Exercise ADR Game; Let us play with ADRs!

Aim
The aim of this exercise is to practice clinical reasoning and causality reasoning when it comes to diagnosing an ADR and asking the right questions for an ADR anamnesis.
This exercise is suitable for training PV 3 (Recognizing ADR).

Source
The Netherlands Pharmacovigilance Centre Lareb, WHO Collaborating Centre for Pharmacovigilance in Education and Patient Reporting

Learning outcomes
The student …
- … can ask relevant questions for assessing causality of an ADR
- … develops an open mind for adverse drug reactions with pharmacotherapy
- … acknowledges the need for pharmacovigilance in pharmacotherapy

Description
This game can be used during lectures to groups of maximum 20-25 students or during working groups. The game makes use of a simulated patient and refers to a retrospective case diagnosis. This game is interchanged by a power point presentation on causality assessment, for example as part of the content of the 5 PV key aspects for PV education at universities. Steps to take:

- Start with an explanation of the “rules” of the game.
    - There are 3-4 rounds for asking questions. Each round for 1 or 2 minutes.
    - Round 1: each group can ask 1 closed-end question, answer Yes/No is available for all groups
    - Round 2: each group can ask 1 closed-end question, answer is secret for this group only
    - Round 3: 1 minute Internet consultation
    - Round 4: 1 closed-end question, loudly for all groups to hear
    - Final: in secret the groups tell or write down their diagnosis
- Participants are asked to split into groups of maximum 5 participants.
- One participant (or the teacher) simulates the patient (description is given).
- Each group of participants represents a doctor or healthcare professional receiving the patient.
- The ”patient” comes for consulting and presents his/her case.
- The members of each group discuss altogether and they decide of a question that they want to ask. A first designed member of the group asks the question to the patient.
- The patient gives the answer loudly.
- The other group asks a second question and the patient asks the question loudly.
- Then the first group designs another member of the group to ask a second question but, at this time, the patient will answer secretly, not telling the other group the answer.
- Same thing for the second group, etc.
- Depending on the number of groups there is another loud questions and another secret one.

- All groups are asked if they know what happened to the patient and if they could explain what their management steps will be.
- The winner will be the group who has asked the right questions to register and analyse the ADR and give information about what to do and who has answered correctly to the quiz.
- Then, this is followed by a short presentation about the importance of PV and questions related to causality assessment. In this presentation there will be some multiple choice questions in order to get a discussion in the group.
- Then, there will be a short presentation about preventing and managing ADRs, including ADR reporting.
- At the end there will be a discussion (coordinated by the teacher) leading to a take home message. It will be discussed if they took all aspects of preventing, recognizing, managing ADRs into consideration. Also will be discussed if they would reports it and why. Also, this "new" form of education will be discussed.

Examples

1) Dyspnoe

Introductory information (patient introduces himself to group)
Female, 55 years old, suffered from acute and worsening dyspnoe. She also has chills. She went to the pharmacy to buy paracetamol (acetaminophen) for these symptoms and she also buys ascorbic acid for preventing recurrent urinary tract infections (UTI, cystitis).

Background information (for answering questions)
outcome: acute pulmonary reaction with nitrofurantoin; as a hypersensitivity reaction
The patient medical history:

- COPD, for which she uses tiotropium; she has a good adherence to therapy.
- Recurrent cystitis, for which she has used several antibiotics: nitrofurantoin, trimethoprim, amoxicillin.
- Two weeks ago, she started with nitrofurantoin 100 mg once daily for prophylaxis of UTI.
- Her symptoms also started about 2 weeks ago. If asked specifically: the symptoms started recently after start of nitrofurantoin prophylaxis.
- She has no other flu-like symptoms (like sore throat, myalgia, rhinorrhoea).
- Her GP wrote a prescription for fluticasone inhalation one week ago, since he suspected COPD aggravation, but this did not resolve the symptoms.
- On previous use of nitrofurantoin (6 months ago) for short term treatment of cystitis, she also had dyspnoe for a few days.
- She stopped smoking 10 years ago.
- No other chronic medical condition besides COPD and recurrent UTI.
- Renal function is good: > 60 ml/min/1.73m2 mDRD.
- Weight: 65 kg, length 165 cm
- No peripheral edema, no cardiac disorders, no dyspepsia.
- No flu or common colds in her family, work, etc.
- Chills, possibly fever, but she did not measure her body temperature.

2) From flu-like symptoms to lifethreatening situation

Introductory information (patient introduces himself to group)
A 67-years-old male was admitted in the chest ward with fever, sore throat which looked like a common cold, but which were accompanied with generalized pruritus and skin rash for 2 days. He was receiving isoniazid (INH), rifampicin (RFN), ethambutol (EMB), and pyrazinamide (PZN) thrice weekly for sputum-positive pulmonary tuberculosis.

Background information
**** Outcome: Toxic epidermal necrolysis due to ethambutol and pyrazinamide****

- He was not taking any other drug at time of presentation
- He had been using the TB drugs (all 4) for 14 days
- Body weight: 50 kg (BMI 23 kg/m2)
- On examination axillary temperature - 103.1°C, pulse rate - 112/min, respiratory rate - 22/min, blood pressure (BP) - 106/72 mmHg, and SpO_2 – 98%.
- Skin examination revealed presence of blisters on a dusky pruritic macules over front and back of chest and abdomen and both upper and lower limbs, involving 60% of the body surface area.
- Nikolsky′ sign was positive, i.e., it was able to extend the area of superficial sloughing by gentle lateral pressure on the skin surface.
- He also had oropharyngeal, conjunctival, and nasal ulcerations. Examination of other systems revealed no abnormality
- All anti – tuberculous drugs ATD were stopped and he was shifted to intensive care unit.
- Investigations revealed hemoglobin (Hb) - 10.8 g/dl, white blood cell (WBC) - 8.2×10^9/L, neutrophils - 70%, lymphocytes - 26%, eosinophils - 4%, reticulocyte index - 2, erythrocyte sedimentation rate ESR - 90 mm in first hour, fasting plasma glucose - 122 mg/dl, liver function test - normal, serum Na - 123 mg/dl, serum K - 4.5 mg/dl, blood urea nitrogen - 30 mg/dl, and serum creatinine - 1.2 mg/dl. Urine examination was normal.
- Human immunodeficiency virus HIV 1 and 2 serology was nonreactive.
- Sputum smear was positive for active TB. Chest X-ray (posteroanterior view) revealed infiltrations in the left upper and mid zones with cavitation.
- Bacterial culture from the skin lesions revealed no growth.
- He was given intravenous normal saline and nutritional support. Skin care was given with local application of povidone iodine and calamine lotion.
- His general condition improved, and skin and mucosal lesions healed completely by 2 weeks.
- TB treatment was restarted by challenge test
    - INH and RFN were reintroduced one by one in staged fashion. He could be safely put on daily INH - 300 mg and RFN - 450 mg regimen.
    - he developed morbiliform rash with pruritus, fever, and arthralgia within 48 hours of introduction of EMB - 100 mg EMB was immediately withdrawn
    - After normalization of skin rashes, PZA - 250 mg was added but he developed similar skin reaction on the next day and PZA was immediately withdrawn
    - After stabilization, streptomycin (SM) and levofloxacin (LFX) were added and he was continued with daily regimen containing INH - 300 mg, RFN - 450 mg, SM - 500 mg, and LFX - 750 mg
    - There was no reappearance of skin lesion.
    - His sputum became negative for AFB at the end of 2 months. Then he was continued with INH 300 mg and RFN 450 mg for next 7 months

This case was based on:

Sibes Kumar Das, Pulak Kumar Jana, Arun Kumar Bandyopadhyay, and Indranil Biswas. Ethambutol and pyrazinamide-induced toxic epidermal necrolysis in an immunocompetent adult with tuberculosis. Lung India. 2012 Jan-Mar; 29(1): 87–88.
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