UNIVERSITI SAINS MALAYSIA

PEPERIKSAAN TAMBAHAN
PROGRAM SARJANA FARMASI
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FCP 556: BIOSTATISTICS, STUDY DESIGN AND CLINICAL PHARMACOKINETICS

(2 HOURS)

This examination consists of **two sections**

Section A consists of 50 multiple choice questions

Section B consists of **two (2)** long questions

Answer **ALL** questions

Answers to Section A must be entered into the scripts provided

...2/-

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Section A

1. Which of the following is not an aim of research planning?

   ..... (a) To select an appropriate research strategy.

   ..... (b) To ignore previous research evidence.

   ..... (c) To formulate appropriate aims.

   ..... (d) To select relevant variables for study.

2. Thirty-five (35) degree Centigrade is an example of.....

   ..... (a) a ratio.

   ..... (b) a null hypothesis.

   ..... (c) a variable.

   ..... (d) the value of a variable.

3. Which of the following is unique to experimental research strategy?

   ..... (a) Participant observations.

   ..... (b) Selection of cases to be studied.

   ..... (c) Assignment.

   ..... (d) Definition of population.

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4. Which of the following is common to both experimental and non-experimental research strategy?

..... (a) Experimental hypothesis.

..... (b) Selection of cases to be studied.

..... (c) Field research.

..... (d) Assignment.

5. As sample size increases.....

..... (a) the sample becomes more biased.

..... (b) the ecological validity of the investigation increases.

..... (c) the population becomes more accesible.

..... (d) the sampling error decreases.

6. A representative sample .....

..... (a) consists of at least 500 cases.

..... (b) must be a random sample.

..... (c) is defined as the inverse of the square root of the sample size.

..... (d) reflects precisely the crucial dimensions of a population.

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7. If a study is externally valid then.....

..... (a) its results can be generalized to other equivalent settings.

..... (b) it must have been an experiment.

..... (c) quota sampling must have been used.

..... (d) all the subjects in the sample must have been equivalent.

8. Which of the following experimental design could control all the threats to internal validity?

..... (a) The Pre-Test, Post-Test Control Group Design.

..... (b) The Static Group Comparison Design.

..... (c) The One Group, Pre-Test, Post Test Design.

..... (d) The One-Short Case Study.

Question 9 - 12 refer to the following case.

A study to determine the analgesic effect of a new drug (XYZ) was conducted among sample of 50 patients in a medical unit. Measurement of pain threshold (PT) is based on pain reported by patients after pinprick to the right arm. 25 patients were warded on the first floor and given 200mg oral dose of XYZ and the PT was measured 4 hours later. The other 25 patients were warded on the second floor and was given placebo oral tablet and the PT was measured 4 hours later. A significantly lower PT was found in the XYZ group compared to the placebo group which the researcher attribute to XYZ analgesic effect.

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9. The dependent variable in this study is.....

..... (a) the PT

..... (b) drug XYZ

..... (c) the method of assignment

..... (d) the type of treatment.

10. The independent variable in this study is.....

..... (a) the PT

..... (b) drug XYZ

..... (c) the method of assignment

..... (d) the type of treatment.

11. The main threat to internal validity in this research is.....

..... (a) mortality.

..... (b) history.

..... (c) maturation.

..... (d) regression to the mean.

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12. What type of experimental design has been employed by the researcher?

..... (a) The Solomon Four-Group Design.

..... (b) The Pre-Test, Post-Test Control Group Design.

..... (c) The Static Group Design.

..... (d) The One-Group, Pre-Test, Post-Test Design.

13. Which of the following tests is appropriate for analyzing data where 3 or more groups were used ?

..... (a) t-test

..... (b) z-test

..... (c) Sign test

..... (d) Chi-square test

14. Which of the following statement is true ?

..... (a) ANOVA is a non-parametric test.

..... (b) Chi-square test should be used for nominal data.

..... (c) The choice of a statistical test is not dependent on the study design.

..... (d) Z-test is appropriate for data on a ratio scale.

15. Which of the following statements is true ?

..... (a) Cmax after an IV bolus dose is affected by the half-life of the drug.

..... (b) Amount of drug in the body after an IV injection is linearly related to plasma concentration.

..... (c) The unit of clearance is HOUR.

..... (d) The half-life of a drug usually changes with dose.

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16. Which of the following factors can decrease theophylline clearance ?

..... (a) Marijuana

..... (b) Children of aged 1 - 9 years.

..... (c) Phenytoin therapy

..... (d) Cor pulmonale

17. Which of the following conditions is not an indication for theophylline serum level monitoring ?

..... (a) Asthmatic with cardiac decompensation, liver cirrhosis, and respiratory insufficiency.

..... (b) Patients developed tachycardia on IV aminophylline infusion.

..... (c) Chronic asthmatic with variable response despite daily theophylline dose of 25 mg/kg.

..... (d) Chronic bronchitic on beta-agonist, anticholinergics and theophylline developed fine tremors.

18. Which of the following drugs may significantly increase theophylline serum concentrations ?

..... (a) Isoniazid

..... (b) Phenobarbital

..... (c) Oral contraceptive

..... (d) Rifampicin

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19. Which of the following combinations is true ?

..... (a) Pneumonia - increased theophylline concentration

..... (b) Influenza - decreased theophylline concentration

..... (c) Hyperthyroidism - increased theophylline concentration.

..... (d) Heart failure - decreased theophylline concentration

20. Which of the following is the rationale for early conversion from intravenous to oral theophylline therapy ?

..... (a) Oral theophylline therapy is less expensive than IV therapy.

..... (b) Oral theophylline therapy is as effective and cause no more adverse effects than IV therapy.

..... (c) Continuous IV theophylline infusion does not always infuse as ordered (e.g. pump failure, nurse error).

..... (d) All of the above

21. Which of the following statement is not true ?.

..... (a) Rapid IV administration of theophylline is usually associated with hypotension, vascular collapse and flushing.

..... (b) Bradycardia is the most common sign associated with theophylline toxicity.

..... (c) The occurence of seizures may not be correlated to theophylline serum levels.

..... (d) The incidence of theophylline toxicity is variable due to different parameters used in most studies.

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22. Which of following may not be contributed to the failure of theophylline therapy ?

..... (a) Possibility of irreversible component of the airways disease.

..... (b) Possibility of theophylline overdoses.

..... (c) Possibility of unresolved concurrent pulmonary infection.

..... (d) Possibility of ethylenediamine hypersensitivity.

23. Which of the following is/are measure(s) of disease occurrence?

..... (a) Incident rate

..... (b) Cummulative incidence

..... (c) Prevalence

..... (d) All of the above

24. Which of the following can be classified under observational study design ?

..... (a) Case reports

..... (b) Case series

..... (c) Incidence studies

..... (d) All of the above

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25. Which of the following is the strongest study design for inferring causal relationship ?

..... (a) Cohort study

..... (b) Case-control study

..... (c) Cross-sectional study

..... (d) Randomised clinical trial

26. A study that starts with the identification of persons with the disease of interest and a suitable control group of persons without the disease to establish a causal association between a disease and an exposure is known as a .....

..... (a) cohort study

..... (b) case-control

..... (c) randomised trial

..... (d) cross-sectional study

27. A case-control study is also known as a.....

..... (a) retrospective study

..... (b) prevalence study

..... (c) prospective study

..... (d) disease frequency survey

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28. A study that observes a population for a sufficient number of person-years to generate reliable incidence or mortality rates in the population subsets is known as a ...

..... (a) cohort study

..... (b) case-control

..... (c) randomised trial

..... (d) cross-sectional study

29. Which of the following are advantages of a case-control study ?

(i) It is well suited to the study of rare diseases

(ii) It is relatively inexpensive

(iii) It requires relatively few subjects

(iv) It allows study of multiple potential causes of a disease

..... (a) (i) and (iii) only

..... (b) (ii) and (iv) only

..... (c) (i), (ii) and (iii) only

..... (d) (i), (ii), (iii) & (iv)

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30. Which of the following are limitations of a case-control study ?

(i) It relies on recall or records for information of past exposures

(ii) Validation of information is difficult or sometimes impossible

(iii) Selection of an appropriate comparison may be difficult.

(iv) Rates of disease in exposed and unexposed individuals cannot be determined

..... (a) (i) and (iii) only

..... (b) (ii) and (iv) only

..... (c) (i), (ii) and (iii) only

..... (d) (i), (ii), (iii) & (iv)....

31. Which of the following are advantages of a cohort study design?

(i) It is well suited to the study of rare diseases

(ii) It allows for calculation of rates of disease in exposed and unexposed individuals

(iii) It requires relatively few subjects

(iv) It allows study of multiple potential effects of a given exposure

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..... (a) (i) and (iii) only

..... (b) (ii) and (iv) only

..... (c) (i), (ii) and (iii) only

..... (d) (i), (ii), (iii) & (iv)

32. Which of the following are limitations of a cohort study design ?

(i) It requires large numbers of subjects to study rare diseases

(ii) Relatively expensive to conduct

(iii) Maintaining follow-up is difficult

(iv) Validation of information is difficult or impossible

..... (a) (i) and (iii) only

..... (b) (ii) and (iv) only

..... (c) (i), (ii) and (iii) only

..... (d) (i), (ii), (iii) & (iv)

33. All of the following are observational study design used in epidemiological research except....

..... (a) cohort study

..... (b) case-control

..... (c) randomised trial

..... (d) cross-sectional study

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34. Feature(s) of a good clinical trial includes .....

..... (a) randomized

..... (b) blinded

..... (c) prospective

..... (d) All of the above

35. A drug exposure and disease status or symptoms are determined at the same point in time. This kind of study is called....

..... (a) a cohort study

..... (b) a clinical trial

..... (c) a case-control study

..... (d) a cross-sectional study

36. Randomization is the most essential feature of .....

..... (a) a case-control study

..... (b) a cohort study

..... (c) a cross-sectional study

..... (d) none of the above

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37. Prevalence of a disease in a population can be estimated from ...

..... (a) a case-control study

..... (b) a cohort study

..... (c) a cross-sectional study

..... (d) a randomised clinical trial

38. Which of the following observational study design is not analytical in their approach ?

..... (a) a cohort study

..... (b) a case-control study

..... (c) a cross-sectional study

..... (d) a population-based mortality studies

39. Which of the following observational study design is descriptive in their approach ?

..... (a) A case report

..... (b) A case series

..... (c) An incidence studies

..... (d) All of the above

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40. Which of the following is true about low frequency effects ?

..... (a) It can only be detected in large populations

..... (b) It manifest after long period of use

..... (c) It manifest after long latency period

..... (d) None of the above

41. If an adverse effect is suspected to occur in one out of 50,000 subjects, how many subjects need to be observed in order to be 95% likely to detect it ?

..... (a) 100,000

..... (b) 150,000

..... (c) 200,000

..... (d) 250,000

42. Which of the following is not a modifier of efficacy ?

..... (a) Concurrent drugs

..... (b) Disease severity

..... (c) Lifestyle

..... (d) None of the above

43. A valid study means that....

..... (a) the results are consistent

..... (b) the results are reproducible

..... (c) it accurately measures the outcome of interest

..... (d) all of the above applies

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44. A reliable study means that...

..... (a) the results are consistent

..... (b) the results are reproducible

..... (c) both (a) and (b) applies

..... (d) none of the above applies

45. Which anticonvulsant drug requires therapeutic monitoring of phenobarbital serum levels as well as its own ?

..... (a) Phenytoin

..... (b) Primidone

..... (c) Carbamazepine

..... (d) Ethosuximide

46. Auto-induction is a unique characteristic of .....

..... (a) phenytoin

..... (b) primidone

..... (c) carbamazepine

..... (d) ethosuximide

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47. Which of the following is true regarding post antibiotic effect of aminoglycosides ?

..... (a) It is the toxic effect associated with the high post aminoglycoside concentrations.

..... (b) It correlates with the extent of peak concentration above the minimum inhibitory concentration.

..... (c) It is the toxic effect associated with high pre-aminoglycoside concentration.

..... (d) It can be prevented by giving single daily doses.

48. Which of the following contributes to the variability in phenytoin plasma concentrations ?

(i) Nonlinear kinetics

(ii) Bioavailability

(iii) Drug interactions

(iv) Non compliance

..... (a) (i) only

..... (b) (i) and (ii) only

..... (c) (i), (ii) and (iii) only

..... (d) (i), (ii), (iii) and (iv).

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49. Which of the following is/are true regarding drug metabolism ?

(i) Administration of phenobarbitone to a pregnant mother may result in increased drug metabolism in neonates.

(ii) Antipyrine is not useful as a model to estimate hydroxylation kinetics of drugs.

(iii) Rifampicin is a metabolic inducer.

(iv) Non-linearity is seen with phenytoin kinetics at therapeutic doses.

..... (a) (i) only

..... (b) (i) and (ii) only

..... (c) (i), (ii) and (iii) only

..... (d) (i), (ii), (iii) and (iv).

50. Which of the following is/are considered for the selection of an appropriate statistical test?

(i) The scale of measurement.

(ii) Measurements from independent subjects or repeated in the same subject.

(iii) The number of groups studied.

(iv) Sample size.

..... (a) (i) and (iii) only.

..... (b) (ii) and (iv) only.

..... (c) (i), (ii) dan (iii) only.

..... (d) (iv) only.

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Section B

1. Mr. D.E., is a 76 year old man who has been on aminophylline constant IV infusion at a rate of 25mg/hr for 15 hours. A theophylline concentration determined at this time (15 hours after the start of the infusion) is 16.2 mcg/ml.

Baseline data:

Weight: 45 kg
Medical history: Congestive heart failure for 10 years
Peptic ulcer x 5 years
Social history: Smokes 2 packs per day
Concurrent medications:
Digoxin 0.125mg OD
Cimetidine 800mg q hs
Salbutamol inhaler ii puffs QID
Becotide inhaler ii puffs QID

A. Is the measured theophylline concentration at steady-state ?

Give your reasons and state any assumption(s) you make.

(10 marks)

B. Decide if the administration rate should be changed. Give reasons for your decision.

(15 marks)

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2. A. Write short notes on the following :

(i) State the differences between statistical and clinical significance of a statistical test.

(5 marks)

(ii) Explain the meaning of a statistical power in a study.

(5 marks)

(iii) State the criteria for the selection of a statistical test.

(2 marks)

B. (i) Explain the major differences between a case-control and a cohort study. Provide example(s) to illustrate these differences.

(9 marks)

(ii) List the advantages and disadvantages of each of these methods.

(4 marks)

Appendix

Normal Laboratory Values

1.	Ammonia	80-110 mcg/dl or	47-65 umol/L
2.	Amilase	4-25 IU/ml	
3.	Billirubin		
	- Direct	0-0.2 mg/gl	0-3 umol/L
	- Indirect	0.2-0.8 mg/dl	30-14 umol/L
	- Total	0.2-1 mg/dl	30-17 umol/L
4.	CO_2	20-30 mEq/L	24-30 mMol/L
5.	pCO_2	35-45 mmHg	
6.	CI	100-106 mEq/L	100-106 mMol/L
7.	Cpk	50-170 U/L	
8.	Creatinine (SCr)	0.6-1.5 mg/dl	60-130 umol/L
9.	Random blood sugar	70-110 mg/dl	3-10 umol/L
10.	Iron	50-150 mcg/dl	9.0-26.9 umol/L
11.	Lactic dehydrogenase	70-210 IU/L	
12.	Magnessium	1.5-2.0 mEq/L	0.8-1.3 mMol/L
13.	pO_2	75-100 mmHg	
14.	pH	7.35-7.45	
15.	Acid phosphatase		
	Male	0.13-0.63 IU/ml	36-176 nmol s^{-1}/L
	Female	0.101-0.65 IU/ml	2.8-156 nmol s^{-1}/L
16.	Alkaline phosphatase	39-117 IU/L	
17.	Phosphorous	3.0-4.5 mg/dl	1.0-1.5 mMol/L
18.	Potassium (K+)	3.5-5.0 mEq/L	3.5-5.0 mMol/L
19.	Calcium (Ca^{2+})	8.5-10.5 mg/dl	2.1-2.6 mMol/L
20.	Sodium (Na+)	135-145 mEq/L	135-145 mMol/L
21.	Bicarbonate (HCO_3-)	24-38 mEq/L	24-28 mMol/L

22.	Protein		
	- Total	6.0-8.5 g/dl	60-85 g/L
	- Albumin	3.5-5.0 g/dl	35-50 g/L
	- Globulin	2.3-3.5 g/dl	23-35 g/L
	- Transferrin	200-400 mg/dl	2.0-9.0 g/L
23.	Transaminase (SGOT)	0-40 IU/L	0-0.32 umol s^{-1}/L
24.	BUN	8-25 mg/dl	2.9-8.9 mMol/L
25.	Uric Acid	3-7 mg/dl	0.18-0.42 mMol/L
26.	Blood Pictures		
	Red blood cell (RBC)		
	Male	4.8-6.4 x $10^6/mm^3$	
	Female	4.2-5.4 x $10^6/mm^3$	
	White blood cell(WBC)	4.0-11.0 x $10^3/mm^3$	
	P	60-75%	
	L	20-40%	
	M	4-8%	
	B	0-1%	
	E	1-3%	
	Platelate (Plt)	200-400 x $10^3/mm^3$	
27.	ESR Male	0-10 mm/jam (Wintrobe)	
	Female	0-15 mm/jam (Wintrobe)	
28.	Hematocrit		
	Male	45-52%	
	Female	37-48%	
29.	Hemoglobine (Hgb)		
	Male	13-18 g/dl	
	Female	12-16 g/dl	
30.,	Prothrombin time (PT)	75-100% nilai asas	
31.	APTT	25-37 saat	
32.	Creatinine Clearance (CrCl)	105-150 ml/min/1.73 m^2	
33.	TT_4	3.0-7.5 mcg/dl	
34.	RT_3U	25-35%	
35.	FTI	1.3-4.2	

-ooOoo-

NORMAL HEMODYNAMIC VALUES AND DERIVED INDICES

		Normal Value	Units
BP S/D/M	Blood Pressure Systolic/Diastolic/Mean	120/80/93	mm Hg
CO	Cardiac Output	4-6	Liters/min.
RAP	Right Atrial Pressure (Mean)	2-6	mm Hg
PAP S/D/M	Pulmonary Artery Pressure Systolic/Diastolic/Mean	25/12/16	mm Hg
PCWP	Pulmonary Capillary Wedge Pressure (mean)	5-12	mm Hg
CI	Cardiac Index $CI = \frac{CO}{\text{Body Surface Area}}$	2.5-3.5	Liters/min/m^2
SV	Stroke Volume $SV = \frac{CO}{\text{Heat Rate}}$	60 - 80	ml/beat
SVI	Stroke Volume Index $SVI = \frac{SVI}{\text{Body Surface Area}}$	30 - 50	ml/beat/m^2
PVR	Pulmonary Vascular Resistance $PVR = \frac{MPAP - PCWP}{CO} \times 80$	< 200	dynes.sec.cm^{-5}
TPVR	Total Peripheral Vascular Resistance $TPVR = \frac{MBP - RAP}{CO} \times 80$	900-1400	dynes.sec.cm^{-5}
LVSWI	Left Ventricular Stroke Work Index $LVSWI = (MBP-PCWP)(SVI)(.0136)$	35-80	gm-m/m^2/beat