FROM MOLECULES TO MEDICINES :

AN IN-DEPTH LOOK INTO TODAY DRUGS

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From Molecules to Medicines: An In-Depth Look Into Today Drugs

1st Lecture

Overview by first speaker: Dr Alora (Professor in Medicine and Bioethics, Phillipines)

Speaker quoted a few cases where patient died following consumption of prescribed medicines:

Panama story: 365 people died following consumption of cough medicine. Investigation revealed harmful substances Diethylene Glycol which was substituted for glycerine.

Bohol story: A 41 year old lady died of uterine atony following the usage of Methylergometrin maleate

Questions: What is the PROBLEM? Something wrong with GENERIC formulation. Should everyone receive branded, ORIGINAL drugs?

What is the threat of **substandard** drugs?
Patients must be protected?

2nd Lecture by Prof Palapac (Pharmacologist, Phillipines)

Title: Good Manufacturing Practice (GMP)

Late 2007, Heparin products of Baxter
-causing allergic reaction in children: difficulty breathing, nausea
-350 patients affected
-Investigation showed contaminant: highly sulfated form of chondroitin
-home message: GMP non compliance
-conclusion: many factors in the manufacturing process affect quality of drugs

Factors affecting quality of drug

1. material
2. procedures
3. packaging
4. storage

Material
Expecting 100% purity
Impurity is the cause for side effects

Procedures
Different in bioequivalent of the product

Packaging
Properties of drugs: clavulanic should not be wet , amoxicillin should not be dry
Drug is sensitive to the external environment
Hence appropriate protective packaging is important

Storage
Storage condition affect drug stability

3rd Lecture
Dr Suzette Lazo (Pharmacologist, Phillipines)

Drug Development

Discovery of drug molecules
↓
Preclinical testing
↓
Phase I
↓
Phase II
↓
Phase III

Phase I
Involving 20-30 healthy volunteers

Phase II
200-300 volunteers used to check efficacy and side effects of each drugs
-Does it works in patients?

Phase III
Is it safe and more effective versus the gold standard
1000-3000 patient volunteers used to monitor drug reaction in long term

Basic principle

Drug (tab, capsule)
↓
Dissolve in stomach
↓
Absorbed in upper intestine
↓
Enter blood circulation and goes to liver
↓
Distributed to other organs in the body
↓
Reaches target organ and receptors
↓
Response

Absorption in the gut wall→portal vein→ liver→ distributed in systemic circulation→ organ/tissue
↓
Excreted in kidney

D→A→C→ Ce→R

	Absorption		PKs		PKe		pharmacodynamic response	
D	→	A		→C		→ Ce		→R
Drug		absorbed drug		blood concentration		effect Site Concentration		response

PKs= pharmacokinetic process
PKe= equilibrium process

Bioavailability
Bioavailability is the rate and extent to which the active ingredient or active moiety is absorbed from the active site.

Supra-bioavailable→ increase risk of ADRs
Sub-bioavailable→ result in treatment failure

Bioequivalence (BE)

Generic versus pioneer

Drug product change after approval versus product before the change
Alternative dosage form, eg immediate vs extended
New route of administration
Significant manufacturing change which may affect the bioavailability of a drug

Types of BE studies
Pharmacologic end-point BE studies
Clinical end-point BE studies
Blood level BE studies
Urine BE studies

Definition of bioequivalent

The absence of significant different in the rate and extent to which the active ingredient in pharmaceutical equivalent or pharmacologic alternatives become available at the site of drug action.
To be BE, 90% confident interval with AUC and Cmax of the test drug must fall within 80% to 125% of the reference standard (innovator).
Bioequivalent should be done for generic drugs.

Parameter of BE study
Eg :
Cmax
AUC
Confident interval 80-120%

Characteristics of good drugs:
Correct solution
Practice GMP
Testing for quality

Substandard drugs: fake, imported

Quality versus substandard drugs

Quality drugs	Substandard drugs
effective	harm
Save	ineffective
cure	dangerous

HOW? WHAT TO DO WHEN YOU SEE NEW DRUGS

1. Use good prescribing habits
-know the patient, drug and law
-demand to see objective and credible evidence
-choose drugs wisely
-monitor deligently
2. Learn and share learning
-clinical and formulary experience research
3. educate others
-patients, other healthcare providers, public
-be aware and vigilant of substandard drugs

4. support effort of others
-Hospital therapeutics committees
-Government regulators
5. initiate alliances
-form committees within your professional societies
-influence advertising

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