Knowing the differences in the class effect of pharmacologic agents will improve our individualized medical prescription

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For more than 3 decades ago there has been an increasing interest and utilization of the phrase "class effect" given to a group of drug agents that somehow share similar pharmacologic and therapeutic effects sharing some pharmacodynamics characteristics. There has been a tendency to express this "class effect" with anti-arrhythmic agents, angiotensin converter enzyme (ACE) inhibitors, beta-blocker agents, anti-dyslipidemic drugs, and the list goes on. Although, there is no accepted definition of the term "class effect" in the literature, it is widely used [1,2]. This tendency to call "class effect" happens with practically every group of drug agents when most of the times the only similarity they share is to be in the same class group.

The relatively similar results of some randomized clinical studies on ACE inhibitors done in the 80s lead to the intuitive generalization of their clinical effects facilitating the superfluous assumption that all ACE inhibitors share the "class effect" that makes them identical [3-5]. However, studies performed in the new millennium era have shown the differences between drug agents that belong to the same class group. The pharmacological agents are typically grouped based on one common mechanism of action. The different drugs of a class group are often divided into subclasses based on the chemical structure. It is also interesting to note that all drugs usually have multiple mechanisms of action determined by their unique chemical structure. The scientific knowledge about these drugs have proved variations in the half-life, in the liposoluble properties, the route of metabolism and elimination, serum and tissue levels, the dose-response relation, and the route of administration for a better therapeutic effectiveness. When it is considered the marked differences in the chemical structure among the different drugs of a same group, it is not surprising that they may have different clinical actions and outcomes. Indeed, the pharmacodynamic differences determine the different results obtained on later studies performed with ACE inhibitors [6-8]. Those ACE inhibitors with longer half-life and better tissue penetration had more significant reduction in clinical events. For example, it was surprising to learn about the adverse effects, negative results and increased mortality with intravenous enalapril in patients with myocardial infarction in the CONSENSUS II trial [9]. Specially, after knowing about the beneficial effects of oral enalapril utilized in the CONSENSUS I trial [3]. The adverse events probably occur due to the pro-ischemic effects of the secondary hypotension with the intravenous administration of enalapril. Evidently, if the same drug with a comparable dose utilized for the same disease but with a different route of administration can generate surprisingly different results, how much more different would be the use of two drugs that share the same class group. The scenario

turns even more confusing when we learn the results of the SAVE trial showing that an ACE inhibitor significantly reduces ischemic events [10]. Later on, it is demonstrated a variety of their positive effects on the vascular endothelium and mediator substances of inflammation [10-13]. In this context, it is well known that some patients may present torsade des points after the intravenous administration of amiodarone, while they did not have any pro-arrhythmia on long-term oral amiodarone [14-16]. This fact underlines the different results with different routes of administration of the same drug.

Other clinical studies have shown beneficial effects of the ACE inhibitors on sudden cardiac death, and on atrial fibrillation, while others demonstrated a deleterious effect [17-20]. The mechanisms responsible for these diverse actions are produced by the various tissular effects of the drug on the vascular endothelium in individual subjects. Therefore, while the ACE inhibitors can share a hemodynamic effect and a similar clinical outcome in heart failure patients, the tissular effect of the drug varies considerably [13].

Are we prescribing the correct drug to the adequate patient according to medicine based evidence? Sometimes, industrial marketing and several other factors may exert certain pressure on the clinician to utilize a cheaper agent, or to employ a lower dose than the one that was shown to be effective in the clinical trials. It is highly prudent to assume that untested drug agents of a certain class are not interchangeable for a specific indication until there is enough scientific clinical evidence. A drug agent that has not been tested in clinical trials with long-term follow-up lacks the appropriate long-term safety. This is a very important matter since a number of individual pharmacological agents of established drug classes have been found to cause major complications and deleterious effects leading to drug withdrawal after FDA approval and post-marketing of the drug. Large-scale, randomized clinical trials with long-term follow-up can provide the necessary tools to properly evaluate long-term safety and for determining adequate data for risk-benefit ratios. We should be prescribing the specific pharmacological

agent utilized in the randomized clinical trial at the same dose and for the same illness of the specified population in order to obtain similar beneficial results as the clinical study. Two drug agents of the same class group should not be considered to have similar therapeutic effects until this similarity is proved in a head-to-head comparison in large scale, controlled, double blind, and randomized clinical trials with long-term follow-up.

Therefore, all pharmacologic agents of the same class group are not the same, and the medicine based evidence supports in favor of a detailed and meticulous analysis of the concept of "class effect". It is surprising that the discovery of the vast complexity and enormous differences of the pharmacologic agents of the same class group could not eradicate the concept of "class effect" ingrained in physicians. The complete understanding of the explosive scientific, social and medical evolution, besides, the recognition of the proper correction of wrong medical concepts should modify the point of view of the physician about the conception of the "class effect" of drug agents. This is with the sole intention of dissipating and eliminating this vague concept from the minds of physicians.

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