



## COVID-19-related acro-ischemia and topical calcium channel blockers: A useful therapeutic adjunct

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### Abstract

It is gradually now clear that one of the mainstays of COVID-19 infection lethality is represented by disseminated intravascular coagulation and venous thromboembolism, eventually leading to multiple pulmonary embolisms with subsequent profound hypoxia and respiratory failure in the adult patient.

In this article we discuss if the severity of lesions in the critically affected adults is due to the combined effect of both a generalized coagulation disorder and a peripheral vasoconstriction, mainly due to the profound hemodynamic derangement and the effect of inotropic and vasoactive drugs used in the intensive care setting.

**Keywords:** COVID-19, acroischemia, calcium channel blockers, nifedipine

### Introduction

Since December 2019, the new coronavirus disease-2019 (COVID-19) pandemic started in Wuhan, Hubei, China has posed serious and substantial threats to national healthcare systems all over the world. COVID-19 pandemic has been officially declared “a public health emergency of international concern” on 30 January 2020 by the World Health Organization (WHO) [1].

While research all over the world is striving to assess efficacy of the currently used drugs –as well as testing new molecules- against this infection [2, 3], a parallel scientific effort is being deployed in describing the clinical picture of the disease, with many case series from many countries [4, 6]. From a clinical point of view, it is gradually becoming clear that one of the mainstays of COVID-19 infection lethality is represented by disseminated intravascular coagulation and venous thromboembolism [7] eventually leading to multiple pulmonary embolisms with subsequent profound hypoxia and respiratory failure in the adult patient [8].

One of the most striking and clinically evident manifestation so far reported of this thrombotic diathesis is the occurrence of acral ischemia (or acro-ischemia) in affected patients; it presents particularly at fingers and toes with cyanosis, chilblain-like lesions, skin bulla and, eventually, dry necrosis of the part. This clinical manifestation has been documented both in adult [9] and pediatric patients, although for the latter –despite multiple reports in local pediatric and dermatologic networks- no published literature to date exists in support.

According to currently available knowledge, presentation of acro-ischemic lesions in the pediatric age is usually milder, and spontaneous recovery of the affected limbs usually occurs in two weeks; on the contrary, adult reports are much more concerning, and often the severity of the lesions poses a threat for the vitality of affected limbs [9].

It is reasonable to hypothesize that the severity of lesions in the critically affected adult is due to the combined effect of both a generalized coagulation disorder and a peripheral vasoconstriction, mainly due to the profound hemodynamic

derangement and the effect of inotropic and vasoactive drugs used in the intensive care setting.

Capillary (particularly, arteriolar) vasospasm is also implied in the reversible ischemia typical of the Raynaud phenomenon. In this clinical context, calcium channel blockers such as nifedipine are commonly used to relieve symptoms and to reduce the recurrence and severity of attacks, particularly when an actual danger of tissue injury exists [10].

Interestingly, to avoid systemic collateral effects, topical nifedipine-based ointments have been recently developed [11]. These topical nifedipine formulations -combined to appropriate systemic treatment aiming to correct disseminated intravascular coagulation- [7] might prove useful also in COVID-19 patients exhibiting acro-ischemia, in order to counterbalance acral capillary vasoconstriction with on-site pharmacological action, avoiding systemic damage to the already impaired hemodynamics of the critically ill patient.

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