

## Useful Side Effects of Some Medicines

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### Editorial

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### Editorial

Man has suffered from diseases of all kinds since the beginning of human life several millennia or centuries ago. Uncountable illnesses, both those that science can easily explain and those that to date are inexplicable, have affected, killed and weakened many from antiquity till now. In man's attempt to be productive and avoid morbidity, numerous products and substances have been used to mitigate, treat or cure diseases. Additionally, other substances that promote good health and well-being have been used and continue to be used by man in order to help avoid or prevent some sicknesses. The products or substances that have been used for diagnosis, management, treatment and prevention of diseases are termed medicines or drugs. These terms (medicine and drugs) are mostly used interchangeably, except that medicine can also refer to a practice – the practice of healing.

Just as there are numerous diseases so are numerous medicinal products or drugs used in their management and/or treatment. Many methods of classification of drugs are used; some are based on the chemical nature of the active ingredient(s) and others, how the drugs are used to treat specific disease conditions. Common groups of drugs include analgesics for relief pain; antimicrobials used to treat infections; anti-hypertensives and anti-diabetics for management of hypertension and diabetes respectively. There are also the stimulants and the depressants.

Drugs do not always give only the useful effects they are expected to render. Their administration sometimes come with side effects, adverse drug event (ADE), or adverse drug reaction (ADR). The World Health Organization (WHO) defines ADE as "any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this

treatment". It also defines ADR as "a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function" [1].

For most drugs, the side effects are minor, causing just a little inconvenience such as little nausea or mild gastrointestinal disturbances, normally for oral medications; or slight skin irritation for topical products. Additionally, for most drugs, with proper dosing there will not be any noticeable side effect. There is also a section of the population who may be allergic to some drugs that majority of users tolerate without problems. Such allergic reactions may differ from individual to individual; ranging from itching and general rashes to a more serious condition like anaphylactic shock. Unwanted effects of drugs can result from the administered drug alone, or concomitant administration with other products such as other drugs, herbal products, food supplements or food itself. Specific drugs may have unique side effects and adverse effects, and in fact some drugs present serious ADRs which may include death, congenital deformities, permanent damage to organs of the body and other complex complications [2]. For example, the corticosteroids such as dexamethasone and prednisolone normally used to treat or manage allergic reactions, some inflammatory conditions and some types of cancers, can have serious adverse effects when used at high doses or for a prolonged period of time. Such effects include high sugar levels in the blood which can worsen diabetes, fluid and some salts retention leading to swelling [3]. Use of most chemotherapeutic agents, such as methotrexate, in management of different types of cancers are also associated with severe side effects such as bone-marrow suppression,

loss of hair (alopecia), foetal death and congenital deformities and tumour lysis syndrome [4].

More often than not drug regulatory bodies in various countries, such as the Food and Drugs Administration (FDA) in the United States of America, ensure that drugs that come into the market have the claimed therapeutic activities and additionally are deemed safe. This is achieved through the extensive and detailed clinical trials before release of the drug to the market. However, not all side effects, and even sometimes the indications of the drug, are known during clinical trials. Most regulatory agencies and other bodies encourage post-marketing surveillance programmes on drugs in order for healthcare professionals and individuals to report any adverse or side effects of the drug. From 2011 to mid-2017, the FDA received more than 5.4 million reports of prescription drug adverse events, including more than 1 million deaths [5].

Interestingly, not all *side* effects of drugs are unwelcome; some are useful and in fact in some cases that effect takes over the actual indication(s) of the drugs in some areas or localities and among some people. A typical example of a drug whose other effect is now being used extensively is Tramadol. Tramadol is an opiate analgesic used in management of moderate to moderately severe pains. It is a synthetic analogue of neither codeine that binds to opiate receptors and inhibits nor epinephrine and serotonin reuptake [6]. The BNF reports malaise as a common side effect of Tramadol, with diarrhoea, flatulence, gastritis as uncommon side effects; it further reports that rarely the drug can cause hypertension, anorexia, anxiety, abnormal coordination, bronchospasm and seizures [4]. However, recent use of Tramadol among many young men in some countries is its ability to prevent premature ejaculation; a situation where a male ejaculates with a minimal sexual arousal before or shortly after vaginal penetration, typically lasting less than 2 minutes. Here the person discharges the semen before he wishes to do so. The use of Tramadol to prolong ejaculation has been corroborated by many studies, that the drug has impressive results in delaying ejaculation [7,8]. The mechanism by which Tramadol delays ejaculation is not fully elucidated.

Another drug whose other effects are more widely used perhaps than the main indication is cyproheptadine. Cyproheptadine is an antihistamine drug used in management of histamine-associated symptoms such as runny nose, watery eyes, pruritis, etc. It mainly works by antagonizing the activities of histamine on HA-receptors, thereby causing a reduction in undesirable indications brought about by the histamine HA-receptor binding. This drug has an additional effect of being able to stimulate appetite, and

this use supersedes its anti-allergic activities, at least in Africa. In Ghana for example, there are many brands of cyproheptadine-containing preparations that serve as appetite stimulating haematinics; haematinic because in most cases other minerals and vitamins that enhance erythropoiesis (blood formation) have been incorporated. These over-the-counter appetite stimulating products are highly patronised in the market.

Metformin, a biguanide, is principally an anti-hyperglycemic agent that improves glucose intolerance in patients with Type II Diabetes, where it lowers both basal and postprandial plasma glucose concentrations. One use of metformin, though unlicensed for that purpose according to the BNF (4), is its use in treatment of polycystic ovary syndrome (PCOS). PCOS is a condition which embraces a broad spectrum of signs and symptoms of ovary dysfunction with fundamental features of hyperandrogenism and polycystic ovary morphology [9]. Metformin has become a therapy for PCOS which results in weight reduction, improvement in insulin resistance, restoration of normal ovulatory cycles, increase in fertility, decrease in hyperandrogenism, decrease in the rate of spontaneous abortions and decrease in the risk of gestational diabetes mellitus [10].

In research and development of drugs a product developed for a particular indication sometimes end up being used for a totally different condition. An example of such drug is minoxidil which is used to stimulate hair growth and slow balding. This drug was originally launched in 1979 for treatment of hypertension. Currently there are many over-the-counter topical preparations containing minoxidil for treatment of baldness. Another example drug whose initial indication changed is Sildenafil (Viagra). Viagra was designed for treatment of angina, but was not very successful for that purpose during trials. However, many male users reported dramatic improvement in penile erection during the clinical trials. Today Sildenafil is an enormous hit in the management of erectile dysfunction, and in fact that is the current indication.

Drugs are very useful products that have saved humanity from premature death and weakness in several ways. Whilst they sometimes come with unwanted effects which in fact in most cases are transient, there are instances they offer additional useful effect which are unreported. And this is where individuals experiencing any off-label effect, being it positive or negative, is encouraged to report to designated agencies for proper investigation. Indeed through such reports and investigations there may be some other serendipitous discoveries from existing drugs.

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