**Primum Non Nocere: In Search for Its Origin**

The so-called Hippocratic injunction to do no harm has been a traditional philosophy in clinical pharmacology and medical education. Many authors believe incorrectly that the author of this aphorism was Hippocrates. Most physicians have a false notion that it was there in the Hippocratic Oath. Recent scholars have established that the Latin expression was not specifically used by the legendary Greek physician Hippocrates, and it was not in the Hippocratic writings collected in the Middle Ages. The origin of the phrase remains debated and different scholars attributed it to different legendary physicians, including Galen, Ambroise Paré, Thomas Inman, and Oliver Wendell Holmes.[1]

**Primum Non Nocere: But How?**

It is true that every weapon in the physician’s armamentarium is double edged. As physicians, we need to understand that we are not immune to harming. We, as today’s physicians, also need to allow our patients to know why and how it is never possible to “first, do no harm.” Every drug, every medical intervention has a potentiality to cause adverse effect, and in the realms of statistics, all that doctors do is basically calculating the risk–benefit ratio. Yet, paradoxically, this noble intention may become the nemesis of many patients and this principle of *Primum Non Nocere* may be defeated. While cutaneous adverse drug reactions (CADRs) are possibly as old as medicine itself, with changing time and advent of newer drugs, the study of CADR is becoming more challenging.[2]

**Definition**

An ADR has been defined as “a response to a drug that is noxious and unintended and which occurs in doses normally used for the treatment, prophylaxis, or diagnosis of disease, or the modification of physiological function.” The definition excludes poisoning and unintended but beneficial effects.[3] The European Union definition encompasses harm from off-label use, overdose, misuse, abuse, and medication errors. Hence, any harm from a medicine, particularly if serious or unusual, should be reported.[4] Serious, here, means fatal and life-threatening diseases and diseases causing or prolonging a stay in hospital.

However, more often than not, possibility of ADRs is clinically challenging, as there are many other differentials. Roujeau’s criteria attempted to simplify defining cutaneous ADRs, (a) other causes for the eruption, such as viral exanthema, should be excluded, (b) a temporal relationship between the drug and onset of rash should exist, (c) improvement should be noted following drug cessation, (d) reactivation upon challenge should be noted, and (e) cutaneous reaction is known to be associated with the drug.[5]

The term, severe cutaneous adverse reaction (SCAR), was proposed for such conditions, as they were (a) severe, (b) unpredictable, and (c) drug induced. SCARs encompass a heterogeneous group of delayed hypersensitivity reactions, which are most frequently caused by drugs.[6] The designation SCAR most commonly includes Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), SJS/TEN overlap, drug reaction with eosinophilia and systemic symptoms/drug-induced hypersensitivity syndrome, and acute generalized exanthematous pustulosis.[7]

**Epidemiology of Severe Cutaneous Adverse Reaction**

Adverse drug reactions are responsible for up to 7% of hospital admissions.[8] Up to 30–45% of the ADRs are skin related, 2% of which may be severe and may have mortality rate as high as 10–30%.[9] More than 200 drugs have been implicated in the literature that can cause SCARs. Causality of the ADR can be measured using the WHO-UMC causality assessment system, which grades the assessment across a spectrum from “certain” to “unlikely” to “unclassified.”[10]

Advent of newer drug, newer modality of drug delivery, and polypharmacy are throwing newer challenges in the field of CADRs. Continuous learning and careful vigilance can lead to early diagnosis and avoidance of considerable mortality and morbidity.

**Symposium Philosophy**

SCAR can be a life-threatening disease and one of the important fields in hospital-based dermatology practice. Knowledge has evolved on the immunopathogenesis of SCARs by which drugs activate T cells. In vivo and ex vivo diagnostics are being increasingly employed to aid causality assessment. Knowledge of cross-reactivity between structurally related medications is still rudimentary but may avoid precipitating subsequent severe episodes and minimize unwarranted restriction of therapeutic options. Newer pharmacogenomic discoveries associating severe T-cell-mediated drug hypersensitivity syndromes have created the hope of prevention.

Improved understanding has also led to considerable new hope in the management of SCAR. However, for the
treating physicians, this era is particularly challenging to stay in touch with the latest developments. This symposium targets to make a comprehensive compendium of the latest developments in the field of the SCAR.

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