OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Review Article **Pharmacy**

Laboratory Tests for the Early Detection of Adverse Drug Reaction

Hameed Manahi R Alrwayli[1*], Bassam Ghadeer Shanwan Alanazi[1], Muhanna Musafiq Sameer Alanazi[2], Ahmed khalaf Diri Alanazi[2], Abdullah Ibrahim A Alenezi[2], Majed Jawban Nadyan Alruwili[2], Maher Aziz Essa Alanazi[3], Abdullah Taher Alturqi Alanazi[4], Fayez Hamed Fayyadh Alanazi[2], Mohammed Munahi Rasheed Alruwaili[5], Sultan Mheel F Alenazi[6]

[1]Pharmacist, Pharmacy of the Extended Care Hospital, Arar, Saudi Arabia
[2]Laboratory Technician, Laboratory and Blood Bank, Mental Health Hospital, Arar, Saudi Arabia
[3]Laboratory Specialist, Laboratory and Blood Bank, Maternity and children Hospital, Arar, Saudi Arabia
[4]Laboratory Specialist, Laboratory and Blood Bank, Mental Health Hospital, Arar, Saudi Arabia
[5]Laboratory Technician, Laboratory and Medical Technology, North Medical Tower Hospital, Arar, Saudi Arabia
[6]Vaccinations and Health Certificates Center, Arar, Saudi Arabia

DOI: 10.36348/sjmps.2023.v09i12.009 | **Received:** 03.11.2023 | **Accepted:** 07.12.2023 | **Published:** 12.12.2023

***Corresponding author:** Hameed Manahi R Alrwayli
Pharmacist, Pharmacy of the Extended Care Hospital, Arar, Saudi Arabia

Abstract

The Food and Drug Administration (FDA) of the United States has approved drugs for sale in the country only if they are both safe and effective, meaning that the advantages of the medication must outweigh any known hazards. But over-the-counter (OTC) and prescription medications also have negative effects. (FDA) reactions, sometimes referred to as side effects, are undesired side effects that may be connected to a medication. Side effects can range in severity from little issues like a runny nose to potentially fatal situations like heart attack and in some case may lead to death. Age, use of other drugs, vitamins, or diet supplement, amount of drug, and route of administration can affect on degree of side effect as in IM or IV adverse effect is faster and stronger to appear than in oral route. According to laboratory tests, many tests have been done to detect impact of drug on body. In drugs cause liver failure tests appear elevated in liver enzyme as alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate aminotransferase (AST). In kidney failure laboratory test indicate elevated in lipase and amylase serum.in drugs high cholesterol level such beta blocker, prednisone, and anabolic steroid in lab test detect high cholesterol level above 200mg\dl. Drugs elevate blood glucose as statins, corticosteroid, and beta blocker indicated elevation of blood glucose level above the normal. Analytical methods can consider also laboratory method as have been done in labs, it help in identification and separation of drugs so identify the drug these analytical method as spectrophotometry, gas chromatography, high performance liquid chromatography (HPLC).

Keywords: FDA, side effect, ALT, AST, analytical method, HPLC.

INTRODUCTION

Adverse drug reactions (ADRs) is also mean undesirable effect, reasonably associated with the use of the drug that may occur as a part of the pharmacological action of a drug or may be unexcepted in its occurrence on the patient. ADR can occur in all settings where healthcare is provided, most of the current evidence comes from hospitals because the risks associated with hospital treatment are higher. Many such events occur in other healthcare settings such as consulting rooms, nursing homes, pharmacies, community clinics and patients' homes [1].

A branch of clinical pharmacy or clinical pharmacology that deals with drug or drug metabolite levels in the blood is therapeutic drug monitoring. Monitoring is necessary because, when the dosage is raised from a low to a high level, the patient may experience hazardous symptoms as a result of the high dose. Depending on the patient's status and state of illness, different responses occur at different doses. The patient may find the measurement's result acceptable or undesired, or it may have therapeutic ramifications that are unpleasant. There are two main scenarios where drug monitoring is employed. The first is the adoption of preventative measures to ensure that there are no clinical disorders present, such as organ rejection, cardiac arrhythmia, depression or manic episode relapse, or seizures. The second purpose is to prevent major toxicity of amino glycoside antibiotics, such as nephrotoxicity [2].

Therapeutic drug monitoring (TDM) aims to provide a reference concentration range that physicians may use as a guide and laboratories can reference. The range that produces the optimal response for a given patient is known as their "therapeutic concentration range," and it should be chosen based on their symptoms and any related dangers. This approach's drawback is that, in certain people, maximum benefit will only be obtained above minimum hazardous quantities, which carries a risk of negative side effects [3].

The old concept of one drug, one target, and causal effect paradigm is inadequate, as evidenced by recent studies on the adverse side effects (ADR) of medications in cells. These days, medications are made to control the actions of particular target proteins, or "drug targets". In order to provide desired "on-target" effects, effective medications can overcome human barriers to absorption, distribution, metabolism, and excretion. Drugs, however, can also attach to proteins that are off-target, which could result in adverse drug reactions (ADRs), which can range from moderate sleepiness to fatal cardiotoxicity [4].

It is commonly known that many adverse effects are not noticed in clinical trials and are only discovered once the medication is on the market. Because of this, medication side effects continue to be the primary cause of morbidity and mortality in the medical field, costing billions of dollars each year. A number of computer methods have been put up to forecast a drug's negative effects. However, because these approaches can only predict the existence or absence of a pharmacological side effect—not its frequency—their application in drug risk-benefit assessment is restricted. Accurately estimating side effect frequencies is critical for clinical practice patient care, but it's also critical for pharmaceutical companies because it lowers the risk of a drug being taken off the market or requiring an expensive reevaluation of side effect frequencies through additional clinical trials [5].

Various approaches have been proposed for the prediction of pharmacological targets. In 2008 campillos create a comprehensive drug-side effect data collection and use it in conjunction with chemical attributes, in order to build a similarity score between medications; they find comparable medications to a query drug and suggest their targets as potential targets for the drug [6].

Mutsumi Fukuzaki employed gene expression patterns and cooperative pathways to expect ADR. However, there was no mention of large-scale validations or performances. Canonical correlation analysis and a network-based diffusion were used by Nir Atias. To predict ADRs, with prediction precision of little less than 0.5. Nir Atias's research also mentions the use of chemical structure based techniques for off-target and adverse drug reaction prediction. Although Andreas Bender showed that this kind of method is highly sensitive in predicting ADR, on average, the positive predictive value is quite modest, averaging less than 0.5 [7].

Impact Side Effect of the Drugs on the Body:

ADRs can impact a large number of the body's organ systems and vary in severity from mild to severe, mild reactions such as a skin rash or mild elevation of liver enzymes that stop when the causing drug is stopped. In severe reaction it may reach fatal reactions like skin blistering reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis, and fulminant liver failure and may lead to death [8].

Carbamazepine and Phenytoin which used in treatment of Epilepsy, Allopurinol which used in gout, Nevirapine and abacavir used it HIV this side effect appear on skin that cause hypersensitivity. Flucloxacillin used in Gram +ve bacterial infection, Co-amoxiclav used in Bacterial infection, Nevirapine used in HIV, Minocycline used in Bacterial infection cause Hepatotoxicity in Gastrointestinal. 5-aminosalicylic acid used in inflammatory bowel disease cause Nephrotoxicity in renal. Warfarin used as Anticoagulant may cause bleeding in cardiovascular system [9].

In cancer patient platinum based drugs has sever side effect that have been detected and must avoid it, Cisplatin, carboplatin, and oxaliplatin are the three platinum-based medications that are used to treat cancer worldwide. Additionally, four platinum-based medications heptaplatin in Korea, lobaplatin in China, miriplatin and nedaplatin in Japan have regulatory approval in their respective countries. More than 40 distinct adverse effects are possible for patients using the three platinum medications; they can be roughly categorized into seven groups: nephrotoxicity, ototoxicity, neurotoxicity, cardiotoxicity, hematological toxicity, hepatotoxicity, and gastrointestinal toxicity. Patients may need to have their platinum medication doses reduced by 25% to 100% due to side effects. In addition, patients need close monitoring of their kidney and liver functions, hearing tests, and their biochemistries, depending on the medication [10].

Monitoring of Liver Function:

It is commonly recognized that cirrhosis can develop progressively from chronic hepatitis. Developing precise treatment approaches that target liver disease and inflammation is essential. The most popular clinical technique at the moment for evaluating liver function is measuring the levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT). When making judgments, doctors often refer to elevated ALT and AST levels as markers of liver damage. Nonetheless, some patients with advancing hepatitis may have normal or perhaps slightly raised serum ALT and AST levels. By this way we can detect drugs that may damage liver [11].

According to the US Food and Drug Administration's (FDA) authorized labeling for statins, liver function tests should be carried out prior to starting medication, six and twelve weeks after starting treatment or increasing dosage, and then semiannually after that. Acute liver failure (ALF), hepatitis, cholestasis, and increasing of transaminases are the four hepatic syndromes must take in consideration [12].

Numerous case reports and case series have provided compelling evidence of the liver damage caused by some medications. Numerous of these medications have recognized clinical characters of liver damage as phenotype, amoxicillin-clavulanate, halothane, isoniazid, and chlorpromazine are a few examples. In Early DILI research frequently indicated halothane and chlorpromazine as causes of hepatotoxicity [13]. Therefore, detection of adverse drug reactions of these drugs can be done by monitoring liver enzymes.

Monitoring Kidney Function:

Decreased renal function, shown as decreased urine production and elevated serum creatinine levels, is the hallmark of acute kidney injury (AKI). In clinical contexts, such as renal transplantation for patients with end-stage renal disease (ESRD), renal ischemia-reperfusion leads to an increase in immune activation and antibody generation, which exacerbates graft failure and the loss of renal grafts. During the reperfusion phase, oxygen free radicals are generated, leading to lipid peroxidation and tissue damage. Cell death and apoptosis can be brought on by lipid membrane peroxidation, oxidative damage to proteins and DNA. antioxidant enzymes like glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD) may be reduced as a result of Ischemia-Reperfusion Injury (IR) injury so reduction of these enzymes prove side effect of drugs taken. Ghrelin increase 2.8 times in case of end stage renal disease, aldosterone level also increased in renal tissue, urine and plasma in acute renal injury [14].

Drugs cause renal failure as antiviral agents cidofovir, adefovir, and tenofovir as well as the bisphosphonate pamidronate, antiparasitic drug as sulfadiazine that induce crystal nephropathy as crystal formation lead to renal failure [15].

Therefore, detection of adverse drug reactions of these drugs on the kidney can be achieved by monitoring level of its enzymes.

Monitoring Glucose Level on Blood:

Many drugs as corticosteroid may raise glucose blood level in the blood [16]. Hyperglycemia is commonly found in critically ill patients as a result of numerous processes such as increased gluconeogenesis and glycogenolysis caused by elevated levels of corresponding hormones and insulin resistance. Various approaches, including more complex ones like mass spectrometry and infrared spectroscopy, are being utilized to quantify glucose. However, the majority of routine analytical techniques used in central laboratory analyzers, point of care testing (POCT) devices used in hospital and outpatient clinic settings, and even homecare glucose meters for patient self-testing are based on enzymatic techniques [17].

We measure blood glucose level in lab test in fasting time of patient if blood glucose level (100-125 mg\dl) it detect prediabetes, if lower than (70 mg\dl) detect hypoglycemia, if higher than (126 mg\dl) detect diabetes [18].

So we can detect drugs cause hyperglycemia as an adverse drug reaction by blood glucose level measurement.

Analytical Methodologies for Metallomics Investigations of Medications:

In biological systems, the majority of trace elements are attached to biomolecules. As biological catalysts that control reactions and physiological processes in cells and organs, metal-binding substances perform crucial roles. For example, metalloenzymes, which are metalloproteins that catalyze biological reactions, are involved in several critical biological processes. Degeneration processes also involve metal-binding biomolecules; for example, traces of Fe, Cu, and Zn contribute to the formation of neurotoxic amyloid fibrils that facilitate the advancement of Alzheimer's disease. We can use analytical methods to detect Pt in drugs used as antitumor; these analytical methods which are adsorptive stripping voltammetry (ASV), neutron activation analysis (NAA), absorption and emission atomic spectroscopy, and inductively coupled plasma mass spectrometry (ICP-MS) seem to be the most powerful elemental technique because of its high sensitivity [19].

Analytical Method for Drug Monitoring:

Therapeutic drug monitoring involves highly sensitive, ultrafast, microvolume, and expensive advanced equipment like liquid chromatography high resolution TOF mass spectrometry LC/MS/M in small volume. Atenolol was found using a liquid chromatography high resolution TOF mass spectrometry (LC-HRMS), which measures the target analyte's mass to charge ratio precisely [2]. Other analytical methods that have been done in lab are spectrophotometry and Fluorometry: these techniques have a sensitivity level in the region of μg/ml. Thin layer chromatography is a technique for drug identification and quantification. It takes longer and is less sensitive, GLS with HPLC: This approach is very specific, accurate, and sensitive. But after time, column degradation happens and extraction is needed. GLC is not as preferred as HPLC. Radioimmunoassay (RIA): This technique needs radio nucleotides but is sensitive and accurate [20].

LIMITATION

Limited availability of comprehensive and up-to-date literature on laboratory tests for early detection of adverse drug reactions. Lack of standardized protocols for laboratory testing across different healthcare settings and regions.

CONCLUSION

In conclusion, laboratory tests play a crucial role in the early detection of adverse drug reactions. However, the literature on laboratory tests for this purpose is limited, and there are several limitations to consider when interpreting the available data. Variability in the sensitivity and specificity of laboratory tests, lack of standardization in testing protocols, limited access to advanced testing facilities, and potential bias in study selection are among the key limitations. Despite these challenges, laboratory testing remains an important tool for healthcare providers in identifying adverse drug reactions and improving patient outcomes. Future research should focus on developing standardized laboratory testing protocols and identifying new biomarkers for the early detection of adverse drug reactions.

REFERENCE

1. Alomar, M. J. (2014). Factors affecting the development of adverse drug reactions. *Saudi pharmaceutical journal*, *22*(2), 83-94.
2. Gawade, S. P. (2016). Overview on monitoring of therapeutic drugs. *Indian Journal of Pharmacy Practice*, *9*(3).
3. Jacob, S., & Nair, A. B. (2016). An updated overview on therapeutic drug monitoring of recent antiepileptic drugs. *Drugs in R&D*, *16*, 303-316.
4. Huang, L. C., Wu, X., & Chen, J. Y. (2011). Predicting adverse side effects of drugs. *BMC genomics*, *12*(5), 1-10.
5. Galeano, D., Li, S., Gerstein, M., & Paccanaro, A. (2020). Predicting the frequencies of drug side effects. *Nature communications*, *11*(1), 4575.
6. Atias, N., & Sharan, R. (2011). An algorithmic framework for predicting side effects of drugs.
7. Pauwels, E., Stoven, V., & Yamanishi, Y. (2011). Predicting drug side-effect profiles: a chemical fragment-based approach. *BMC bioinformatics*, *12*(1), 1-13.
8. Wade, O. L., & Beeley, L. (2013). *Adverse reactions to drugs*. Elsevier.
9. Carr, D. F., & Pirmohamed, M. (2018). Biomarkers of adverse drug reactions. *Experimental Biology and Medicine*, *243*(3), 291-299.
10. Oun, R., Moussa, Y. E., & Wheate, N. J. (2018). The side effects of platinum-based chemotherapy drugs: a review for chemists. *Dalton transactions*, *47*(19), 6645-6653.
11. Huang, S., Li, C., Guo, J., Zhang, L., Wu, S., Wang, H., & Liang, S. (2019). Monitoring the Progression of Chronic Liver Damage in Rats Using [18 F] PBR06. *Molecular Imaging and Biology*, *21*, 669-675.
12. 12. Sniderman, A. D. (2004). Is there value in liver function test and creatine phosphokinase monitoring with statin use?. *The American journal of cardiology*, *94*(9), 30-34.
13. Björnsson, E. S. (2016). Hepatotoxicity by drugs: the most common implicated agents. *International journal of molecular sciences*, *17*(2), 224.
14. Banaei, S., & Rezagholizadeh, L. (2019). The role of hormones in renal disease and ischemia-reperfusion injury. *Iranian journal of basic medical sciences*, *22*(5), 469.
15. Perazella, M. A. (2003). Drug-induced renal failure: update on new medications and unique mechanisms of nephrotoxicity. *The American journal of the medical sciences*, *325*(6), 349-362.
16. Liu, D., Ahmet, A., Ward, L., Krishnamoorthy, P., Mandelcorn, E. D., Leigh, R., ... & Kim, H. (2013). A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. *Allergy, asthma & clinical immunology*, *9*, 1-25.
17. Wahl, H. G. (2009). How accurately do we measure blood glucose levels in intensive care unit (ICU) patients?. *Best practice & research Clinical anaesthesiology*, *23*(4), 387-400.
18. Dall, T. M., Yang, W., Halder, P., Pang, B., Massoudi, M., Wintfeld, N., ... & Hogan, P. F. (2014). The economic burden of elevated blood glucose levels in 2012: diagnosed and undiagnosed diabetes, gestational diabetes mellitus, and prediabetes. *Diabetes care*, *37*(12), 3172-3179.
19. Esteban-Fernández, D., Moreno-Gordaliza, E., Cañas, B., Palacios, M. A., & Gómez-Gómez, M. M. (2010). Analytical methodologies for metallomics studies of antitumor Pt-containing drugs. *Metallomics*, *2*(1), 19-38.
20. Ansari, S., & Karimi, M. (2017). Novel developments and trends of analytical methods for drug analysis in biological and environmental samples by molecularly imprinted polymers. *TrAC Trends in Analytical Chemistry*, *89*, 146-162.