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Short Commentary

Anosmia in COVID-19: Celecoxib Appears to Speed Recovery

Kevin M Tomera* and Joseph K Kittah

Pulmonary and Critical Care Medicine, Beloit Memorial Hospital, 1905 E Huebbe Parkway, Beloit Wisconsin 53511, USA

Abstract

Abrupt loss of smell (anosmia) is recognized as one of the frequent hallmarks of Covid-19. While it usually recovers within weeks, it may not. Both the SARS-CoV-2 spike protein and nucleocapsid N protein upregulate COX-2. Patients suffering COVID-19 disease often present with markedly elevated levels of Prostaglandin E2 (PGE2). Rapid return of smell in 2-5 days was observed after increasing the dose of celecoxib to 400mg oral twice daily (BID) with high dose famotidine 80mg four times a day (QID) as adjuvant therapy for COVID-19. Magnetic resonance imaging- MRI have shown changes in the olfactory bulbs in patients with anosmia. Consistent with local inflammation, only minor changes in inflammatory markers were sometimes noted when tested. Adjuvant therapy with high dose celecoxib and high dose famotidine appears to be promising and should be studied for this disturbing symptom of Covid-19 and other CNS COVID-19 sequalae.

Keywords: Anosmia; Antihistamine; Celecoxib; Covid-19; Cyclooxygenase inhibitors; Famotidine

Background

Reduction of smell is recognized as one the cardinal symptoms of Covid-19 [1]. Unfortunately, while in most cases return of smell occurs as rapidly as the loss of smell in several weeks too frequently anosmia persists for even months [2].

Both the SARS-CoV-2 spike protein and nucleocapsid N protein upregulate COX-2 [3-5]. Patients suffering COVID-19 disease often present with markedly elevated levels of Prostaglandin E2 (PGE2). A prospective study of adjuvant therapy with celecoxib has moderated covid-19 PGE-2 levels, prevented clinical deterioration and has had rapid improvement in CT-chest [6]. A retrospective study showed adjuvant therapy with celecoxib significantly improved IL-6 serum levels and appeared to improve outcomes [7]. An inclusive consecutive case series of adjuvant therapy with celecoxib in hospitalized patients showed significant clinical responses [8]. Increasing the celecoxib dose to 400mg bid oral appeared to improve clinical response [9].

Clinical Report

Three patients with anosmia and positive PCR tests, one inpatient and two outpatients, given celecoxib 400mg bid oral and famotidine 80mg qid reported recovery of smell in two, three and five days. The inflammatory markers were minimally elevated with baseline biomarkers in the patient tested having a normal d-dimer, ferritin, lactate dehydrogenase, interleukin 6, neutrophil count, lymphocyte count, neutrophil lymphocyte ratio, comprehensive metabolic panel with only a slightly elevated C-reactive protein of 1.6 (normal <0.5pg/ml) and reduced total WBC of 2.4 (normal low 4.1 x 10^3/microliter to normal high 10.4 x10^3/microliter).

Discussion

The minimal change in biomarkers measured in the patient presenting with anosmia suggest that anosmia is a local inflammation not requiring major systemic dysregulation. This appears to be supported by Magnetic Resonance Imaging (MRI) at presentation of COVID-19 patients with anosmia showed transient olfactory bulb edema [10]. Celecoxib has previously been shown to suppress experimental encephalomyelitis through prostaglandin and non-COX-2 pathways [11-13].

However, while celecoxib is hydrophobic and crosses the blood brain barrier it appears to require larger doses explaining why patients at celecoxib 200mg oral bid did not report rapid return of smell [14]. Fortunately, high dose celecoxib, 400mg oral bid for up to six months has been shown to be as safe as low dose celecoxib 100 mg oral bid and as safe as placebo [15]. Adjuvant therapy with celecoxib 400mg oral bid appears safe and promises to mitigate a bothersome symptom of COVID-19 -anosmia and deserves more investigation for not only anosmia but other CNS related COVID-19 sequalae.

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Conflict of interests

None

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***Corresponding author:** Kevin M Tomera, Pulmonary and Critical Care Medicine, Beloit Memorial Hospital, 1905 E Huebbe Parkway, Beloit Wisconsin 53511, USA, E-mail: ktomeramd@gmail.com

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