

CASE STUDIES ON ADVERSE DRUG REACTION

Case:1

The patient is a 59-year-old male with Type 2 diabetes, hyperlipidemia, and hypertension. He has no history of liver disease.

Background:

- Started Drug X on Feb 11, 2016
- Other medications: simvastatin and lisinopril
- Labs drawn on Feb 11 revealed liver enzymes, INR, creatinine, and bilirubin all within normal limits
- No alcohol use
- 8 weeks after starting Drug X, patient presented to ER with 5-day history of jaundice, dark urine, and nausea/vomiting
- He was admitted to ICU and subsequently diagnosed with *acute liver failure*
- Drug X stopped upon admission
- Viral hepatitis was ruled out
- 7 days after stopping the medication, *all lab values returned to normal*

1. List two reasons why this patient may be at risk for an adverse event.

2. Is a temporal relationship of acute liver failure with drug X reported in this case?

Yes or No

3. Based on the information on recovery of acute liver failure reported in this case, the patient experienced:

- A. Positive rechallenge
- B. Negative dechallenge
- C. Positive dechallenge
- D. Negative rechallenge

4. Name two characteristics in this case that support a causal association of acute liver failure with Drug X.

5. Based on this case, should regulatory action be taken to add acute liver failure to the label? If not, what additional information may be helpful?

Discussion:

1. This patient may be at risk for an adverse event because of his age, because he is taking multiple medications, has comorbid diseases, and his use of a drug is chronic (use for 8 weeks).
2. Yes.
3. Positive dechallenge.
4. Characteristics include temporal association, positive dechallenge, alternate causes (viral hepatitis, alcohol use) ruled out, and no prior history of liver disease.
5. These decisions are not always easy and straightforward. In this case, additional information would be helpful to understand several unknown factors:
 - When were lisinopril and simvastatin started and were they discontinued or continued after the event? Simvastatin is labeled for increase LFTs and lisinopril for hepatic failure: two places to check labels (package inserts or prescribing information) are **Drugs@FDA or DailyMed (<https://dailymed.nlm.nih.gov/>)**.
 - Are there any other cases? Usually more than one case is needed.
 - What is the exposure to this drug? For example, did this one patient experience liver failure out of only 10 patients exposed to Drug X (10%), or did this one patient experience liver failure out of millions of patients exposed to Drug X?

Case:2

A 52 year-old patient commenced on allopurinol 300mg for the prevention of another acute attack of gout that recently occurred.

Background:

The patient is known to have moderate to severe renal impairment, but no liver impairment present. Other concomitant medicines:

- iron sorbitol
- insulin (short and long acting)
- calcium carbonate

In the 6th week after starting the medicine, the patient developed severe aplastic anaemia and died.

1 - The aplastic anaemia and subsequent death are adverse events but are they an ADR?

Yes or No

2. What is the likelihood that the aplastic anemia is associated with allopurinol?

- i. Probable**
- ii. Possible**
- iii. Unlikely**

3. Did the patient have any risk factors for prescribing the allopurinol?

Yes or No

4. Is aplastic anaemia a possible known side-effect with allopurinol?

Yes or No

Discussion:

1. YES, It is an ADR if you have a suspicion that the reactions are associated with the medicine(s) prescribed to the patient.

2. This is possible because it is listed under Undesirable Effects in the SPC.

3. YES: the SPC advises that reduced doses should be used in patients with renal impairment. Therefore, the prescriber should take care and make sure to prescribe the appropriate dose.