Drug Calculations in Schizophrenia

The National Institute for Health and Care Excellence (NICE) recommends the use of medication for the acute management of disturbed and violent behaviour (2005). NICE recommends firstly de-escalation and environmental techniques before utilising medication. Benzodiazepines can be used for their anxiolytic effects but antipsychotics can also be used as they can cause sedation and NICE suggests their use when there is a psychotic context to the unsettled behaviour.

A patient is admitted who is acutely psychotic and is very unsettled. If de-escalation attempts fail and his behaviour continues to be dangerous to himself or to others; it is decided to prescribe haloperidol and lorazepam both orally and, when offered and not accepted, intra-muscularly (IM). The manufacturer of lorazepam injection states that before administration, it should be diluted 1:1 with normal saline or water for injection (Pfizer, 2014). 1mg is prescribed as required with a maximum of 4mg in 24hrs. The injection is available 4mg/ml ampoules.

(a) How much mL should be injected to administer 1mg?
(b) How much water for injection should be used to be used to dilute the lorazepam?

Haloperidol 5mg/5mL IM injection has a maximum daily dose of 12mg and oral haloperidol has a maximum daily 20mg daily (Joint Formulary Committee, 2014). In 24 hours the patient was first administered 5mg orally, then 5mg IM later in the day and finally 5mg orally at night.

(c) Was the maximum dose exceeded?

Antipsychotics are also recommended in the treatment of psychosis and schizophrenia (NICE, 2014). In this case, it is recommended that the choice of antipsychotic should be made
jointly by the clinician and patient. Clozapine should be initiated in treatment resistant schizophrenia. Treatment resistant schizophrenia is defined as an inadequate response despite adequate doses and durations of two different antipsychotics, at least one being an atypical.

Olanzapine was commenced and the patient, now more settled, was diagnosed with schizophrenia. The maximum dose of olanzapine was reached after a month and the patient was discharged when more settled. However, a satisfactory improvement was not seen and it was decided to start a depot to assure adherence. The patient is prescribed zuclopenthixol decanoate depot and a dose of 600mg every 14 days is reached. It is available in 500 mg/mL ampoules (Joint Formulary Committee, 2014). Antipsychotic doses represented as percentages of the BNF maximum recommended doses of are calculated to identify when high doses are prescribed (Yorston and Pinney, 2000). A high dose is defined when a dose of an antipsychotic or combined doses of antipsychotics exceed 100% BNF maximum recommended.

(d) How much mL is required to be administered every 14 days?
(e) How many ampoules are used in 28 days?
(f) Referring to the BNF, what is percentage of BNF maximum dose of zuclopenthixol prescribed?

After two months on zuclopenthixol, no response was evidenced and the patient was diagnosed with treatment resistant schizophrenia. It is decided to start the patient on clozapine; a slow titration is necessary to reduce the risk of seizures, sedation and hypotension (Novartis, 2014).

The manufacturer recommends the following regime: 12.5mg once a day for the first day, then 12.5 mg twice a day on the second day (Novartis, 2014). This is followed by 12.5 mg mané and 25 mg nocté on the third day and 25mg twice a day on the
fourth. After this, it is decided to increase by 25mg every day until 300mg/24hours is reached and then assessing efficacy. Tablets are available in 25mg and 100mg strengths, half tablets should be used only when necessary and the unused half tablet to be discarded.

(g) On what day will 300mg/24hrs be achieved? (h) How many tablets of both strengths are required?

Therapeutic monitoring of clozapine and its' metabolite, norclozapine, can be useful when an interacting agent is introduced or discontinued, detecting fast or slow metabolisers, or when adherence is in question (Couchman et al., 2010). Adherence is assured when the norclozapine level is approximately two thirds of that of clozapine. The patients’ clozapine level is 480mcg/L and there norclozapine level is 320mcg/L.

(i) Represent two thirds as a percentage, decimal and as a ratio (j) Has the patient been adherent?

A patient is now currently on clozapine 225mg twice a day and still displaying symptoms. The patient is not able to tolerate any higher doses and it is decided to add another antipsychotic. Combination of antipsychotics is a possible treatment strategy when clozapine monotherapy fails to adequately resolve symptoms (Langan and Shajahan, 2010). What is the percentage of BNF maximum recommended doses of the following antipsychotics combined with the clozapine dose? Which combination(s) would be considered as a high dose?

(k) Aripiprazole 20mg once a day (l) Paliperidone 3mg twice a day (m) Risperidone 8mg twice a day (n) Amisulpride 300mg once a day
References


Novartis (2014), Clozaril 25mg and 100mg Tablets, available at https://www.medicines.org.uk/emc/medicine/1277 last accessed 01/03/15

Pfizer (2014), Ativan Injection, available at https://www.medicines.org.uk/emc/medicine/2196 last accessed01/03/15

Answers

(a) 4mg/ml ampoule
Divide both sides by 4:
1mg/0.25ml required

(b) 1:1 dilution which requires the same amount of mL of sterile water as lorazepam. Therefore 0.25mLs of sterile water required.

(c) First step is to convert all doses into one form. 2 administrations are already oral, therefore convert the one IM dose to the oral equivalent:

Using proportional sets
\[
\frac{20}{12} = \frac{x}{5}
\]
\[
(20 \times 5)/12 = y
\]
y = 8.33mg

Add this to the sum of the other oral doses (10mg) = 18.33mg
This is under the 20mg (max oral dose) therefore it hasn’t exceeded the max daily dose

(d) Each ampoule is 500mg/ml

Using proportional sets
\[
\frac{1}{500} = \frac{z}{600}
\]
\[
(1 \times 600)/500 = z
\]
z = 1.2 mLs required every 14 days
(e)  
2 ampoules required every 14 days, therefore 4 required in 28 days

(f) 100 % BNF dose = 600mg every 7 days  
600mg every 14 days is equivalent to 300mg every 7 days  
Therefore 600mg every 14 days is 50%

(g)

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It will take 14 days to reach 300mg/24hrs

(h) 38 x 25mg required and 11 x 100mg tablets required

(i)  
Decimal: 0.66  
Ratio: 2:3  
Percentage: 66%
(j) Yes, as the norclozapine:clozapine ratio is 2:3

(k) Clozapine dose is (450mg/900mg x 100): 50%
Aripiprazole (20mg/30mg x 100): 66%
Total with clozapine (66% + 50%): 116% - High dose

(l) Paliperidone (6mg/12mg x 100): 50%
Total with clozapine (50% + 50%): 100%

(m) Risperidone (16mg/16mg x 100): 100%
Total with clozapine (100% + 50%): 150% - High dose

(n) Amisulpride (300mg /1200mg x 100): 25%
Total with clozapine (25% + 50%): 75%