SHEET NO. 10

PHARMACOLOGY

DOCTOR 2019 | MEDICINE | JU

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بسم الله الرحمن الرحيم

risk:benefit ratio

With every drug use, unwanted effects must be taken into account. Before prescribing a drug, the physician should therefore assess the risk: benefit ratio.

Risk benefit ratio will stay with us as doctors throughout our lives, when we take the big decision whether to give your patients the drug or not. e.g: a patient has a block in the coronary artery which will lead to myocardial infarction and death, but we have an option to give him an expensive injection to dissolve this clot, which will dissolve other clots in our body and leads to internal bleeding. Which is a critical dilemma whether to give the drug or not, So you should be aware: what is the risk to give this injection, While the benefit is the survival of patient?
Take into consideration, if the benefit outweighs the adverse effects or toxicity or the risk, we give the drug. But we don't take the decision by ourselves, if the patient was sane, he should be involved in taking the decision since we have risk.

-In this, knowledge of principal and adverse effects is a prerequisite.

To measure the risk: benefit ratio, you should have a knowledge of principle and adverse effects, which means knowing the effects and the side effects of the drug that you deal with.

-We talk the last time about that risk:benefit ratio is not an absolute or static ratio,it is a dynamic ratio.
This ratio will change from children to pregnant women to elderly patients, each group will have different risk:benefit ratio for the same drug. So,the following factors will determine whether to give the drug or not:
1)pathophysiology of the patient.
2) age of the patient
3)situation of the patient in the community, because it depends on the patient himself also.
Here is a real example to highlight in your mind that this ratio is a dynamic one: Usually we don't give the Covid-19 patients anti-interleukin 13 drug, or anti-interleukin 6 drug, because it so expensive, but if the situation has worsened, the benefit outweighs the risk, so we give him the drug.

تَعَلَّمُوا العِلْمَ مَا دُمْتُمْ سيدنا عمر بن الخطاب رضي الله عنه وارضاه قال: " تفقهوا قبل ان تسودوا"،اي صِغَارًا قَبْلَ أَنْ تَصِيرُوا سَادَةً رُؤَسَاءَ مَنْظُورًا إِلَيْهِمْ، فَإِنْ لَمْ تَتَعَلَّمُوا قَبْلَ ذَلِكَ اسْتَحْيَيْتُمْ أَنْ تَتَعَلَّمُوا بَعْدَ الْكِبَرِ فَبَقَيْتُمْ جُهَّالاً تَأْخُذُونَهُ مِنَ الأَصَاغِرِ الَّذِينَ لاَ يُحْسِنُونَ الْعِلْمَ فَيُزْرِي ذَلِكَ بِكُمْ.المواضيع التالية ليست للحفظ ولكنها للفهم اكثر لنتقن عملنا كأطباء مستقبليين نتعامل مع مرضى، وفي النهاية نحن طلاب علم قبل العلامة.

COMMUNICATING WITH THE PATIENT

• SPEAKING CLEARLY AND SLOWLY IS VERY IMPORTANT.

• BE AWARE OF THE DIFFFERNT LANGUAGES AND CULTURES.

• PATIENTS WILL SOMETIMES HAVE A DIFFERENT MEANING THAN THE PERSON TEACHING THE INFORMATION.

-So,use clear words with a patient with different dialect or language, and make sure that he understands completely, so he will not do something wrong as a result of misunderstanding.

Hints

• Balance between over-prescription and under-prescription.

Some doctors tend to over-prescribe drugs to meet patients' expectation, which isn't good. Americans for example tend to over-prescribe antibiotics, which leads to antibiotics-resistance and missing out on the sensitivity of microorganism towards antibiotics. In other hand, under-prescription is harmful when there is a need to interferent and prescribe a drug. British doctors are conservative and tend to under-prescribe drugs, so you must not be American or british, but you should be a smart doctor whom depends on a risk:benefit ratio to determine whether to give a drug or not.

• Avoid a pill for every ill.

Lots of diseases don't need drugs, e.g: a flu's patient, or a patient who has sore-throat, doesn't need antiviral drugs because the body will manage the disease. So we will not over-prescribe a drug for many reasons related to viral resistance that we will take it in virology course.

• Always consider non-pharmacological therapy.

Pharmacology means drugs, and drugs are toxins, so we should take this

solution as a final step, when there is no other non-pharmacological therapy. For example: if the patient suffers from hyperlipidemia(increase in lipids in the body), we won't give him a drug which has adverse effects or toxicity, but rather we try to manage the situation with his lifestyle, like instructing him toward a diet that decreases his over-wight, or avoid types of food that cause increase in lipids. only if that isn't working, we go to a drug therapy.

Three STEPS IN PLANNING TO GIVE A MEDICATION

1. **Decide the reason or goal for giving the medication**
   We don't give the drugs just to satisfy our patient, there should be a need and a goal.
2. **Learn specific information about the medication:**
   a. The desired action of the drug.
   b. Side effects that may develop.
   c. The usual dosage, route, and frequency.
   d. Situations in which the drug should not be given(contraindications)
   e. Drug interactions (What is the influence of another drug given at the same time?)

3. **Develop a teaching plan for the patient:**

• a. What the patient needs to know about the medication's action and side effects.

In each leaflet of the drug, there is common side effects, and uncommon side effects that are rare to happen, so we just tell the patient the common ones.

• b. What the patient needs to know about the administration of the medication.

The patient needs to know the drug, amount of dose that should be taken, and any increase or decrease in this amount.

• c. What the patient needs to report to the nurse or physician about the medication. Like the side effects that the doctor told the patient that he will experience.

For example:

Metformin, marketed under the trade name Glucophage, has a common side effect which leads to diarrhea for 20% of the patients in the beginning, but later on it will be decreased to 7% because the body will get used to the drug which will prevent irritation in GI tract, therefore the diarrhea will be stopped. we give Metformin to the patient as 500mg dose for two weeks. if the diarrhea

didn't stop, We change the drug, but if it did stop, we continue with Metformin and elevate the dose to 1500mg-2000mg. So, the patient should aware of that, and tell you if the diarrhea stopped or not, so you make the right decision.
But in special cases you need to tell your patient the uncommon side effects, for example: metformin leads to Ketoacidosis for one patient per 100,000 which may cause death, but for a patient who has kidney failure, this probability will be much higher, and we will not give him the drug. So, you should consider the pathophysiology of the patient and decide whether to tell him the uncommon side effects or not.

Adverse effect:

♣ Type A—Exaggerated pharmacological response (drug dose related)
Type A depends on drug binding to receptor, **so the higher dose of the drug, the higher rate of adverse effect occurrence**, and that's what we mean by exaggeration in pharmacological response. But how?!
1.Pharmacodynamic (e.g., bronchospasm from beta-blockers)
For example: In the normal dose, beta blockers aren't selective enough, so they bind the b1 receptors with 90% in the pharmacological reaction which causes decreasing in heart rate, and it binds b2 receptors with 10% as pharmacological side effect. But if we increase the dose, it will cause bronchospasm. which means if we give the patient 200mg of the drug instead of 100mg, it will bind to b2 receptors with 20mg instead of 10mg, and will lead to bronchospasm, that's why it is dose related.

2) Toxic (e.g., deafness from aminoglycoside overdose)
Another example of dose related is aminoglycoside, the higher we give aminoglycoside, the higher probability we get deafness. That's why we give the drug for one week only. more than one week, it will be accumulated in the body causing toxicity. although it is water soluble drug, but it seems that there is a problem in drug excretion as result of high usage of that drug.

♣ Type B—Nonpharmacological, often allergic, response (not drug related but sensitivity related)
1)Medicine-induced diseases (e.g., antibiotic-associated colitis)
In the normal dose range, whatever amount of dose you take, antibiotic will cause colitis. which means our body is that much sensitive to antibiotic, resulting in colitis with normal dose range. Not in underdose or overdose, that's why it isn't drug related.
2) Allergic reactions (e.g., penicillin anaphylaxis)

Our body deals with penicillin as foreign drug, so it starts allergic reaction, which is an immune response secreting histamine, which causes hypotension and acceleration in heart rate, which describes anaphylaxis. And that happens whether we give the patient 1mg or 5mg, so it's not dose related.

3) Idiosyncratic reactions (e.g., aplastic anemia with chloramphenicol)
This is a special reaction that we don't know about it so much, all that we know is whenever you take chloramphenicol drug, it will cause aplastic anemia.

♣ Type C—Continuous or long term (time related)
After years or 6 months of continuous use of drug, the side effects will appear, that's why we named it long time side effects. so ,you should tell your patient when to stop using the drug, in order to avoid time related side effects. For example: tamoxifen is a drug that used to treat breast cancer, if we used it more than 5 years continuously, it will increase the probability of endometrium cancer occurrence in the ovary from 1% to 4%, so we can have a cancer after years of continuous use, and this probability will increase more and more if used the drug more often.
Another example: Osteoporosis with oral steroids
if we transplant a kidney in certain patient, we give him oral steroids or corticosteroids, like cortisone. But we can't give him the cortisone more than 6 months, because it will cause osteoporosis as a side effect. So, usually we don't use oral steroids more than 6 months

♣ Type D—Delayed (lag time)
This effect needs a time to appear, so it is a time related like type C, but the difference that it is not required to be used continuously in order to have side effect after a certain period. it can be used today, and side effects will appear after 3 months for example, **WITH NO CONTINOUS USE**.
For example: Teratogenic effects with anticonvulsants or lisinopril.
anticonvulsants ((ادوية مضادة للصرع or lisinopril(دواء للسكر), are drugs that contraindicated(يُمنع استخدامها) for pregnant lady. because they have teratogenic effects on certain newly created organ in the fetus, which means these teratogenic effects will appear after 3 or 4 months when this organ is created, a delayed effect which we see it by neural tubes.
You are still not understanding? Another example: a drug for cancer patients is called doxorubicin, which will cause a heart failure after 1 year or 2 years, not immediate but a delayed effect.

♣ Type E—Ending of use (withdrawal)

An example of that is tolerance of beta-blockers. a prolonged use of beta blocker will cause the body to over expression beta receptors, so a sudden stop of beta blockers, will lead to 'attack' from noradrenaline, which was blocked by beta blockers. That will lead to heart rate increase and myocardial infraction.

Another example: Withdrawal syndrome with benzodiazepines
Remember the physiological independence? If we suddenly stopped steroid after 21 days, it will lead to adrenal crisis. Or a sudden stop of benzodiazepines (antidepressant) for addicted patients will lead to withdrawal system (which means A wide range of physical or emotional disorders, including nervousness, headaches, and insomnia).
*so, ending use of a drug is not an easy task, it leads to unwanted adverse effects.

♣ Type F—Failure of efficacy (no response)
For example: Resistance to antimicrobials
A misuse of antibiotics creates resistance among the bacteria in our body.
A patient who takes antibiotics for viral infection, will not treat the infection, but rather will cause another problem which is Resistance to antimicrobials, so the drug won't work, and that's what we call failure of efficacy.
*So, again and again don't ever over-prescribe a drug, but give the patient what he needs only without under-prescription too!

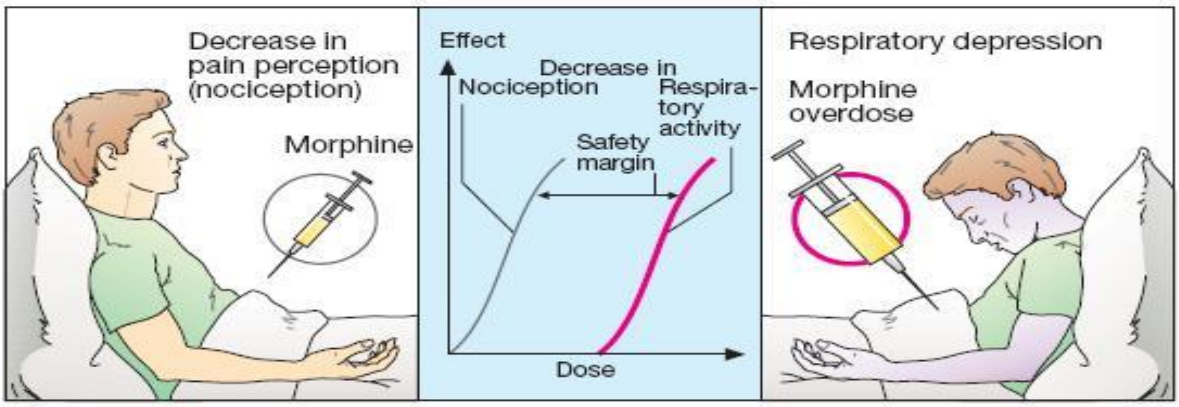
Risk Factors for Adverse Drug Reactions
• Simultaneous use of several different drugs
As the patient increase types of used drugs, we will have a higher Drug-drug interactions, which may increase or decrease the level of the drug in the blood. Increasing the level of the drug in the blood increases the resulting side effects, one of the side effects that would be increased is pharmacological side effect type A.
• Very young, or very old in age
We talked about geriatrics and paediatrics as special situations, as they are more susceptible to adverse effects. For instance, children have reduction in creatinine clearance as their liver and kidney aren't totally developed.
• Pregnancy
Different pathophysiology situation, where is there a fetus, so entering of lipophilic drugs will cause adverse effects to him.
• Breast Feeding
A baby may have diseases due to his mother's bad psychological state, if the

breastfeeding lady tends to be more stressed and tired, then the probability of having diseases for babies will increase.

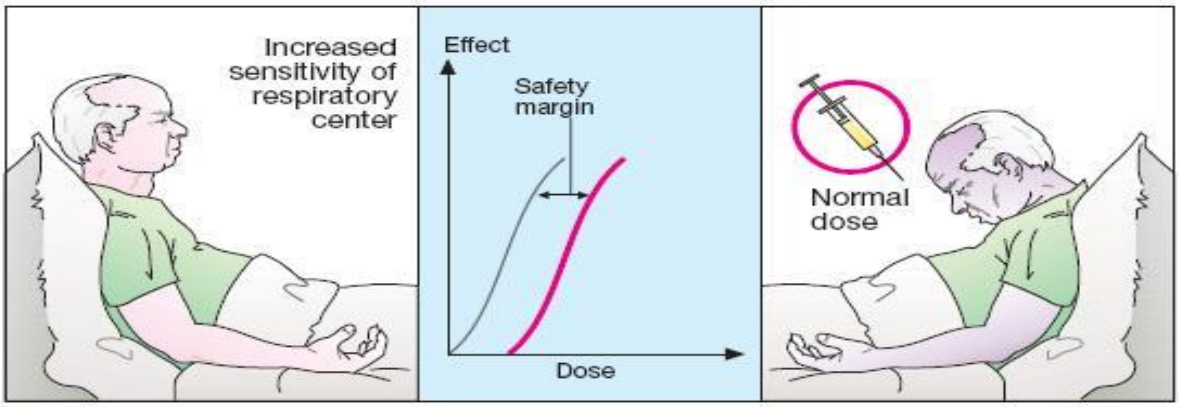
• Hereditary Factors (We will talk about it later)

• Disease states which may effect drug absorption, metabolism, and/or elimination.

If the patient has one of these: kidney failure liver failure, heart failure, a patient with stomach stapling, or have Inflammatory bowel disease, all of these affect kinetics of the drug, and increase side effects of drugs.



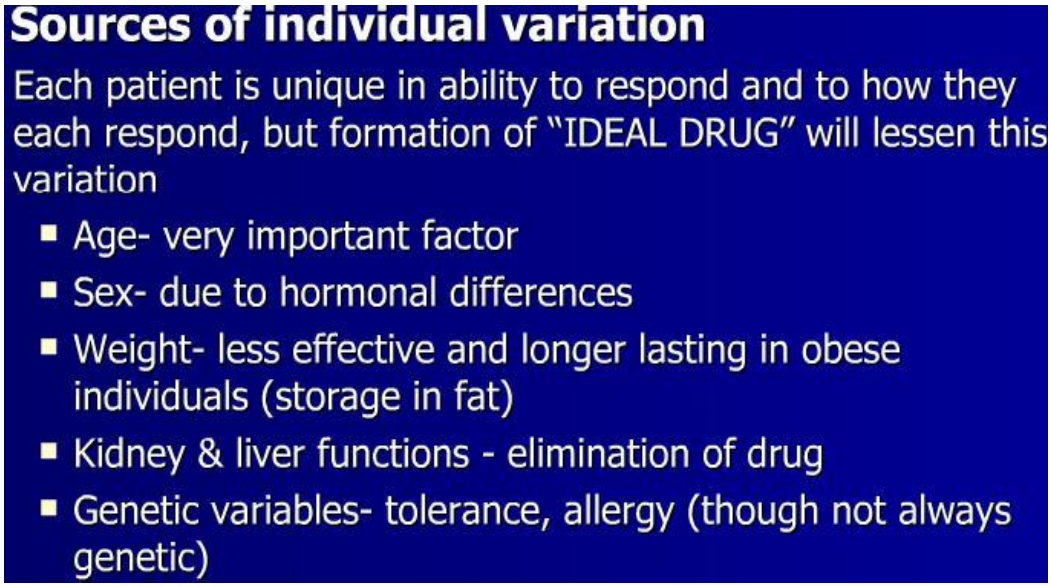
A. Adverse drug effect: overdosing



B. Adverse drug effect: increased sensitivity

-as you can see morphine differs in safety margin between elderly and young people. If the patient is young, margin of safety will be wider, but if he was old, he will have more respiratory depression, so margin of safety will be Narrower. Adverse drug reactions will be increased with the sensitivity of patient. Remember (benefit:risk) ratio is very important as it indicates different situations among patients.

variation in drug responses



- variation among different patients with different pathophysiology, could be solved if we designed a drug for each patient of these.