Pharmacokinetic and pharmacodynamic impacts on well-being: case study

Pharmacology Essay

This essay will explore the pharmacological considerations that may be affecting the wellbeing of a client, Vera. This essay will discuss the pharmacokinetics and pharmacodynamics of each of the medications Vera is taking, in relation to dosage, concurrent use of multiple medications, and other factors that can alter the pharmacokinetic and pharmacodynamic effects of drugs in the body, as well as exploring any possible interactions and adverse effects.

Vera's diet and dietary supplements will also be taken into consideration to determine if they have any possible adverse effects combined with the medication that she is taking.

The medications that Vera is currently taking are Zoloft (sertraline) and Voltaren (diclofenac).

Vera takes Zoloft in a dosage of 50mg daily. She has been prescribed this by her specialist for feelings of depression, loneliness and anxiety. She has been taking it for three months.

The dosage and administration of Zoloft that is indicated for the treatment of symptoms of depression that Vera has been experiencing is at a dose of 50 mg/day, which she is taking.

Zoloft should be administered once a day, and can be administered with or without food. Vera has been taking her dose each morning before breakfast which is in conjunction with safe administration (Pfizer, 2017).

Pharmacodynamic effects

Sertraline is an SSRI, which is a class or drugs which selectively inhibit the reuptake of serotonin in the pre synapse, increasing the available serotonin in the brain.

Sertralines main pharmacological action is to inhibit presynaptic reuptake of serotonin (5-HT) from the synaptic cleft. At clinical doses, sertraline blocks the uptake of serotonin into human platelets (New Zealand Formulary, 2019).

In studies on rhesus monkeys, sertraline has shown to not demonstrate potential for abuse or toxic effects when taken within the dosage range (50mg to 200mg). It did not demonstrate effects greater than a placebo and did not produce either stimulation, anxiety, or sedation (Pfizer, 2017).

Pharmacokinetic effects

Sertraline is absorbed slowly after oral administration, with peak plasma concentrations at about 6-8 hours after administration. Plasma concentrations are directly related to dosage. The elimination half-life of sertraline ranges from 22 to 36 hours, with an average of 32 hours. The onset of therapeutic effects can usually be seen within 7 days after consistent doses (Pfizer, 2017).

Approximately 98% of circulating Sertraline is bound to plasma proteins. Animal studies indicate that sertraline has a large volume of distribution (Pfizer, 2017).

Sertraline is extensively metabolised by the liver, and undergoes first pass hepatic metabolism, meaning that the concentration is greatly reduced before it reaches the circulation. Metabolism of sertraline occurs in the body by demethylation to an inactive metabolite. Evidence shows that several P450 enzymes catalyse sertraline demethylation, including CYP2B6, CYP2C19, CYP2C9, CYP3A4 and CYP2D6. Deamination is catalysed by enzymes CYP3A4 and CYP2C19 (Obach, Cox & Tremaine, 2004).

Sertraline is extensively metabolised in the body and the resulting metabolites are excreted in faeces and urine in equal amounts. Only a small amount, less than 0. 2% of unchanged sertraline is excreted in urine (Pfizer, 2017).

Vera takes Voltaren SR tablets at a dosage of Voltaren SR 75mg twice a day. She was prescribed this for pain and inflammation for her sprained ankle. She has been taking the tablets on an empty stomach on rising in the morning, and before bed, for three weeks. This has helped with the pain and swelling in her ankle, however, since starting it Vera is bruising more easily and has experienced burning discomfort in her stomach.

Voltaren (diclofenac) is indicated for the treatment of post-traumatic pain, inflammation, and swelling, which is the reason Vera has been prescribed it following her ankle injury. The recommended initial daily dose is 100 to 150 mg, a single or divided dosage (Novartis, 2018)

Voltaren is prescribed in doses of 75-100mg daily for milder cases or long term therapy (Novartis, 2018). Vera takes 75 mg twice daily, which adds to 150 mg per day in total. This is the maximum safe dosage recommendation.

Voltaren SR tablets should preferably be taken before meals. The tablets should be swallowed whole with liquid and must not be divided or chewed (New Zealand Formulary, 2019). Vera does this by taking the tablet on an empty stomach before breakfast, and again before bed.

Pharmacodynamic effects

Voltaren (Diclofenac) is in the pharmacotherapeutic class of drugs that are NSAIDs, nonsteroidal anti inflammatory drugs. Voltaren contains diclofenac sodium, a non-steroidal compound with antirheumatic, anti inflammatory, and analgesic properties. One of the therapeutic indications for Voltaren is for inflammation in post traumatic injuries (Novartis, 2018). This applies to Vera's case, as she is taking Voltaren to relieve the inflammation, pain and swelling of her sprained ankle post injury.

The main mechanism of action is the inhibition of prostaglandin synthesis. This is key to its therapeutic effects as prostaglandins play a major role in causing inflammation and pain (New Zealand Formulary, 2019).

Pharmacokinetic effects

The active constituents of Voltaren are slowly released into the GI contents after administration. Diclofenac is absorbed in the GI tract after release from the tablet, and is subjected to first pass metabolism by the liver. Peak plasma concentrations occur about 4. 5 hours after administration when taken with food (Novartis, 2018).

Diclofenac enters synovial fluid, where peak concentrations occur 2 to 4 hours after peak plasma values have occurred. The half life for elimination

from synovial fluid is 3-6 hours (Novartis, 2018). The active substance is 99. 7% bound to plasma proteins, mainly albumin. (Electronic Medicines Compendium, 2019).

The metabolism of diclofenac takes place mainly in the liver by oxidative metabolism and conjugation to glucuronic acid, resulting in several metabolites, two of which are active but to a much lesser extent than diclofenac. (Novartis, 2018).

The terminal half life of diclofenac in the plasma is 1 to 2 hours. About 60% of the administered dose is excreted in the urine in the form of metabolites, and less than 1% in unchanged form. The rest of the dose is eliminated as metabolites through the bile in the faeces (Novartis, 2018).

Potential interactions and adverse effects

There are several possible interactions and adverse effects that may be taking place within the polypharmacy combination that Vera is taking, as well as in conjunction with her dietary supplement and diet.

As well as 50mg Zoloft once daily and 75mg SR Voltaren twice daily, Vera also takes a dietary supplement of Calcium carbonate (1000mg, equivalent to 400mg of elemental calcium). She takes this with grapefruit juice at breakfast time to supposedly increase stomach acid and assist calcium absorption. A friend has also suggested she takes St John Wort tablets, which she wants advice on. The components of her diet which may have possible adverse effects/interactions with other substances that she is taking, are the grapefruit juice and espresso.

Evidence has shown the administration of NSAIDs can cause, among other adverse side effects, gastrointestinal bleeding, ulcers and perforation (Novartis, 2018). On top of that, several recent studies have shown that there is an increased risk of gastrointestinal bleeding when NSAIDs are taken concomitantly with selective serotonin reuptake inhibitors (SSRIs), than when either class of drugs is taken alone. Vera is taking Zoloft, which is a SSRI, and Voltaren, which is a NSAID, the combination of which has been shown to increase the possibility of GI bleeding and ulcers (Pinto, Farrar & Hersh, 2009). One study confirmed that the use of SSRIs in combination with NSAIDS increased the risk of adverse gastrointestinal effects by ten times more than SSRIs alone, and four times higher than the risk for NSAIDs alone (De Jong, Van den Berg, Tobi & De jong-Van den Berg, 2003). As Vera has experienced burning stomach pain and easily bruising since she began taking Voltaren, this could be a result of the concurrent doses of Voltaren and Zoloft that she is currently taking.

Another possible adverse effect to be considered is whether the dosage of Voltaren that Vera is currently taking is safe and appropriate for her needs. Vera takes 75mg of Voltaren twice daily, which adds to 150 mg per day in total. This is the maximum safe dosage recommendation Novartis, 2018). Voltaren, like other NSAIDs, has several contraindications, including gastric or intestinal ulcers, bleeding or perforation, hepatic failure, renal failure, and cardiac failure. Vera has experienced burning stomach pains at night and bruising more easily, which could possibly be related to her dosage and administration of Voltaren, as she is taking it in quite a high dosage for her ankle pain, and also was prescribed by a locum doctor, who may not have

read through her notes properly and had time to take into consideration her other medications.

According to the Medsafe datasheet for Voltaren, if gastrointestinal bleeding or ulceration occurs in patients receiving Voltaren, the medication should be discontinued, and it has more serious consequences if this occurs in the elderly (Novartis, 2018).

Another potential interaction could be between the grapefruit juice that Vera drinks daily, and Zoloft. Grapefruit juice can inhibit cytochrome P450 CYP3A4 metabolism, which metabolises Zoloft, causing increased drug levels in the system and therefore potentially increasing the risk of adverse effects. The effects of grapefruit juice on CYP3A4 levels last at least 48 hours after being taken. It is recommended that the possible risk of adverse effects be taken into consideration when concurrent use of grapefruit juice and any medication metabolized by CYP3A4 is occuring. Patients that are 70 or older, and those taking multiple medications, are also at the greatest risk for a serious interaction to occur (Natural Medicines, 2019). Vera is 69, and is taking multiple medications, which puts her at greater risk, therefore the potential of interactions and adverse effects of grapefruit juice and Zoloft should be considered for her.

Vera drinks two cups of espresso per day after breakfast. According to the Natural Medicines database, there is a moderate possibility of adverse effects when caffeine and Zoloft are taken concurrently. In theory, caffeine can increase the risk of bleeding when taken at the same time as Voltaren, as caffeine is reported to have antiplatelet activities (Natural Medicines,

2019). However, there is not solid evidence of this occurring in humans, so it is just a possible interaction to be aware of, particularly as Vera has experienced bruising easily since beginning to take Voltaren.

Based on the research and evidence I have found about the medications, supplements, and diet that Vera has, as well as exploring and analysing any possible interactions and adverse effects, there are several recommendations that I would make based on critical analysis, and backed up by the scientific evidence discussed and referenced in previous paragraphs.

One important recommendation that I would make is to refer Vera back to her original doctor/specialist in order to ensure that the safety of the combination and dosages of Zoloft and Voltaren that she is concurrently taking. Based on studies and datasheets that I have found, evidence has shown that there are links between gastrointestinal bleeding and ulcers and the combination of taking NSAIDs and SSRI drugs concurrently, as well as NSAID drugs on their own. As Vera is taking the maximum safe dosage of Voltaren, in conjunction with Zoloft, and has experienced burning stomach pains and bruising easily since she began taking Voltaren, I would suggest that she must see her doctor so that he can review the possible interactions between these and decide whether it is safe for Vera to continue taking both Zoloft and Voltaren at their current dosages and administrations. As she was prescribed Voltaren by a locum doctor and not her specialist, this could have been a mistake that slipped under the radar and which her doctor may be able to identify and rectify if it is.

Another recommendation that I would possibly make, based on the evidence that grapefruit juice can interfere with the metabolism and pharmacodynamics of Zoloft, due to inhibiting cytochrome CYP3A4, is that Vera temporarily stops drinking grapefruit juice daily while she is taking Zoloft, to take precautions that they do not interact. I could not find any scientific evidence that proves that grapefruit juice increases the absorption of the calcium carbonate supplements that Vera takes, so it should not make a difference to the absorption of these. I would also recommend that Vera find a caffeine free alternative to the espresso she drinks daily, such as a caffeine free tea, as caffeine has a moderate risk of increasing bleeding when taken concurrently with Zoloft, and Vera has been experiencing bruising easily, so in order to minimize the possibility that the bruising has been a side effect of this combination, I would recommend this.

Based on evidence that I have found, I would also recommend for Vera to not begin taking the St Johns Wort tablets that her friend has recommended to her, in her current circumstances.

According to the Natural Medicines database, Saint John’s Wort, when taken concurrently with Zoloft, has a moderate risk of causing serotonergic side effects, including dizziness, nausea, vomiting, anxiety, confusion and irritability (Natural Medicines, 2019). As Vera is currently taking Zoloft for her symptoms of depression as prescribed by her doctor, I would recommend for her not to start taking Saint John’s Wort while she is taking Zoloft for these symptoms.

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