Review Article

SARS-CoV-2 Interaction and Role of Angiotensin 2 on Oral Wounds - A Questionable Role on Oral Ulcerative Conditions (Wound Aggravation vs Wound Healing)

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ABSTRACT

The alarming spread of novel corona virus, severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), has resulted to an ongoing pandemic of corona virus disease 2019 (covid-19). Angiotensin-converting enzyme 2 (ACE 2) has been shown to be a functioning receptor for SARS-CoV-2 to gain entry into host target cells. Orally, ACE-2 expression is found in epithelial cells. Both ACE-2 and covid-19 has an unclear pathway in pathogenesis and healing of oral ulcers and wounds. Our paper aims at the specific interactions between ACE -2 and covid-19 and their power play in viral diseases and wounds that affect orally.

Keywords: COVID-19, oral ulcer, oral wound, ACE2

Introduction

COVID - 19 (NOVEL CORONA VIRUS) disease 2019 proved itself clearly by spreading at an alarming rate since 2019 December across the world. It has been already known that SARS-COV-2 has a special affinity towards binding with human receptor ACE - 2 (ANGIOTENSIN CONVERTING ENZYME -2).[1] The spike (s) glycoprotein of N-COV - 2019 binds to ACE -2. ACE - 2 is elaborately searched in the world literature and is expressed in different bodily tissues of upper and lowers respiratory tract, myocardium and G-1 mucosa l[2]

In case of oral cavity studies that the expression of ACE-2 in oral cavity has also been explored and it is found that it was highly enriched in the epithelial cells. ACE-2 expression was found to be higher in tongue that buccal mucosa. Oral manifestations have been observed in COVID - 19 patients but were still in a deep question as to say was it a primary presentation of the disease or a

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Received: 11 January 2021
Revised: 05 April 2021
Accepted: 07 April 2021
Published online: 15 April 2021
Citation: Banerjee A, Elangovan E, Sengupta A, Rajguru JP. SARS-CoV-2 interaction and role of angiotensin 2 on oral wounds- a questionable role on oral ulcerative conditions (wound aggravation Vs wound healing). J West Bengal Univ Health Sci. 2021; 1(4):49-52.

secondary manifestation. The presentation in the oral cavity can be in the form of ulcers or geographic tongue.

There are viral diseases which affect the oral cavity either directly or secondarily manifestations of systemic disorders.[3,4]

ACE-2 expressing cells should be considered as potential factor for 2019-N-COVID. ARB s (ANGIOTENSIN RECEPTOR blocker) have similar effects to that of ACE inhibitor, preventing formation of angiotensin - 2, whereas ARB s acts by blocking the binding site of angiotensin. Hence the activity of angiotensin 2 can be modified and hence also acts promising in preventing SARS - COV 2 infections (Figure 1)

There is a report which has come up with recurrent oral ulcers which could be an initial presentation of N-Covid 19.

SARS - COV 2 gain entry through ACE -2 and subsequently down regulates its activity and hence causes organ injury and the accumulated angiotensin - 2 is the main factor for that injury. It leads to facilitation of neutrophil infiltration in response to bacterial endotoxin.[5]

RAAS inhibitors or recombinant ACE-2 normalizes angiotensin-2. Tissue regeneration and normal healing are important aspects of tissue homeostasis. These are impaired by various systemic factors like diabetes, dysfunctional blood vessels etc. There are literature which states that blocking angiotensin -2 can facilitate tissue regeneration in diabetic mice.[6] Tissue homeostasis has three major aspects that is vascular response, decreased pathogenic invasion and tissue remodeling. There are various factors that determine ulceration and wound healing mainly by

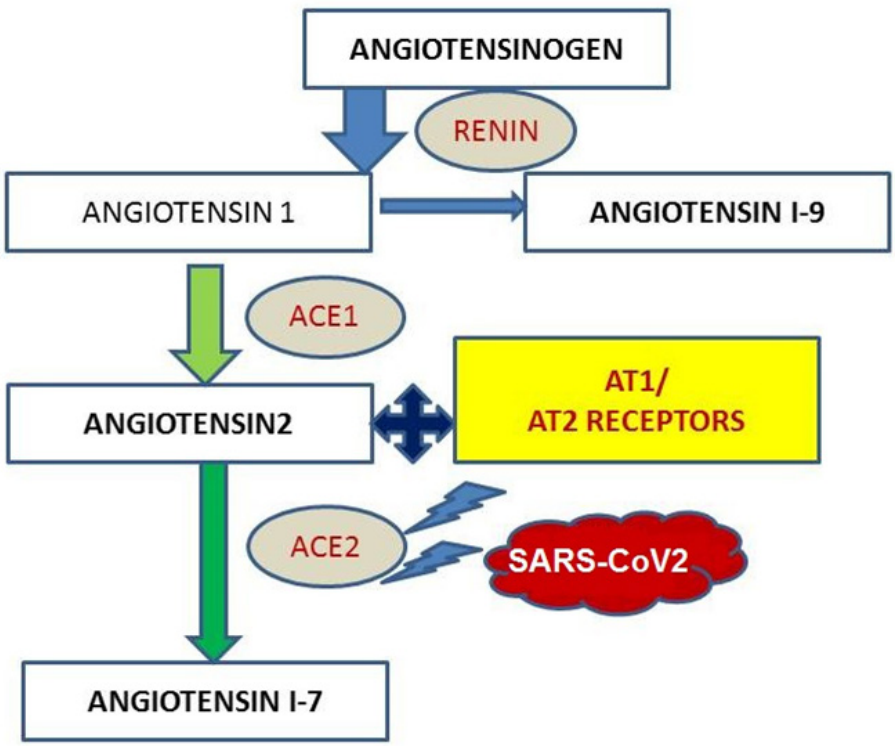

Figure 1: Normal pathway of RAAS and COVID-19 interaction. (AT1- angiotensin 2 type 1 receptor, AT2- angiotensin2 type 2 receptor; ACE- Angiotensin converting enzyme)

expression of various growth factors like EGF, FGF, and VEGF etc. Angiotensin - 2 inhibitions facilitates epidermal wound regeneration in diabetic mice whereas the study done by Takeda H et al shows those angiotensin-2 AT1 blockers suppresses the re-epithelisation of keratinocytes and myofibroblasts recovery.[7]

Renin angiotensin system (RAAS) play a pivotal role in that angiotensin - 2 the biological key component of this system plays an important role.

Angiotensin -2 works by the help of two receptors that is AT1 and AT2. Both the receptors expression was found higher in the initial 7 days of epithelisation of wound (healing) which gradually decreased. This shows that this takes part in wound healing and remodeling.[1,3]

Oral mucosal healing versus aggravation of ulcerative condition

The COVID-19 affected patients are reported to present with oral ulcerations or oral sores occasionally. These ulcerations may or may not be viral manifestations. Stress could be an important factor too in these cases. Numerous patients are admitted to the hospital care with COVID-19 is suffering with co-morbidities

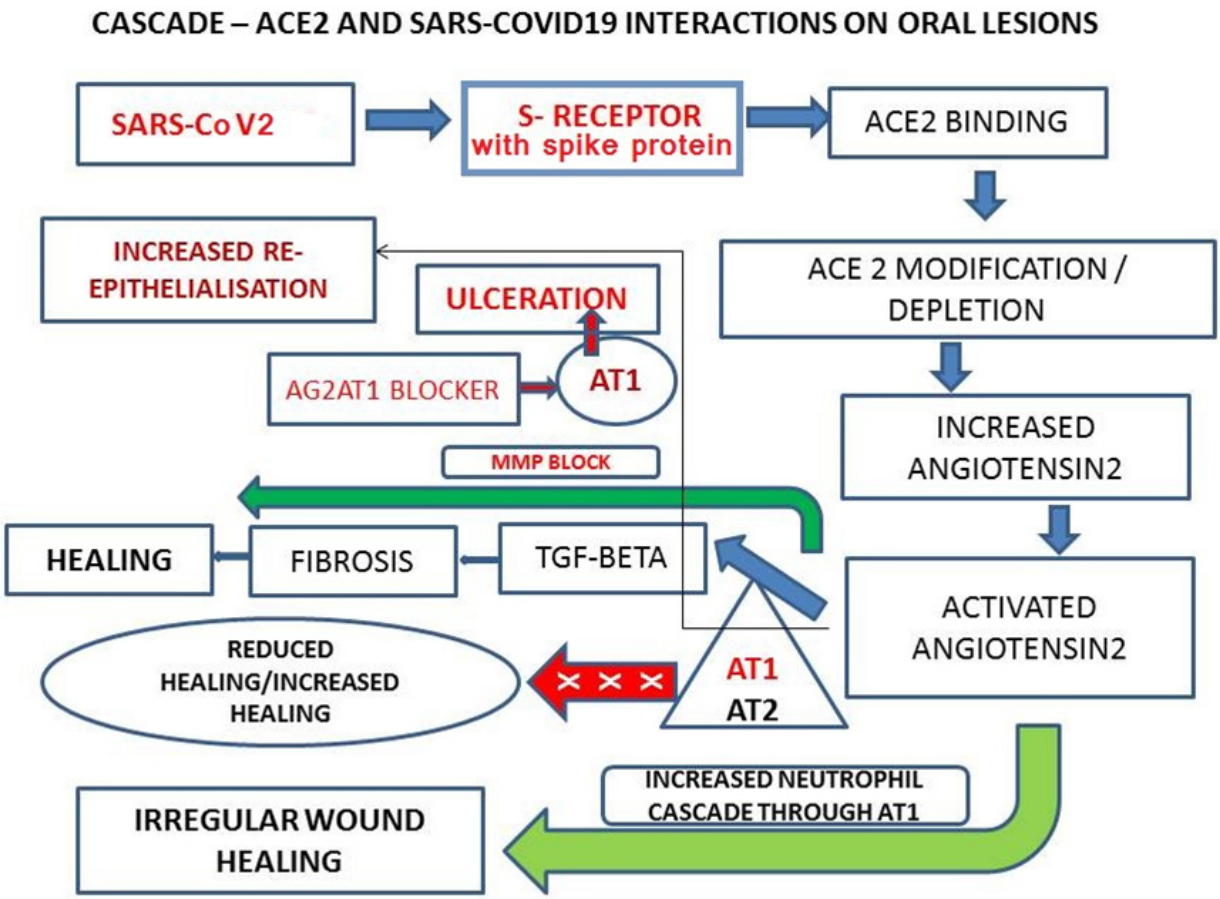

Figure 2: Dual or questionable role of angiotensin 2 and SARS-COV 2 interaction in oral wound aggravation and healing. (AT1- angiotensin 2 type 1 receptor, AT2- angiotensin2 type 2 receptor; ACE- Angiotensin converting enzyme; s- spike protein receptor)

like diabetes, autoimmune disorders, psychological stress etc. On gaining access through ACE2 receptors, the virus enters into the body system and goes through a well designated pathway which is still under debate. Ongoing through numerous published researches on ACE2, angiotensin 2 and its role in tissue homeostasis and wound healing its clearly understood that the mechanisms are very complicated and still under research. ACE2 functions are impaired once viral interaction starts and it has a drastic effect on angiotensin 2(Ag2). There are possibilities that either there is an increase amount of Ag2 failing to be converted to Ag1 which leads to tissue injury by disturbed TGF-beta pathway or there can be an inhibition in the expression of matrix mettaloprotienases and can lead to healing of oral ulcers by fibrosis. (Figure 2)

Our commentary is mainly to evaluate that COVID - 19 infections do play a role in oral mucosal healing or does it aggravate the ulcerative conditions with an active role of ACE2.

Conclusion

The pathways of oral wound formation and wound healing are still a matter need to be looked upon by elaborately studying various signaling pathways. COVID-19 and Ag2 do have a significant role in healing mechanisms of oral wounds considering various other factors like age, systemic conditions and immune status of the patient.

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