THE COLLEGES OF MEDICINE OF SOUTH AFRICA

Incorporated Association not for gain
Reg No 1955/000003/08

Final Examination for the Fellowship of the College of Clinical Pharmacologists of South Africa

17 March 2016

Paper 1 (3 hours)

All questions are to be answered. Each question to be answered in a separate book (or books if more than one is required for the one answer)

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1 A 67-year-old man presents with a history of severe chest pain associated with dizziness, nausea, and palpitations. On examination he was pale, sweaty and tachycardic. An electrocardiogram demonstrated changes consistent with a non-ST-elevation myocardial infarction (NSTEMI) and cardiac troponin was elevated. His BP was 167/90, fasting total cholesterol was 6.9mmol/L, LDL cholesterol 3.5mmol/L and HDL cholesterol 0.8mmol/L. Triglyceride and random glucose values were normal

a) Discuss the acute pharmacological treatment of the NSTEMI. (15)

b) Discuss the treatment of hypertension and dyslipidaemia with concomitant ischaemic heart diseases. (10)

[25]

2 a) A 7-day-old neonate presents acutely ill and shocked with a high anion gap metabolic acidosis on arterial blood gas. On careful history taking the mother reports that wintergreen ointment was continuously applied to the umbilicus. You get consulted and inform your colleagues that wintergreen ointment contains methyl salicylate and request a plasma salicylate concentration. The laboratory reports a salicylate concentration of 53.90 mg/dl (therapeutic range 10 to 30 mg/dl) which confirms salicylate toxicity

i) Discuss the pathophysiology and clinical presentation of salicylate toxicity. (10)

ii) Discuss the management of salicylate toxicity. (10)

b) Discuss the pharmacotherapy of alcohol withdrawal under the following headings

i) Pathophysiology.

ii) Acute withdrawal pharmacotherapy.

iii) Sobriety pharmacotherapy. (10)

c) A 19-year-old male is brought to casualty by his roommate. The presenting complaint is that he is acting strangely. On examination the following is found: visual hallucinations, slurred speech, ataxia, nystagmus, a pulse rate of 120 and blood pressure of 156/96mm Hg. The collateral history is that he frequently uses Benylin™ Dry Cough which contains dextromethorphan. Discuss the pathophysiology and management of dextromethorphan intoxication. (5)

d) Briefly discuss the risk factors for opioid abuse that should be screened for as part of your risk-benefit assessment when considering prescribing opioids for chronic pain. (5)

[40]

PTO/Page 2 Question 3…

3 A small study on the efficacy of artemether-lumefantrine for the treatment of uncomplicated malaria in non-immune travelers in France and Columbia found a trend towards a higher risk of treatment failure in adults weighing over 85kg who were given the currently recommended adult dose. The recommended dose was defined based on studies in Thai adults with a mean bodyweight of 48kg and limited data on those over 65kg. In South Africa, although artemether-lumefantrine is the recommended first line treatment for malaria, it is only registered for use in those weighing up to 65kg so its use in patients weighing more than 65kg is off-label. You have been awarded a substantial research grant to investigate the optimal dosing of artemether-lumefantrine for the treatment of uncomplicated malaria in patients weighing >85kg. Outline the key elements of your study design in terms of

a) Study objective. (2)
b) The study design and comparator arms (if applicable). (3)
c) Inclusion/exclusion criteria. (5)
d) Primary endpoint. (2)
e) Secondary end points. (5)
f) Parameters to consider in the sample size calculation. (3)

[20]

4 a) Compare the mechanism of action, clinical use and toxicity of each of the following 3 anti-emetics

i) Ondansetron.
ii) Domperidone.
iv) Metoclopramide. (9)

b) Write short notes on drug-drug interactions for each of the following

i) St John's Wort.
ii) Gingko biloba.
iii) Kava. (6)

[15]

FC Clin Pharm(SA) Part II

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Paper 2 (3 hours)

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1 a) Discuss the characteristics of a drug that would make it a good candidate for therapeutic drug monitoring. (15)

b) A 26-year-old man presents to you complaining of a six month history of hearing persecutory voices in his head and feeling paranoid as a result of 'those people who are out to get him'. His television often addresses him directly and he says messages are transmitted to him via the television aerial. He has attacked his mother on two occasions believing that she is colluding with the enemy. He displays poor or little insight. You make a diagnosis of paranoid schizophrenia

i) Compare the mechanisms of action, toxicity (short- and long-term), and efficacy of two first-line drugs from different classes. (16)

ii) Discuss the duration of therapy. (4)

iii) If adherence becomes erratic, what are your treatment options? (3)

iv) Name the receptors that Clozapine antagonises. (2)

[40]

2 a) Discuss pharmacotherapy used to treat derangements in calcium and phosphate in patients with chronic kidney disease. (10)

b) Describe the treatment of patients with a thyroid storm, highlighting the mechanisms of action of the medicine/s you select. (10)

c) Describe the principles underpinning a risk management plan (RMP) for a newly registered medicine, and the requirements for a successful RMP. (20)

[40]

3 South Africa has the highest obesity rate in sub-Saharan Africa, with up to 70% of women and a third of men being classified as overweight or obese. A staggering 40% of women in our country are obese, which means they have a body mass index greater than 30kg/m^2. However, this is no longer just an adult problem, 1 in 4 girls and 1 in 5 boys between the ages of 2 – 14 years are overweight or obese

a) Complete the following table to provide THREE important effects of obesity on pharmacokinetic parameters, an example of a drug in which this effect is clinically significant and the dosage adjustment recommended. (9)

Pharmacokinetic parameter	**Effect of obesity**	**Type of drugs affected, with an example**	**Dosage adjustment recommended**
Volume of distribution			
Hepatic clearance			
Renal clearance			

b) A 27-year-old Springbok rugby player and a sedentary 28-year-old obese woman both have a Body Mass Index of 35, yet their body composition is markedly different. Both require surgery under a general anaesthetic including cisatracurium (a highly lipophilic non-depolarising skeletal muscle relaxant with a very large volume of distribution). Neither have any evidence of renal or hepatic impairment. Discuss how their pharmacokinetic parameters for cisatracurium could differ, and the implications for your prescribing of cisatracurium in these two patients. (6)

[15]

4 Based on your prior knowledge and the results presented in the abstract below, draft dosing recommendations and guidance for prescribers on the use of enoxaparin in obese patients for the South African Essential Medicines List. [5]

Thompson-Moore NR, Wanat MA, Putney DR, Liebl PH, Chandler WL, Muntz JE.

Evaluation and Pharmacokinetics of Treatment Dose Enoxaparin in Hospitalised Patients with Morbid Obesity.

Clin Appl Thromb Hemost. 2015 September; 21(6):513-20.

BACKGROUND: The pharmacokinetic properties of enoxaparin may lead to supratherapeutic antifactor Xa (anti-Xa) levels and increased bleeding when standard treatment doses are used in patients with morbid obesity.

OBJECTIVE: To evaluate the dose of enoxaparin needed to achieve therapeutic anti-Xa levels in a prospective, masked observational cohort of heterogeneous inpatients with morbid obesity and to determine whether patients with morbid obesity treated with 1mg/kg of enoxaparin are at

increased risk of supratherapeutic levels and bleeding events compared to patients receiving lower doses.

METHODS: Hospitalised patients with a body mass index ≥40kg/m^2 or actual body weight ≥140kg and prescribed treatment doses of enoxaparin >60mg per day were enrolled and consented to phlebotomy for determination of anti-Xa levels.

RESULTS: Forty-one patients were included for data analysis. The dose of enoxaparin that resulted in therapeutic and supratherapeutic anti-Xa levels at steady state was 0.83mg/kg and 0.98mg/kg (-0.11; 95% confidence interval [CI] -0.20 to -0.01, P = .02), respectively. Enoxaparin dose as mg/kg of actual body weight was an independent predictor of having a supratherapeutic anti-Xa level. Patients with doses <0.95mg/kg versus ≥0.95mg/kg were less likely to have supratherapeutic levels (odds ratio 0.21 [95% CI 0.05-0.84], P = .02) and had similar rates of subtherapeutic levels. Doses <0.95mg/kg and ≥0.95mg/kg resulted in similar bleeding rates of 17.9% and 22.2% (P = .71), respectively.