDC were profoundly communicated with intestinal epithelial cells, since the epithelial intestinal cells were responsible for the changeover of L-DOPA into dopamine.

Low sodium status furthermore makes renal relationship all through COVID-19 infection progressively likely on account of upregulation of film bound ACE2 in the kidney. Verbalization levels of ACE2 have been connected with shortcoming to SARS-CoV and SARS-CoV-2 pollution in different cell lines. In any case, when the coronavirus spike protein binds to ACE2, there is a downregulation of ACE2 which prompts an extraordinary assortment of angiotensin II and diminishing in angiotensin 1-7 (vasodilator, threatening to proliferative and cytoprotective). In specific, the endotoxin induced murine model of animal shows high lung injury while

the dopamine D1 receptor agonist fenoldopam was seemed to tubular aggravation similarly by means of lung vulnerability along with respiratory edema. Apart from this, association of exogenous catecholamines into the distal airspaces could emphasize alveolar fluid breathing space in the human lung, an effect that is intermediate somewhat by cystic fibrosis transmembrane conductance controller. Thus, exogenous β-agonists will probably be required to revive the objectives of alveolar edema in the lungs of patients with aspiratory edema. This is a key request, since the degree of endogenous induction of alveolar fluid opportunity by catecholamines in patients with aspiratory edema will choose whether there can be an additional remedial effect of catecholamines.

Conclusions

The possible defensive job of catecholamines with regards to SARS-CoV2 diseases has been ineffectively researched as of not long ago. Further, works regarding the connections between ACE2 receptors and catecholamines may be carried out in experimental way to manage the SARS-CoV2 infection in an effective manner. Also, in patients experiencing serious types of COVID19, the cateholamine manufactured pathway ought to be investigated in future examinations.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Mehra M and Ruschitzka F. COVID-19 illness and heart failure a missing link?. JACC Heart Fail 2020; 6: 512-514.
2) Watson AMD, Gould EAM, Penfold SA, Lambert GW, Pratama PR, Dai A, Gray SP, Head GA and Jandeleit-Dahm KA. Diabetes and hypertension differentially affect renal catecholamines and renal reactive oxygen species. Front Physiol 2019; 10:309.
3) Nolan R and Gaskill PJ. The role of catecholamines in HIV neuropathogenesis. Brain Res 2019; 1702: 54-73.
4) Armando I, Villar VA and Jose PA. Dopamine and renal function and blood pressure regulation. Compr Physiol 2011; 1: 1075-1117.
5) Takekoshi K, Ishii K, Shibuya S, Kawakami Y, Isobe K and Nakai T. Angiotensin II Type 2 receptor counter-regulates type 1receptor in catecholamine synthesis in cultured porcine adrenal medullary chromaffin cells. Hypertension 2002; 39: 142-148.
6) Felder RA and Jose PA. Mechanisms of disease: the role of GRK4 in the etiology of essential hypertension and salt sensitivity. Nat Clin Pract Nephrol 2006; 2: 637-650.
7) Serge N. An alteration of the dopamine synthetic pathway is possibly involved in the pathophysiology of COVID-19. J Med Virol 2020; 92: 1743-1744.