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Perspective

Underlying Pharmacology of Adverse Effects of Medicines

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Abstract

Pleitropism underlies the biological adverse effects induced by medicines. Drugs and vaccines are two different types of medicinal compounds which hit biological targets to produce desired beneficial effects. However, the targets may be expressed at multiple sites and therefore partly underlie some adverse effect. Vaccines, primarily designed to target immune system B lymphocytes, are a combination of several immunogens as well as non-immunogenic booster molecules, each of which harbours the potential to produce distinct biological effects by gaining access to different and multiple targets *in vivo*, therefore compounding the adverse effects.

Keywords: Drugs; Vaccines; Adverse effects; Pleitropism

Introduction

Human Immunodeficiency Virus/HIV surfaced on science radar in the eighties decade and exploded on social scene [1]. HIV prostrated humanity as an uncontrollable Acquired Immunodeficiency Syndrome/AIDS epidemic engulfed populations across the globe. The rapidity with which HIV spiralled across the globe remains a perplexing issue particularly because AIDS is neither air nor water borne but rather spreads through blood products/sex. Scientists have not yet found an ideal approach to stem AIDS rampage although biochemical strategies using anti-retroviral drugs/ARVs form the basis of AIDS retroviral therapy/ART, currently in practice to limit viral replication *in vivo* [2]. More recently, scientists have discovered that cows have evolved a robust immune system which can generate large amounts of broad spectrum bioneutralizing antibodies/bNAbs, effective against survival of several HIV strains [3]. The worth of this novel strategy as AIDS preventing vaccine will become clear when clinical trials have been accomplished.

The immunization approach involving injection of vaccines directly into the blood is a great gift of translational medicine to humanity albeit it's become a prickly issue lately [4]. Adverse effects experienced by some vaccinated individuals have spawned the vaccine adverse events reporting system/VAERS [5,6]. Vaccines basically introduce antigenic molecules directly into the blood stream, designed to raise a humoral immune response from the antibody producing B lymphocytes [7]. Inherent in this approach is the risk of introducing cross species transfer of host infectious agents which have the potential to communicate host disease agents, along with other chemical components added to boost the immune response [8]. These biomeds/vaccines suffer from the same drawbacks as other drugs, primary drawback of both being pleitropic effects [9].

Perspective

Probable causes of adverse effects of medicines involve pleiotropism. Pleitropic effects occur owing to the fact that a drug molecule can gain access to a target expressed in multiple sites *in vivo* [10]. Whereas a drug is a single molecule, a vaccine is a mixture of several molecular components. Therefore the risk of adverse biological effects is enhanced several fold [11,12]. Dosage is the second issue common to both types of meds, another potential cause of adverse effects. Dosage is an issue because all recipients receive the same dose of a these meds while some patients could be sensitive to higher doses. However, whereas adverse effects caution is mentioned on the brochures of drugs, this convention is not followed for vaccines. Third issue common to both types of meds is genetic sensitivity. Most doctors try to ascertain before prescribing a drug whether a patient suffers from sensitivity to any drugs. But this convention is again not observed during immunizations. Fourth issue pertains to duration of treatment/exposure to both types of medicines. Whereas drugs are prescribed for a limited period of infection, vaccines are delivered as preventive meds against infections acting *in vivo* over longer periods. Fifth issue pertains to timing of exposure. Age is relevant issue while prescribing meds. Whereas separate formulations of drugs are prescribed for adults or children most vaccines are delivered to babies during developmental years, age at which potential for adverse effects is enhanced [13]. Lastly, and most importantly, while the drugs have to undergo stringent toxicology testing before getting clearance for use in human beings, vaccines appear not to follow the clearance protocol applied to other drugs. Had the same stringent checking been applied to vaccines, VAERS would never have emerged as a serious issue with legal implications. In case of vaccines, which are a mixture of several chemical components, there is more to adverse effects/VAERS than pleiotropism. Vaccinations would be fraught with the risk of inflammations and a host immune response involving elaboration of a glut of inflammatory cytokines or hypercytokinemia [14-17].

Adverse biological effects have a biochemical basis. Cells are equipped with 'eyes' to perceive chemicals/infectious agents in the form of receptor proteins and enzymatic proteins. Such *in vivo* proteins are referred to as targets for extraneous chemicals. The cellular targets may not be very unique and may be expressed in multiple tissues. The targets proteins are mediating various functions. Drugs introduced *in vivo* can have access to all these targets. Concentration of these drug molecules *in vivo* depend upon the dose

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and duration of exposure. Adverse effects are produced when targets expressed in several tissues are gradually accessed by drugs as a result of higher concentrations produced over time, disrupting biological functions of the accessed targets. Vaccines are biomeds, a different category of 'drugs' in the sense that not only do these contain multiple components, each of which can access a target in multiple sites, but also produce vaccinogens that eventually 'target' B lymphocytes of the host immune system. Vaccines carry infectious agents that first infect host cells and then get processed in infected cells to generate novel immunogenic subunit peptide fragments, eventually displayed on their surface. The immunogenic peptides of exogenous origin would then induce the secretion of antibodies, binding or neutralizing, from the B lymphocytes which would either bind to or neutralize the infectious agents/immunogen-flagged infected cells [18]. Whereas this antibody induction strategy is mimicking the response of the host immune system to natural infections, the non-immunogenic chemical components of the vaccines, which are most certainly not a part of the former, access multiple targets in various tissues, especially in a developing stage, and produce adverse effects associated with vaccines/VAERS. Apart from this, even the exogenous immunogenic peptide fragments produced through vaccination maybe a part of the adverse effects too owing to the fact that the antibodies so generated could cross the tissue barriers, notably the developing brain and target some native functional proteins, exposed during development when the blood tissue barriers are still developing, leading to autoimmune diseases. Whether Autism can be considered to be autoimmune VAERS remains a moot point.

Implications

The protocols for testing the toxicology of vaccines should be made as stringent as that of other drugs intended for human use in order to minimize VAERS. Age at which vaccinations are started should be taken into consideration. In particular, the developmental phase of the nervous system should be avoided in order to prevent potential long term harmful effects. It would be an inherently better strategy to develop bioneutralizing vaccines [19-22] which could be administered, if necessary, at a later age rather than mandatory preventive vaccine shots at a vulnerable age.

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