Lecture 1+2

Therapeutics

Medication Safety Principles and Practices
AND
Evidence Based Medicine and Clinical guidelines

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References:


Introduction

• Rational prescribing (i.e. effectively, safely and at low cost) is a challenging task for every medical doctor as it involves a mixture of knowledge, skills and attitudes integrated into the complex social context of the clinical workplace.

• Poor prescribing may result in prescribing errors and adverse drugs reactions, which could adversely affect patient outcomes, leading to hospitalization or even death.

• There is considerable evidence that junior hospital doctors in the first 2 years of practice after graduation make relatively many prescribing errors (8–10% of prescriptions) and are more likely to make these errors than consultants.

• This is particularly worrying as junior doctors write a large proportion (68%) of hospital prescriptions.
Introduction

• Studies have identified a range of factors underlying the poor prescribing skills of junior doctors, including the following factors
  1. Individual (e.g. lack of experience),
  2. Environmental (e.g. high workload),
  3. Organizational (e.g. lack of standardization) and
  4. Patient (e.g. polypharmacy).

• A lack of prescribing competencies (i.e. knowledge, skills and attitudes) among junior doctors is frequently mentioned, which might be due to inadequate undergraduate education and training in clinical pharmacology and therapeutics (CPT).
Although few studies have attempted to assess the impact of changes in undergraduate medical curricula on prescribing, it is likely that the reduction in CPT teaching has contributed to the 500% increase in patient deaths due to ADRs since the early 1990s, and the rising incidence of medication errors and ADRs in the UK.
Solution in the UK

• The British Pharmacological Society and MSC Assessment are working together to deliver the Prescribing Safety Assessment (PSA) that allows all students to demonstrate their competencies in relation to the safe and effective use of medicines.
Medication Safety Principles and Practices
Medication Safety Principles and Practices

• Medical errors are not a new phenomenon.

• Medical errors causing harm may lead to devastating effects on patients.

• In 1991, the Harvard Medical Practice Study showed that a significant number of people are victims of medical errors, and a subset experienced medication errors (MEs).

• Examples of mistakes noted in the Harvard study included renal failure from angiographic dye and a missed diagnosis of colon cancer. Drug complications were the most common type of outcome attributed to negligence, accounting for 19% of these preventable adverse events.
Medication Safety Principles and Practices

• **The goal** of medication therapy is achieving defined therapeutic goals to improve a patient’s quality of life while minimizing harm.

• Known and unknown risks are associated with the therapeutic use of prescription and non-prescription drugs and drug administration devices.

• **Mishaps related to medication** therapy include both adverse drug events (ADEs) and MEs.
Medication Safety Principles and Practices

• Medication errors negatively affect patients’ confidence in the healthcare system and increase healthcare costs.

• Research conducted by the American Society of Health-System Pharmacists (ASHP) showed that 61% of patients surveyed reported that they were “very concerned” about being given the wrong medicine during a hospital stay.

• MEs are also very costly—to healthcare systems, patients and their families, and healthcare workers. The emotional cost of an ME is also significant, including the burden on the family for grieving loss or stress for the healthcare worker (often referred to as the "second victim") involved in an ME that caused harm.
HOSPITAL MEDICAL ERRORS KILL 98,000 AMERICANS EACH YEAR. -- HEARST NEWS INVESTIGATION
Prevalence

• Preliminary data from the Centers for Disease Control and Prevention (CDC) list accidents (of which MEs are included) as the fifth leading cause of death in the United States in 2010.

• The 1999 report “To Err Is Human” by the Institute of Medicine (IOM), stated that medical mistakes kill 44,000 to 98,000 patients annually in the United States, causing more deaths than breast cancer, motor vehicle accidents, and infections of human immunodeficiency virus.
Definitions

• **ADE**: An *injury* resulting from medical intervention related to a drug, which can be attributable to *preventable* and *non-preventable* causes.

• **ME**: Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer.
Metoclopramide and Ondansetron in patients taking Cisplatin
Angioedema and ACEI
Definitions

• **ADE**: An *injury* resulting from medical intervention related to a drug, which can be attributable to *preventable* and *non-preventable* causes.

• **ME**: Any *preventable* event that *may* cause or lead to inappropriate medication use or patient *harm* while the medication is in the control of the healthcare professional, patient, or consumer.
The patient has a dysrhythmia!

I'll give them a little lidocaine, that will fix it!

It was a 3rd degree heart block

It was a 3rd degree heart block
• Patients can experience an ADE even if the correct medication was prescribed and administered because an ADE refers to the effect the drug had on the patient, not necessarily that an error occurred in the medication process.

• MEs involve any mistake in the medication process, regardless of patient outcome. Not all MEs lead to serious consequences.

• All ADEs cause patient harm, but are not necessarily preventable. All MEs are preventable, but do not necessarily cause patient harm.
Although MEs can occur at any stage in the medication-use process, upward of 80% of errors reported are in either the ordering and transcribing or administration processes.
The NCCMERP Index for Categorizing Medication Errors Algorithm

NCC MERP Index for Categorizing Medication Errors Algorithm

Harm
Impairment of the physical, emotional, or psychological function or structure of the body and/or pain resulting therefrom.

Monitoring
To observe or record relevant physiological or psychological signs.

Intervention
May include change in therapy or active medical/surgical treatment.

Intervention Necessary to Sustain Life
Includes cardiovascular and respiratory support (e.g., CPR, defibrillation, intubation, etc.).

*An error of omission does reach the patient.

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This system allows for comparison of numbers and types of MEs across health systems. It takes into account whether or not the patient received the medication, what if any treatment or monitoring was required, and lastly, the outcome.
Causes of Medication Errors

• Medication selection and procurement is the first step in the medication process.

• MEs in this step include failing to order adequate stock of a medication to meet patient needs, ordering expired or adulterated medication, confusion with substitutions during product shortages and recalls, and ordering the incorrect product, strength, or dilution.
Counterfeit drugs
• The second step is storage.

• An ME occurs when any medication that has been stored improperly is subsequently given to a patient.

• This could include failing to refrigerate a medication or failing to protect a medication from light.
• The third step is **ordering and transcribing**. MEs in ordering occur when the **drug selected** and/or its **dose**, **frequency**, or **dosing duration** is not appropriate for the patient’s disease or physiologic condition.

• MEs in the transcribing phase include **failure** to correctly interpret the medication order.
Drug selection

Enalapril and angioedema

Dimercaprol and anaphylactic shock
Dose selection

- Serum concentrations of 0.8 to 1.2 ng/mL are desirable for atrial fibrillation or flutter, whereas lower concentrations of 0.5 to 0.9 ng/mL are targeted for systolic heart failure.
Frequency

- Vitamin D3
Dosing duration
Transcribing phase error
Look-alike, sound-alike drugs

- Amiodarone, Amlodipine, Amiloride
• During **preparing and dispensing**, health professionals must obtain and package the **correct drug**, **dose**, or **dilution** of a product.

• Medication dispensing errors are defined as any discrepancy between the medication dispensed and the original prescriber’s order.
BAU 5th year clinic

Dr [signature]
As-Salt
Jordan

Patient Name
Adress:

Age: Gender:

Rx

[Signature]

Gasa 1×2
BAU 5th year clinic

Dr
As-Salt
Jordan

Patient Name
Age:
Gender:
Adress:
Date:

Rx

Bipap 12.5 1X1
• Bisoprolol
• ME in *administration* is any discrepancy between how the medication is given to the patient and the *administration directions* from the physician or hospital guidelines.
• Septic shock and norepinephrine
• Medication errors involved in monitoring and evaluating the effects of medication are defined as not ensuring proper follow-up of the therapeutic effect of a medication or failing to recognize an adverse effect of a medication.
# COPD exacerbation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reading</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>SrCr</td>
<td>0.83</td>
<td>0.7-1.36 mg/dl</td>
</tr>
<tr>
<td>ClCr</td>
<td>95</td>
<td>&gt;= 90 ml/min</td>
</tr>
<tr>
<td>BUN</td>
<td>20.9</td>
<td>6.8-21 mg/dl</td>
</tr>
<tr>
<td>Na</td>
<td>141</td>
<td>135-152 mmol/L</td>
</tr>
<tr>
<td>K</td>
<td>2.5</td>
<td>3.5-5.3 mmol/L</td>
</tr>
</tbody>
</table>

### Medication list

- Hydrocortisone, 100mg, 1x3, IV
- Pulmicort, Formoterol+Budesonide, 12+500 mcg, 1x2, nebulizer
- Combivent, Albuterol+Ipratropium, 100+20 mcg, 1x4, nebulizer
- Prednisolone, 30mg, 1x1, PO
- Lasix, Furosemide, 40mg, 1x2, PO
- Tienam, Imipenem, 500 mg, 1x4, IV
- Valsartan, 80mg, 1x1, PO
- Simvastatin, 20mg, 1x1, PO
- Heparin, 5000U, 1x3, SC
• One analysis showed that the **most common errors** involved prescriptions in which a medication was **incorrectly prescribed** (18.5%), dosage or quantity was **incorrectly interpreted during dispensing** (25.5%), and **omission** (25.6%), in which the prescribed medication was not administered.

• A majority of errors in the ordering phase are wrong dose or frequency, known drug allergy, and drug-drug interactions.

• Many errors occur in the administration phase, such as wrong dose or incorrect drug administration technique.
Medication errors occur for a number of reasons, including the following:

1. Ambiguous strength designation on labels or in packaging
2. Drug product nomenclature (look-alike or sound-alike names, use of lettered or numbered prefixes and suffixes in drug names)
3. Equipment failure or malfunction
4. Improper use of electronic order entry systems
5. Inaccurate dosage calculation
6. Inadequately trained personnel
7. Inappropriate abbreviations used in prescribing
8. Labeling errors
9. Excessive workload
10. Lapses in individual performance
11. Medication unavailable
Preventing Medication Errors

• Errors can occur at any step in the medication-use process. For each type of error, it is important to determine the root cause, or main reason, for the error.

• After researching the error and determining its root cause, a tracking system for MEs should be created.
The ASHP Guidelines on Preventing Medication Errors in Hospitals classifies errors as following:

<table>
<thead>
<tr>
<th>Type of Error</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribing error</td>
<td>Incorrect drug selection (based on indications, contraindications, known allergies, existing drug therapy, or other factors), dose, dosage form, quantity, route, concentration, rate of administration, or instructions for use of a drug product ordered or authorized by physician (or other legitimate prescriber); illegible prescriptions or medication orders that lead to errors that reach the patient</td>
</tr>
<tr>
<td>Omission error</td>
<td>Failure to administer an ordered dose to a patient before the next scheduled dose</td>
</tr>
<tr>
<td>Wrong time error</td>
<td>Administration of medication outside a predefined time interval from its scheduled administration time (this interval should be established by each individual healthcare facility)</td>
</tr>
<tr>
<td>Error Type</td>
<td>Description</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Unauthorized drug error&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Administration of medication not authorized by a legitimate prescriber for the patient</td>
</tr>
<tr>
<td>Improper dose error&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Administration of a dose that is greater than or less than the amount ordered by the prescriber or administration of duplicate doses to the patient (ie, one or more dosage units in addition to those that were ordered)</td>
</tr>
<tr>
<td>Wrong dosage-form error&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Administration of a drug product in a different dosage form than ordered by the prescriber</td>
</tr>
<tr>
<td>Wrong drug-preparation error&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Drug product incorrectly formulated or manipulated before administration</td>
</tr>
<tr>
<td>Wrong administration-technique error&lt;sup&gt;g&lt;/sup&gt;</td>
<td>Inappropriate procedure or improper technique in the administration of a drug</td>
</tr>
<tr>
<td><strong>Deteriorated drug error</strong>&lt;sup&gt;h&lt;/sup&gt;</td>
<td>Administration of a drug that has expired or for which the physical or chemical dosage-form integrity has been compromised</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Monitoring error</strong></td>
<td>Failure to review a prescribed regimen for appropriateness and detection of problems, or failure to use appropriate clinical or laboratory data for adequate assessment of patient response to prescribed therapy</td>
</tr>
<tr>
<td><strong>Adherence error</strong></td>
<td>Inappropriate patient behavior regarding adherence to a prescribed medication regimen</td>
</tr>
<tr>
<td><strong>Other medication error</strong></td>
<td>Any medication error that does not fall into one of above redefined categories</td>
</tr>
</tbody>
</table>
Implementation strategies to reduce MEs:

1. Computerized provider order entry (CPOE)
2. Automated drug-distribution cabinets enabled with bar-code scanning
3. Robotic drug dispensing systems (intravenous and oral products)
4. Bar-code-assisted medication administration (BCMA)
5. Smart IV infusion pumps with a two-way interface to an electronic medical record (EMR)
• Studies have shown many MEs and ADEs are preventable.

• Numerous studies have shown roughly 25% of all MEs and ADEs would never have occurred if various strategies had been implemented.

• **CPOE** has been shown to reduce preventable ADEs by 17% and decrease non-intercepted serious MEs by 50%.
Evidence-Based Medicine: The Basics
Outline

• What is evidence-based medicine?
• Why?
• SIX-A
• Asking the right clinical questions
• Hierarchy of evidence
Practical definition

• EBM is the integration of clinical expertise, patient values, and the best evidence into the decision making process for patient care.
• Clinical **expertise** refers to the clinician's **cumulated experience**, education and clinical skills.

• The **patient** brings to the encounter his/her own personal and unique concerns, expectations, and **values**.

• The **best evidence** is usually found in **clinically relevant** research that has been conducted using sound **methodology**.
• The evidence, by itself, does not make a decision for you, but it can help support the patient care process.

• The full integration of these three components into clinical decisions enhances the opportunity for optimal clinical outcomes and quality of life.
• The practice of EBM is usually triggered by patient encounters which generate questions about

1. the effects of therapy,
2. the utility of diagnostic tests,
3. the prognosis of diseases,
4. the etiology of disorders.
Evidence-based medicine requires new skills of the clinician, including efficient literature-searching, and the application of formal rules of evidence in evaluating the clinical literature.
The Steps in the EBM Process

| The patient | 1. Start with the patient -- a clinical problem or question arises out of the care of the patient |
| The question | 2. Construct a well built clinical question derived from the case |
| The resource | 3. Select the appropriate resource(s) and conduct a search |
| The evaluation | 4. Appraise that evidence for its validity (closeness to the truth) and applicability (usefulness in clinical practice) |
| The patient | 5. Return to the patient -- integrate that evidence with clinical expertise, patient preferences and apply it to practice |
| Self-evaluation | 6. Evaluate your performance with this patient |
Why is EBM important?

• Studies of information-seeking habits of physicians, have shown that when asked, physicians reported that their practice generated about **2 questions for every 3 patients**.

• Only 30% of physicians' information needs were met during the patient visit, usually by a colleague.
Instead of routinely reviewing the contents of dozens of journals for interesting articles, EBM suggests that you **target your reading** to issues related to specific patient problems.

Developing clinical questions and then searching current databases may be a more productive way of keeping current with the literature.
Anatomy of a good clinical question

- **P**: patient or population
- **I**: Intervention
- **C**: Comparison
- **O**: Outcome
Types of Questions and Studies

• Two additional elements of the well-built clinical question are the type of question and the type of study.

• This information can be helpful in focusing the question and determining the most appropriate type of evidence.
The type of question is important and can help lead you to the best study design:

Example:

- Therapy --------- RCT
- Diagnosis --------- prospective, blind comparison to a gold standard
- Prognosis--------- cohort study > case control > case series
Evidence pyramid

- Meta Analysis
- Systematic Review
- Randomized Controlled Trials
- Cohort Studies
- Case Control Studies
- Case Series/Case Reports
- Background Information / Expert Opinion
• If it is a therapy question, the best evidence would be a randomized controlled trial (RCT).

• If we found numerous RCTs, then we might want to look for a systematic review or a meta analysis.
Evaluating the Validity of a Therapy Study

• We have now identified current information which can answer our clinical question.

• The next step is to read the article and evaluate the study.
Example of the appraising an article RCT

• Was the assignment of patients to treatment randomized?
• Were all the patients who entered the trial properly accounted for at its conclusion?
• Was follow-up complete?
• Were patients analyzed in the groups to which they were (originally) randomized?
• Were patients, clinicians, and study personnel "blind" to treatment allocation?
• Were the groups similar at the start of the trial?
• Aside from the experimental intervention, were the groups treated equally?
• Are the results of this study valid?
Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomised controlled, double-blind study.

Rabe KF, Atienza T, Magyar P, Larsson P, Jorup C, Laloo UG.

Abstract

BACKGROUND: The contributions of as-needed inhaled corticosteroids and long-acting beta2 agonists (LABA) to asthma control have not been fully established. We compared the efficacy and safety of three reliever strategies: a traditional short-acting beta2 agonist; a rapid-onset LABA (formoterol); and a combination of LABA and an inhaled corticosteroid (budesonide-formoterol) in symptomatic patients receiving budesonide-formoterol maintenance therapy.

METHODS: We did a 12-month, double-blind, parallel-group study in 3394 patients (aged 12 years or older), in 289 centres in 20 countries, who were using inhaled corticosteroids at study entry and symptomatic on budesonide-formoterol (160 microg and 4.5 microg, respectively), one inhalation twice daily, during a 2-week run-in. After run-in, patients were randomly assigned budesonide-formoterol maintenance therapy plus one of three alternative as-needed medications-terbutaline (0.4 mg), formoterol (4.5 microg), or budesonide-formoterol (160 microg and 4.5 microg). The primary outcome was time to first severe exacerbation, defined as an event resulting in hospitalisation, emergency room treatment, or both, or the need for oral steroids for 3 days or more.

FINDINGS: Time to first severe exacerbation was longer with as-needed budesonide-formoterol versus formoterol (p=0.0048; log-rank test) and with as-needed formoterol versus terbutaline (p=0.0051). The rate of severe exacerbations was 37, 29, and 19 per 100 patients per year with as-needed terbutaline, formoterol, and budesonide-formoterol, respectively (rate ratios budesonide-formoterol versus formoterol 0.67 [95% CI 0.56–0.80; p<0.0001]; budesonide-formoterol versus terbutaline 0.52 [0.44–0.62; p<0.0001]; formoterol versus terbutaline 0.78 [0.67–0.91; p=0.0012]). Asthma control days increased to a similar extent in all treatment groups. As-needed formoterol did not significantly improve symptoms compared with as-needed terbutaline. All treatments were well tolerated.

INTERPRETATION: Both monocomponents of budesonide-formoterol given as needed contribute to enhanced protection from severe exacerbations in patients receiving combination therapy for maintenance.
Clinical Practice Guidelines

Hey! These really INFORM us!

This is easy and accessible

WE are made WITH you and FOR you!
What are clinical practice guidelines?

- Clinical practice guidelines (or simply “clinical guidelines”) are recommendations on how to diagnose and treat a medical condition.

- They are mainly written for doctors, but also for nurses and other health care professionals.
Clinical guidelines are meant to help ensure that patients receive appropriate treatment and care.

Guidelines
1. summarize the current medical knowledge,
2. weigh the benefits and harms of diagnostic procedures and treatments,
3. give specific recommendations based on this information.
4. provide information about the scientific evidence supporting those recommendations
5. updated regularly.

Guidelines aren’t legally binding. In other words, doctors don’t have to follow the recommendations if they don’t think they are suitable for certain patients. But deviations from guidelines must be justified.
How are clinical practice guidelines developed?

• Ideally, clinical guidelines should be developed systematically – in other words, following a certain procedure:

1. First a guideline committee is formed, including specialists to cover all the important aspects of the medical condition in question. The committee is usually led by a member of the medical association responsible for the medical condition.

2. It collects as much information as possible from different sources and assesses the information based on predetermined criteria. The various assessments and opinions of the committee members are discussed and taken into consideration when writing the guidelines. In other words, the recommendations are "consensus-based."

3. The committee members have to declare any conflicts of interest. For instance, they have to say whether they have worked for a pharmaceutical company that makes medication to treat the medical condition that the clinical guidelines are being written about.
• **Good** clinical guidelines should be based on up-to-date scientific knowledge, and it should be possible to follow the recommendations in daily medical practice.

• International uniform standards are now used worldwide for the assessment of clinical guidelines.
Types of guidelines

1. **S1 guidelines:** These guidelines summarize the recommendations of experts. The recommendations made in S1 guidelines aren’t very reliable.

2. **S2K guidelines:** S2K guidelines are developed by a committee of specialists in the medical field in question. The recommendations made are consensus-based. However, they aren’t very reliable.

3. **S2e guidelines:** Here the guideline committee systematically compiles the medical knowledge from different sources. But if the members of the committee disagree, they do not use a consensus-based approach to develop the guidelines.

4. **S3 guidelines:** This is the only category of guidelines that meets all of the following requirements:
   ✓ The guideline committee includes experts representing various areas of the field in question,
   ✓ The medical knowledge is systematically collected and assessed,
   ✓ If different members of the committee have different views, a specific procedure is followed in order to develop consensus-based recommendations.

   • S3 guidelines are the most reliable kind of guidelines, but they also involve the most effort: It can take several years to develop them. When S3 guidelines are developed for doctors and health care professionals, patient guidelines are usually developed too.
Thank you