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Editorial

Pharmacology: Clinical Applications and Therapeutics

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It gives me a great pleasure, to write this editorial to the journal of Acta Scientific; Pharmacology (AS Pharmacology). Editorials by nature, are opinion articles expressing a point of view. In this day and age of Personalized or Precision Medicine, definitions and boundaries of various medical specialties are fast disappearing. Pharmacology as we knew, when we studied several decades ago, was the branch of medicine concerned with the uses, effects, and modes of action of drugs. Wikipedia describes pharmacology, as the branch of pharmaceutical sciences, which is concerned with the study of drug or medication action, where a drug can be broadly or narrowly defined as any man made, natural or endogenous molecule, which exerts a biochemical or physiological effect on the cell, tissue, organ or organism. With ever increasing global burden of metabolic diseases such as hypertension, excess weight, obesity, diabetes, and vascular diseases, individuals are under multiple drug regimen. In view of this fact, pharmacology should be considered as how the drug (s) affect a biological system, and how the body responds to the drug (s). In view of this observations, a pharmacology journal should welcome articles in the emerging areas of translational, predictive and personalized medicine; new therapeutic modalities including topics such as gene expressions, role of microRNAs(miRNAs), cellular and molecular therapies, pharmacogenomics, proteomics, metabolomics, microbiomes, bioinformation and applied systems biology and other complementing areas. In addition, it should be noted, that risk of drug-drug interactions increases exponentially with the number of drugs given to a patient. An updated database system on drug interactions, monitored by a pharmacist in hospitals as well as at pharmacies worldwide, could ensure rational, safe drug therapy, and prevent the occurrence of serious and clinically significant adverse events [1].

At the University of Minnesota, when we were working on isolation and characterization of prostanoids (Eicosanoids), using sheep seminal vesicular gland enzymes, we found active metabolites of arachidonic acid (AA), that aggregated platelets and induced secretion of granule contents [2]. Later we discovered, that these active lipid molecules were prostaglandin (PG) endoperoxides PGG2 and PGH2, - transient metabolites of substrate arachidonic acid. Platelet cyclooxygenase (COX-1) converts AA to transient metabolites, -endoperoxides, which are further converted to thromboxanes, by thromboxane synthetase. All these three metabolites of AA are potent platelet agonists. Aspirin irreversibly inhibits COX-1 enzymes by acetylating the serine residue on the enzyme. When we were working on the mechanism of action of Aspirin like drugs, we discovered that Ibuprofen (Motrin, Advil), a non-steroidal anti-inflammatory (NSAID) drug, also inhibits COX-1 enzymes, but its action on the enzyme was reversible and short acting. Furthermore, to our surprise, we found that it bocks the action of Aspirin, if taken before aspirin ingestion [3]. Although we described our findings in the early 80s, these findings did not reach public attention till FitzGerald's group from University of Pennsylvania published their findings in the New England Journal of Medicine [4].

Since we are discussing about Ibuprofen, it is important to discuss some recent findings about drug interactions that may result in more harm than benefit. As I write this editorial, there is a global public health and economic crisis shaping up, with the introduction of COVID-19 virus (unprecedented pandemic). At the time of this writing, this novel viral disease has swept into at least 114 countries, according to World Health Organization (WHO). As the infection is followed by dry cough and high fever, those affected usually reach out for Ibuprofen (Nurofen, Motrin or Advil) to combat the fever and pain. Just 17 hours ago (March 18, 2020), WHO officially announced to avoid taking Ibuprofen if you are suspected of COVID-19 infection. Ibuprofen and similar acting drugs are well-established medicine that have been used safely, as self-care fever and pain reducers, including in viral illness, for more than 30 years. However, the health minister of France, Oliver Veran, has issued a blunt warning about painkillers taken by people ill with the coronavirus: "Stay away from drugs like ibuprofen and aspirin." Aspirin an irreversible inhibitor of COX-1 enzymes, acetylates COX-2 enzymes

and switches its catalytic activity for conversion of AA to 15R-HETE in lieu of prostanoids. The third major pathway of AA metabolism involves aspirin mediated activation of COX-2 and Lipoxygenases [5]. As to how these products of AA metabolism, increase the risk of coronavirus infections is not well understood at this time.

Dr Veran's warning was followed by a letter published in the Lancet, by the researchers, Fang and associates from University of Hospital, Basel, Switzerland and Aristotle University of Thessaloniki, Greece, which suggested increased risk for COVID-19 infection in patients with hypertension and diabetes [6]. According to their findings, human pathogenic coronaviruses bind to their target cells through angiotensin-converting enzyme 2 (ACE2), which is expressed by epithelial cells of the lung, intestine, kidney and blood vessels. The expression of ACE2 seems to be substantially high in patients with diabetes, who are treated with ACE inhibitors and angiotensin 11 type-1 receptor blockers. These findings if found true, could lead to further conflict in disease management, as ACE2 reduce inflammation had has been suggested as a potential new therapy for inflammatory lung diseases, cancer, diabetes, and hypertension.

To add to this confusion, Director (Dr Michele Barry) of the Center for Innovation in Global Health at Stanford University says that there is no reason to think that infected patients should avoid temporary use of Ibuprofen. Whereas, Dr Garret FitzGerald, Chair of the Department of Pharmacology at the Perlman School of Medicine at the University of Pennsylvania says, "It's all anecdote, and fake news of the anecdotes". Well this is the 'World We Are Living In". or to put it the other way, - this is the price we pay for Globalization.

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