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RESEARCH ARTICLES

DOXYCYCLINE – ONLY AN ANTIBIOTIC?

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ABSTRACT

Doxycycline is a synthetic antibiotic of the Tetracycline family with probably the highest number of non-antibiotic properties. Clinically developed in the early 1960s, it was approved by the FDA in 1967 (1). As an antibiotic, its use in the treatment of bacterial pneumonia, acne, chlamydial infections, Lyme disease, cholera, typhus and syphilis is already well established. However, its use in the treatment of other infectious and non-infectious conditions is not very well known. It is amazing to realize that this rather conventional and simple salt is equipped with such a wide plethora of actions. In this review, we attempt to address the non-antibiotic properties of Doxycycline in a serial manner.

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INTRODUCTION

Antimalarial: Doxycycline is a partially efficacious causal prophylactic drug and a slow acting blood schizontocidal agent which is highly effective for the prevention of malaria. When used in conjunction with a fast acting schizontocidal agent, it is also highly effective for malaria treatment. It also finds use as prophylactic agent in areas with chloroquine and multidrug-resistant Plasmodium falciparum malaria. (2), (3)

Antihelminthic: Doxycycline reduces the transmission of diseases such as onchocerciasis and elephantiasis by killing the symbiotic bacteria, Wolbachia, in the reproductive tracts of parasitic filarial nematodes, rendering the nematodes sterile. In 2005, field trials demonstrated an almost complete elimination of the release of microfilariae by an eight-week course of doxycycline (4).

Anti-allergic: Allergic rhinitis and asthma are allergic disorders which result partly due to allergen-specific IgE binding to its receptors on the surfaces of mast cells and basophils (5).

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There are no current allergy/asthma therapies that inhibit IgE production. It has been demonstrated in numerous studies that Doxycycline leads to reduction in the IgE levels in vitro as well as in vivo. Raised IgE levels are frequently encountered in atopic diseases such as allergic asthma. The only currently available treatment approved specifically for allergic asthma is omalizumab, an anti-IgE monoclonal antibody injected once or twice per month. It is a useful adjunct for allergic asthma as it binds to pre-formed IgE. However, omalizumab is an expensive treatment that is not easily obtainable for many patients. (6). Doxycycline has been shown to modulate and reduce the secretion of IgE by the cells, a quality which has not been seen till now with any group of drugs. Doxycycline suppressed the C. pneumoniae-induced production of IgE and IL-4, but not IFN-γ, in PBMCs from IgE+ allergic asthmatic subjects. These findings resulted from the immunomodulatory anti-allergic properties of tetracyclines (7).

Anti-asthmatic: Its efficacy against Chlamydia Pneumoniae and Mycoplasma Pneumoniae gives it an edge over others as chronic infection with these atypical organisms is implicated in a significant subset of patients with asthma exacerbations. It has been observed by Clinicians that treatment with Doxycycline gives benefits to patients in terms of less dyspnoea and reduced severity of the overall disease. Toluene Diisocynate (TDI) is a leading cause of Occupational Asthma

in which inflammatory disease of the airways characterized by airway remodeling caused, at least in part, by an excess of extracellular matrix deposition in the airway wall. Matrix metalloproteinases (MMPs) are major proteolytic enzymes that are involved in extracellular matrix turnover because of their ability to cleave all proteins constituting extracellular matrix. have reported that MMP-9 might play a role in chronic airway. Doxycycline with its significant MMP inhibiting properties showed a significant improvement in TDI induced Asthma. (8).

Anti-rheumatic: Doxycycline is a safe Disease modifying anti-rheumatoid drug (DMARD) in Rheumatoid Arthritis whose effect is sustained at six months. It compared favorably with methotrexate over a six month follow up (9).

Anti-fibrotic: The potential role of a class of zinc-requiring endopeptidases called matrix metalloproteinases (MMPs) in the pathogenesis of IPF has attracted attention (10). The role of doxycycline as an inhibitor MMPs showed significant improvement in a small case series of IPF patients in terms of change in 6 Minute Walk Test, Saint George Respiratory Questionnaire (SGRQ), Forced Vital Capacity (FVC) and quality of life (11).

In Sarcoidosis: These results support that minocycline and doxycycline may be beneficial for the treatment of cutaneous sarcoidosis (12). CS using clarithromycin (200-400 mg/day) and doxycycline hydrochloride (100-200 mg/day) has shown a good safety profile in these patients. Thus, clarithromycin (400 mg/day) and doxycycline hydrochloride (100 mg/day) administered in this trial may be an appropriate dose for the treatment of CS. (13)

As Renal protective: Doxycycline ameliorated CDDP-induced AKI through its pleiotropic effects. Our results suggest that Dox may become a novel strategy for the prevention of CDDP-induced AKI in humans. (14)

Anti-Cancer: In regional lymph node and distant organ metastasis of oral squamous-cell carcinoma (OSCC), Doxycycline was found to be associated with decreased invasion of oral SCC in vitro. Moreover, Doxycycline exerted a significant suppressive effect on tumor growth in an in vivo nude mice model. Taken together, these results, to our knowledge, may imply that Doxycycline has an adjuvant therapeutic effect on OSCC that is associated with inhibition of MMPs expression (15).

Miscellaneous: Pyoderma gangrenosum is a rare, noninfectious neutrophilic dermatosis characterized by long standing ulcers in which Doxycycline may be useful (16). Pemphigus vulgaris (PV) is an acquired autoimmune bullous disease with notable morbidity and mortality if not treated appropriately due to loss of epidermal barrier function and subsequent infection and loss of body fluids. (17).

It seems a little unfortunate that this salt with protean qualities remains mostly underrated and underutilized. It can be concluded with the axiom that Old is Gold. The New era has ushered the concept of repurposing of old drugs for novel actions in newer diseases. However, it will require a lot of randomized trials before the supposed valuable properties of this old salt with be established as its true virtues.

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