Category :**Respiratory: ARDS**

A252 - ***A novel definition and treatment of hyperinflammation in covid-19 based on purinergic signalling***

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Introduction:

Hyperinflammation plays an important role in severe COVID-19. Using inconsistent criteria, researchers define hyperinflammation as a form of very severe inflammation with cytokine storm. Our paper gives a novel definition. Subsequently, we describe the treatment of ICU-patients with COVID-19 requiring ECMO and/or mechanical ventilation.

Methods:

We searched scientific articles on P2X7 purinergic receptors (P2X7Rs) to underpin our definition of hyperinflammation. We found that lidocaine can block P2X7Rs. The issue is that the half-maximal effective concentration of lidocaine for P2X7R inhibition is much higher than the maximal tolerable plasma concentration. To overcome this, we selectively inhibit the P2X7Rs of the cells of the lymph nodes. We do this by subdermal infusion of lidocaine HCL inducing clonal expansion of Tregs in local lymph nodes. Secondarily, these Tregs migrate throughout the body suppressing systemic hyperinflammation (figure). We treated six COVID-19 ICU-patients with subdermal lidocaine infusion (1 mg/kg/hr).

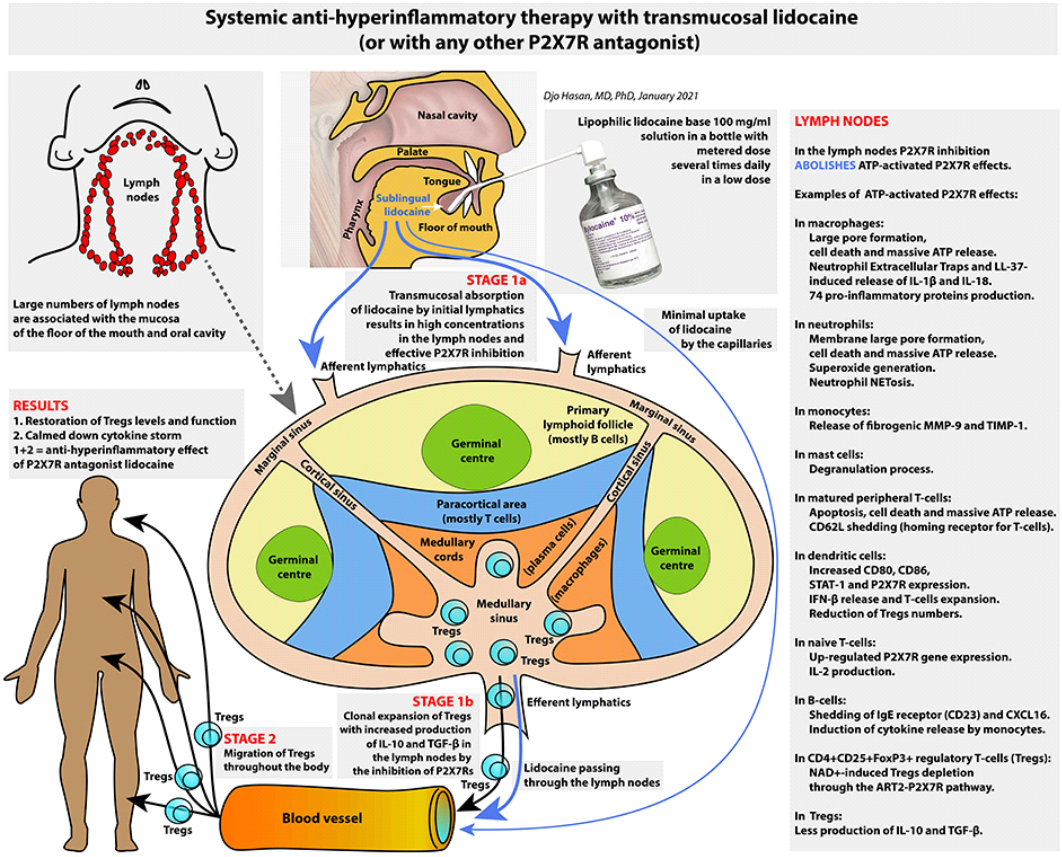
Results:

We found 437 articles to underpin our definition of hyperinflammation. The essence is that hyperinflammation is initiated when SARS-CoV-2 infection causes prolonged and vigorous activation of the P2X7Rs of the immune cells. This leads to cytokine storm and desensitisation of purinergic receptors of immune cells other than the P2X7Rs, resulting in immune paralysis with secondary infections. The six ICU-patients with COVID-19 we treated with lidocaine all recovered completely.

Conclusion:

Applying consistent criteria, we defined hyperinflammation as prolonged and vigorous activation of P2X7Rs of the immune cells and established that selective inhibition of these receptors can calm down cytokine storm in COVID-19. Our experience with subdermal administration of lidocaine in the ICU made clear that this method may not be suitable outside hospitals. Therefore, we developed a novel oral transmucosal administration route using Xylocaine 10% spray, as shown in the figure.

Image :



A graphical summary of the future development of the administration of lipophilic lidocaine base in the sublingual region or elsewhere in the oral cavity. We postulate that selective inhibition of the P2X7Rs of the immune cells of the lymphatic system by lidocaine suppresses hyperinflammation in two stages. Stage 1: The selective inhibition of the P2X7Rs of the immune cells residing in the lymph nodes (stage 1a) induces clonal expansion of Tregs with improved function in these lymph nodes (stage 1b); Stage 2: Subsequently, these Tregs migrate throughout the body exerting anti-inflammatory activities reducing systemic and (distant) local hyperinflammation. Source: Hasan D, et al. (2021) doi:10.1007/s11302-021-09814-6, with permission.