January 2021 Tweetorial JPP

Theophylline

Day 1: [#theophylline](https://twitter.com/search?q=%23theophylline) was extracted from green & black tea leaves in 19th Century; Theophylline is a natural derivative of the purine ‘xanthine’ & structurally similar to caffeine. Used from 1902 as a diuretic & since 1930s for asthma. Oral preparation as a m.r formulation & given i.v as aminophylline (more soluble)

Day 2: Indications for [#theophylline](https://twitter.com/search?q=%23theophylline) include adult & children over 5 (UK step 3+) for chronic asthma (specialist use <5). Adults only use in severe acute asthma/COPD. Asthma 2-11yrs 9mg/kg every 12 hrs, can increase to 10-16mg/kg; 12-17 yrs 200-400 every 12 hrs; COPD 200-400mg twice daily.

Day 3: Kinetics; [#theophylline](https://twitter.com/search?q=%23theophylline) thought 100% bioavailable orally! Metabolised in liver & this process determines blood levels. Approximately 10% is renally excreted as unchanged drug. Prolonged release tablets t½ 7 hrs. Caution in hepatic impairment, heart failure & viral infection. Can use in pregnancy.

Day 3 (cont); [#theophylline](https://twitter.com/search?q=%23theophylline) clearance can be altered by age, weight, diet, smoking, some disease e.g cardiorespiratory & hepatic. [#theophylline](https://twitter.com/search?q=%23theophylline) is a drug with a narrow therapeutic index; monitor at the start & with each dose adjustment or change to clearance e.g altered smoking habit

Day 4: Mechanism of action is unknown for [#theophylline](https://twitter.com/search?q=%23theophylline). Thought to inhibit phosphodiesterase & antagonise adenosine, thus regulating calcium flow leading to relaxation of bronchial smooth muscle. Also stimulates the CNS & cardiac muscle, induces diuresis & increases gastric acid secretion

Day 5: The frequency of ADRs is largely unknown for [#theophylline](https://twitter.com/search?q=%23theophylline) as it pre-dates licensing regs. Include arrhythmias, anxiety, nausea /vomiting, rash, abdominal discomfort, tremor, sleep disorders, convulsions. Risk of severe hypokalamia when used with beta2 agonists (not exhaustive) Prolonged release preparations can cause delayed toxicity

Day 6: Drug-drug interactions for [#theophylline](https://twitter.com/search?q=%23theophylline) include numerous ‘severe’ interactions from either hypokalaemia e.g citalopram, clarithromycin, as well as asthma drugs e.g salbutamol; OR via enzyme induction e.g St John’s wort, or drugs which can worsen respiratory function e.g beta blockers

Day 7: Interesting fact; At lower concentrations [#theophylline](https://twitter.com/search?q=%23theophylline) is believed to exert an anti-inflammatory effect in lungs, reducing the number of eosinophils & IL-8. Theories include inhibition of prostaglandin levels, T cell apoptosis, antagonism TNF-alpha while increasing IL-10 (anti-inflammatory).

CPD: in addition to the tweets, read the BNF section on Airways disease, obstructive’, as well as the monograph on theophylline under ‘Xanthines’. Another useful source is the Summary of Product Characteristics for theophylline – see links below

<https://bnf.nice.org.uk/drug/theophylline.html>

<https://www.medicines.org.uk/emc/product/1021/smpc#gref>

CPD questions (most but not all answers will be in the tweets). There is only one correct answer per question

1. Theophylline is a drug with a narrow therapeutic index

TRUE or FALSE

1. Renal function is more important than hepatic function when managing plasma concentration

TRUE or FALSE

1. Which is TRUE?
2. Smoking induces liver enzymes which increases theophylline levels
3. Smoking induces liver enzymes which decreases theophylline levels
4. Smoking causes lung broncho-spasm and opposes the drug effects
5. Smoking reduces lung absorption of theophylline, so higher drug doses are needed
6. Which of the following does NOT exacerbate hypokalaemia when taken with theophylline?
7. Salbutamol
8. Prednisolone
9. Indapamide
10. Rifampicin
11. Theophylline has sedative effects

TRUE or FALSE

1. Theophylline toxicity can manifest as
2. Bradycardia and hypoglycaemia
3. Tachycardia and seizure
4. Rash and urinary retention
5. Hypotension and renal failure
6. An important drug-drug interaction pathway is caused by enzyme inducers, such as carbamazepine

TRUE or FALSE

1. Which best describes the action of theophylline on bronchial smooth muscle?
2. Opposing adenosine activity means less histamine and calcium availability to the smooth muscle
3. Stimulates epinephrine, which opens up the airway
4. Prevents constriction by lowering histamine levels
5. Opposes lung damage caused by smoking
6. Theophylline is related to caffeine

TRUE or FALSE

1. Theophylline is introduced at step 3 and above on the algorithms for chronic asthma treatment for people over 5 years old

TRUE or FALSE