Interferences in the laboratory assays and minimizing the risk: A case of a patient receiving Exemestane

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Immunoassays are laboratory technologies used for cost-effective and sensitive assessment of many different analytes. These analytes account for about 25% of the tests done at large regional laboratories and include tests ranging from those for specific drugs like Dilantin and Digoxin; proteins like PSA, Troponin, and Ferritin; vitamins like Vitamin B12 and Folate; and hormones like TSH, free T4, Estradiol, Progesterone, and Testosterone, and many others. Recognition of the analyte by the assays occurs through complex interaction of antibodies within the assay reagent with certain parts of the analyte molecule.

Interferences in laboratory assays arise from presence of interfering substances in the patient sample. The interferent could be a drug taken by the patient, the antibodies of monoclonal therapy received by the patient, or could be endogenous metabolites or antibodies produced by the patient. One type of the interferences may occur through recognition by the assay of a drug metabolite that structurally resembles the analyte being measured. Depending on the mechanism involved, the interferences are classified into several types, reviewed elsewhere (reference 1). A classic example of interference in immunoassays is a “cross-reaction” of the over-the-counter medications with the drug of abuse screening causing a “false positive” result. For this reason, positive screen results should always be used with caution and confirmed by a more specific assay. Interference by antibodies produced by the patient typically results in higher than expected results, lower than expected results, and unusual test result combinations such as a high TSH coupled with high free T4 on the same sample. Laboratories have a number of strategies to investigate for these types of interferences once questions about the result reliability are brought to light. These types of interferences are sample-specific and it is not practical to screen every sample for interferences nor are these interferences detected by routine quality assurance processes.

A case of interference in an Estradiol assay
Estradiol testing is carried out in five laboratories in NL. Recently a laboratory in NL reported the Estradiol level of about 260 pmol/L in a female patient. The test was performed by an immunoassay method that is widely used and monitored by both internal quality control and external proficiency testing programs. The patient’s physician became concerned about the result because the patient was receiving Exemestane (Aromasin) and the low Estradiol levels were expected. The laboratory was contacted and the sample was re-measured by a different laboratory using a different immunoassay method, and also by a reference laboratory using a reference method that employed mass spectrometry. The Estradiol level in the same sample was about 60 pmol/L using the other immunoassay method and less than 37 pmol/L using the reference method.
The result from the reference method is the most accurate; however, the method is costly and is not universally available. The laboratory contacted the manufacturers of the immunoassays and performed investigations to determine potential causes of the aberrant results. There was no evidence for interference from endogenous antibodies. There was also no evidence of interference by Exemestane on Estradiol results, leaving the interference from a drug metabolite as the most plausible explanation. We are not aware of any other similar cases in our practice or reported in the literature.

Exemestane is an oral steroidal aromatase inhibitor that is used in therapy for Estradiol-receptor-positive breast cancer. Having structural similarity to steroid hormone molecules, Exemestane irreversibly binds to aromatase enzyme hereby preventing conversion of precursor steroids into estrogens. Therapy with Exemestane typically suppresses Estradiol levels. Without the careful consideration of test results and the potential for interference as an explanation of the unexpected test result by a physician, this anomaly would have gone unrecognized and potentially leading to inappropriate patient care decisions. Simply repeating the test using a different method in this case would have revealed the erroneous test results.

**Identifying aberrant test results caused by immunoassay interference**

The aberrant result observed in the patient receiving Exemestane is an illustration of how analytical interference in clinical chemistry assays may produce errors in laboratory results despite the sophisticated quality assurance schemes used in the clinical laboratories. Laboratories in many cases have no practical way to identify presence of interferences. Implications to a patient from erroneous results arising from interference can be avoided only through appreciation of limitations of the current testing technologies and the potential for inaccurate results. Clinicians should consult with a laboratory whenever test result does not fit the clinical picture. It is only through collaborative efforts from laboratories and clinicians that diagnostic errors with potentially devastating consequences to a patient can be avoided. When patients are found to have factors within their system that can cause erroneous test results, special testing arrangements are often made to mitigate the impact of the interfering substance.

**Key points**

- Immunoassay test interferences are difficult to identify in advance.
- Interferences may not be detected by routine laboratory Quality Control practices.
- Awareness of this limitation of lab tests by physicians is essential to identification.
- Suspect test results must be brought to the attention of the laboratory for investigation.
- Persisting test interferences for specific patients usually require special testing arrangements to minimize the impact on patient care decisions.

**References:**


**IF YOU HAVE ANY QUESTIONS OR COMMENTS PLEASE CONTACT:**

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