

Pharmacovigilance Consider as a Leader for Drug Design

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Abstract

Pharmacovigilance tell us the side effects of the drugs after introduce to the market and used by patients, hence some drugs e.g., thalidomide when used to treat the emesis in pregnant women appear the phocomelia which characterized by abnormal development of limbs where the long bones (like: humerus - femur) or either shortened or absent causing the hands and feet to be attached close to the body, this is due to isomer of thalidomide (S) which is teratogenic but the (R) is a sedative and more safe due to the pharmacovigilance of thalidomide so that the pharmacovigilance led us to use (R) isomer but not (S) isomer in medicine.

Captopril appears to cause cough in patients when used as an antihypertensive drug, due to the SH group of captopril. Hence, captopril was modified to enalapril to avoid the cough symptom that appears when using captopril.

Cimetidine is H₂ antagonist, the first H₂ antagonist modified from histamine to used treatment peptic ulcer, the pharmacovigilance tell us with side effects of cimetidine, the major of them decrease the blood cell counts especially WBCs (agranulocytosis), so the cimetidine modified to synthesis of famotidine which is less side effect than cimetidine.

Keywords: pharmacovigilance, thalidomide, ACE inhibitor, H₂ antagonists, isomers, stereochemistry

1. Introduction

The pharmacovigilance is the science and activities focus on detecting, assessing, understanding and preventing adverse effects or other medicine related problems associated with pharmaceutical products. It is critical processes for insuring the safe use of medicines and

vaccines. The main job of pharmacovigilance is monitoring medications even after they are approved for use as some side effects may only apparent with wider use, where detection concern identifying the adverse effects or other problems related to medication, assessment concern with evaluating the likelihood and

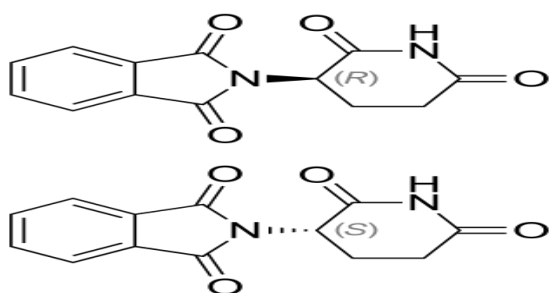
severity of side effects understanding concern with analyzing the causes and contributing factors to side effects, prevention concern to take the action to minimize or prevent future occurrence of side effects and monitoring concern with continuously tracking the safety of medicines after they are on the market.

Pharmacovigilance is important for ensuring patient safety and public health, and it contributes to the overall safety of the healthcare system. It supports the continuous improvement of drugs to increase efficacy and reduce side effects. Informed decision-making supports healthcare professionals and regulators, and global collaboration between various stakeholders—including regulatory agencies, pharmaceutical companies, healthcare professionals, and patients—is essential.

Pharmacovigilance is a vital process for ensuring that the medications we use are as safe and effective as possible. For example, thalidomide, which was used to treat emesis in pregnant women, led to serious birth defects; captopril, used for hypertensive patients, caused cough; and cimetidine, an H₂ antagonist used to treat peptic ulcers, showed side effects—especially on blood—such as decreased RBC count and agranulocytosis.

2. Chemistry and Pharmacology

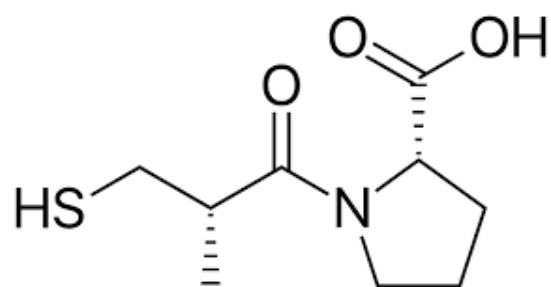
(1) Thalidomide:



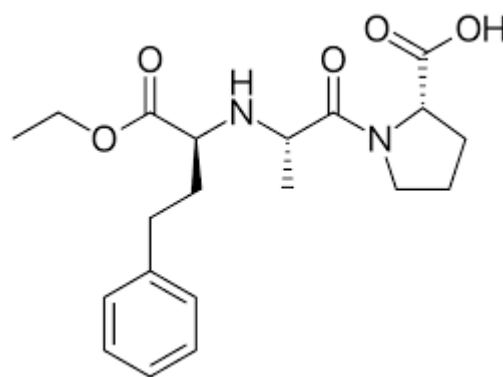
1- Thalidomide was first used in the late 1950s. It was very effective as an antiemetic and was used to treat morning sickness in pregnant women. However, after delivery, some babies were born with phocomelia—a condition characterized by abnormal limb development, where long bones (e.g., humerus, femur) are shortened or absent, causing the hands and feet to be attached close to the body. These characteristics prompted scientists to investigate the cause, which was found to be related to the (S)-isomer of thalidomide. In contrast, the

(R)-isomer was relatively safer, showing sedative and anti-inflammatory properties. Although thalidomide was initially withdrawn, it was later modified to synthesize several anticancer drugs—for example, those used to treat multiple myeloma, graft-versus-host disease, and several dermatological conditions such as leprosy complications. Thalidomide has also been used to manage conditions associated with HIV, including aphthous ulcers and Kaposi's sarcoma.

(2) Captopril and enalapril:



(Captopril)



(Enalapril)

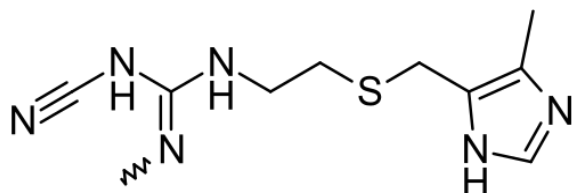
Captopril is used to treat high blood pressure (hypertension), which, if left uncontrolled for a long time, adds to the workload of the heart and arteries, and may cause them to not work properly.

Captopril is an angiotensin-converting enzyme (ACE) inhibitor that blocks the conversion of angiotensin I to the potent vasoconstrictor angiotensin II, and simultaneously inactivates the vasodilator peptide bradykinin. Besides its blood pressure-lowering properties, it also exhibits various immunomodulatory functions.

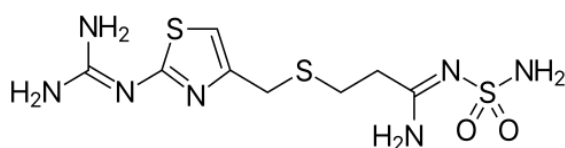
Captopril revealed some side effects after its use by patients, e.g., itching and cough, which led scientists to investigate these effects. The

presence of a sulfhydryl (–SH) group was found to be responsible for these side effects. Hence, enalapril was developed as a modified version of captopril that does not cause itching and cough, due to the absence of the sulfhydryl group present in captopril.

(3) Cimetidine and famotidine:



(Cimetidine)



(Famotidine)

Cimetidine is a modified drug for histamine and was used to treat peptic ulcer, which acts as an H₂ receptor antagonist, competitively blocking the histamine from stimulating the H₂ receptors located on the gastric parietal cells. These cells are responsible for hydrochloric acid secretion and secretion of the intrinsic factor. But the side effects of cimetidine, e.g., breast enlargement in men (gynecomastia) and decreased RBC count, were revealed through pharmacovigilance. So the scientists modified the cimetidine into famotidine, which does not reveal gynecomastia and decrease in RBCs and agranulocytosis. The pharmacovigilance was important for the withdrawal of the drugs from the markets which cause teratogenicity, e.g., (S) isomer, and modified the (R) isomer to be used for treatment of many diseases. The first ACE inhibitor, captopril, is modified to the more effective and less side effect enalapril through the pharmacovigilance of captopril, and cimetidine is withdrawn from the market.

The pharmacovigilance is considered a leader of drug design and lead us modification of some drugs.

3. Conclusion

Pharmacovigilance is a vital post-marketing tool that ensures the continued safety and effectiveness of drugs by identifying and analyzing adverse effects. Historical examples such as thalidomide, captopril, and cimetidine

demonstrate how pharmacovigilance has guided safer drug development. The discovery of the teratogenic (S)-isomer of thalidomide led to the selective use of the safer (R)-isomer. Captopril's side effects, including cough, led to the development of enalapril, while cimetidine's hematological side effects prompted the creation of famotidine. These cases illustrate how pharmacovigilance not only protects public health but also drives innovation and improvement in pharmaceutical therapy.

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