Pharmacology of Diabetic, Antihypertensive, and Antidepressant Drugs

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Living with diabetes oftentimes goes hand in hand with hypertension, and it is not uncommon for depression to result as part of living with comorbidities. W.L.R. is an 80 year old Caucasian male presenting with the following diagnoses: type 2 diabetes, hypertension, and depression. W.L.R. is a widow, has two children, lives alone, independent, and has a limited activity level. He currently takes several medications at different times throughout the day to control his diagnosed conditions. In addition to the diabetic, hypertensive, and antidepressant medications, he also takes medication to prevent acid reflux. The purpose of this paper is to address the pathophysiology of the above diagnoses, as well as the pharmacologic interventions for the various medications, specifically the home management plan for this client.

Diabetes mellitus is a disorder of carbohydrate, protein, and fat metabolism (Widmaier, Raff, & Strang, 2006b). Diabetes is characterized as a disorder of insulin availability or as an imbalance between insulin availability and insulin need (Matfin, Kuenzi, & Guven, 2007). The decreased insulin secretion occurs when the pancreas does not secrete enough insulin in response to glucose levels. People with uncontrolled diabetes are unable to transport glucose into fat and muscle cells. Therefore, the body cells are starved and begin to increasingly breakdown fat and protein (Matfin et al., 2007).

The pathophysiology involves both genetic and environmental factors (Matfin et al., 2007). Type 2 diabetes results from the combination of beta cell dysfunction and insulin resistance (Matfin et al., 2007). Insulin resistance is the result of a normally functioning endocrine system with hormone secretion, in which the target cells do not respond normally to the hormone (Widmaier et al., 2006b). A genetic predisposition for insulin resistance initially stimulates an increase in insulin secretion where the beta cells attempt to maintain a normal

blood glucose level (Matfin et al., 2007). The increased insulin secretion demand leads to beta cell exhaustion and failure. Therefore, the increased glucose production in the liver leads to hyperglycemia (Matfin et al., 2007). The pathophysiology of type 2 diabetes mellitus is characterized by peripheral insulin resistance, impaired regulation of hepatic glucose production, and declining ß-cell function, which eventually leads to ß-cell failure (Mahler & Adler, 2006).

Hypertension is a chronic condition in which the arterial blood pressure is consistently elevated (Widmaier et al., 2006a). Primary hypertension occurs from chronic elevation of blood pressure without evidence of other disease and the cause of arteriolar constriction is unknown (Roush, 2009). Secondary hypertension is when the elevation of blood pressure results from another disorder, such as kidney disease. Renal hypertension is caused by reduced renal blood flow and activation of the renin-angiotensin aldosterone mechanism (Porth & Matfin, 2007). Reduced blood flow causes the affected kidney to release excess amounts of renin which increases the circulating level of Angiotensin II (Porth & Matfin, 2007). Angiotensin II "acts as a vasoconstrictor to increase peripheral vascular resistance and as a stimulus for increasing aldosterone levels and retention of sodium by the kidneys" (Porth & Matfin, 2007, p. 369).

Depression is explained by the role neurotransmitters have in maintaining normal brain functioning (Kozy & Varcarolis, 2010). Neurotransmitters are chemical messengers that transmit nerve impulses from neuron to neuron at the synaptic cleft, in which they are synthesized in the brain and help control functions of the brain (Widmaier et al., 2006b). The monoamines groups affect depression (Kozy & Varcarolis, 2010). A deficit of norepinephrine and serotonin is what is thought to contribute specifically to the mood disorder (Kozy & Varcarolis, 2010). According to Kozy & Varcarolis, depression results from a dysregulation of a number of neurotransmitter systems, in addition to serotonin and norepinephrine. The dopamine, acetylcholine, and gamma-

aminobutyric acid systems are also believed to be involved in the pathophysiology of a major depressive episode (Kozy & Varcarolis, 2010).

Hypertension and diabetes are both independent risk factors for developing cardiovascular disease. Oftentimes, these diseases are coexisting, in which hypertension occurs twice as frequently in patients with diabetes than those without (Kloner et al., 2008). According to a study by Dobesh (2006), the American Diabetes Association presents guidelines for the use of angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) as the first line of initial treatment therapy to lower blood pressure in type 2 diabetics. ACE inhibitors or ARBs are chosen as the first line of treatment in patients with hypertension and diabetes due to the protective effects of these agents on the renal system (Kloner et al., 2008).

W.L.R. was prescribed the ACE inhibitor Lisinopril (Zestril) at the time of his diabetes diagnosis. His current dosage is one 40 mg tablet by mouth, once a day. The usual maintenance dosage is 20-40 mg once daily (Lehne, 2010d). Lisinopril is an ACE inhibitor and its mechanism of action works by reducing the levels of angiotension II, thus dilating the blood vessels and reducing the blood volume (Lehne, 2010d). Additionally, ACE inhibitors, such as lisinopril, can prevent or reverse pathological changes in the heart and blood vessels (Lehne, 2010d). The desired effects of using lisinopril are lowering blood pressure in hypertensive patients, reducing cardiovascular disease, and preventing problems associated with the kidneys in diabetic patients (Dobesh, 2006). Another mechanism of action for lisinopril is increasing levels of bradykinin which causes some of the common side effects of this drug, such as cough and angioedema (Lehne, 2010d). Angioedema is rare but can be fatal due to facial and tongue swelling which can cause constriction of the airways (Lehne, 2010d). Other common side effects include first dose hypotension, hyperkalemia, renal failure, fetal injury, dysgeusia, and rash (Lehne, 2010d). A rare

but serious adverse effect is neutropenia which is often associated with patients experiencing renal impairment (Lehne, 2010d).

The nurse will monitor blood pressure closely two hours after the first dose and periodically thereafter to assess for the first dose effect (Lehne, 2010d). Prior to administrating each dose of lisinopril the nurse will check blood pressure and ascertain if the medication is working properly (Lehne, 2010d). The nurse will also monitor the patient for signs of angioedema and stop immediately if any occur (Lehne, 2010d) The nurse should provide the patient with education about avoiding potassium supplements, lying down if hypotension should occur, notifying the physician of signs of infection or reaction to medication, and compliance is very important so if the patient misses a dose they should take it as soon as possible but not too close to the next dose (Lehne, 2010d).

"Most patients with diabetes will require two or more antihypertensive therapies from different classes with complementary mechanisms of action to control their blood pressure" (Dobesh, 2006, p.1144). Antihypertensive monotherapies are unlikely to achieve the recommended blood pressure for patients with diabetes (Kloner et al., 2008). Therefore, combination therapy is needed for the majority of patients to attain their blood pressure goal (Kloner et al., 2008). According to Kloner et al., calcium channel blockers, such as amlodipine, are effective antihypertensive agents and can be used in multidrug regimens for blood pressure control.

Calcium channel blockers (CCBs) can be added to ACE inhibitor or ARB treatment to achieve target blood pressure (Dobesh, 2006).

Amlodipine (Norvasc), a calcium channel blocker, was prescribed to W.L.R. as a mutlidrug therapy with lisinopril, for the treatment of his hypertension in combination with

diabetes. His current dosage is one 5 mg tablet by mouth, twice a day. The usual dosage for treating hypertension with Amlodipine is 5 mg once a day (Lehne, 2010c). Amlodipine blocks calcium channels in the vascular smooth muscle, which prevent calcium from entering the cells (Lehne, 2010c). Vasodilation occurs when calcium channels are blocked in the peripheral arterioles, therefore lowering the arterial pressure (Lehne, 2010c). Amlodipine works by reducing the peripheral vascular resistance and increasing the cardiac output and blood flow (Lehne, 2010c). The desired effect is to treat and lower the blood pressure in patients with hypertension (Lehne, 2010c). Additionally, amlodipine can be combined with ACE inhibitors to treat hypertensive patients with diabetes (Dobesh, 2006). Some common side effects of this drug are flushing, dizziness, headache, peripheral edema, and gingival hyperplasia (Lehne, 2010c). A life threatening adverse effect could occur with toxicity of amlodipine, evidenced by severe hypotension, bradycardia, AV block, and ventricular tachydysrhythmias (Lehne, 2010c).

While a patient is taking amlodipine, the nurse will monitor the blood pressure for therapeutic effects, as well as before administering each dose (Lehne, 2010c). The nurse will also monitor heart rate for dose-related palpitations (Lehne, 2010c).The nurse should inform the patient to report peripheral or facial edema, shortness of breath, palpitations, or irregular heartbeat to their doctor (Lehne, 2010c). Additionally, the nurse should educate the patient to use caution or support when walking or standing due to possible dose related dizziness (Lehne, 2010c).

Doxazosin (Cardura) is another antihypertensive medication prescribed as part of combination therapy for W.L.R. His current dosage is a 4 mg tablet by mouth, once a day. The starting dosage is 1 mg once a day but can be increased gradually up to 16 mg for the treatment of hypertension (Lehne, 2010a). Doxazosin is a selective alpha adrenergic blocker. The action of

this drug is dilation of the arterioles and veins producing the desired effect of lowering blood pressure in hypertensive patients (Lehne, 2010a). Common side effects of this medication include orthostatic hypotension, headache, nasal congestion, and headache (Lehne, 2010a). The most serious of the side effects is orthostatic hypotension (Lehne, 2010a).

There are several nursing implications and patient education that go along with doxazosin. The nurse will monitor blood pressure and heart rate before administering medication as well as educate the patient to do the same at home (Lehne, 2010a). The nurse should also monitor blood pressure after the initial dose or after any dosage increases because that is when postural hypotension is most likely to occur (Lehne, 2010a). The nurse should instruct the patient to take the first dose at night to minimize the "first dose" effect (Lehne, 2010a). In addition to warning the patient about the "first dose" effect, the nurse should advise the patient against driving or other hazardous activities within 12-24 hours of taking the initial dose (Lehne, 2010a). The nurse should educate the patient about the symptoms of hypotension and advise them to sit or lie down if any should occur (Lehne, 2010a). Lastly, the nurse will advise patients to change positions slowly to avoid orthostatic hypotension (Lehne, 2010a).

Insulin glargine (Lantus) is long acting drug used to treat diabetes mellitus (Lehne & Shlafer, 2010). W.L.R. administers 50 units of insulin glargine subcutaneously at bedtime. The usual dosage begins at 10 units given at bedtime but can be increased to be individualized to the patient (Lehne & Shlafer, 2010). Insulin glargine is a human insulin analogue that exhibits constant absorption from the injection site (Kacerovsky-Bielesz, Dressler, & Freunscht, 2006). There are no pronounced peaks in blood insulin levels and a long (24 hours) duration of action is present in patients with Type 2 diabetes (Kacerovsky-Bielesz et al., 2006). The desired response is for glycemic control and lowering of the blood glucose over extended periods of time,

resulting in less risk of hypoglycemia and hyperglycemia (Lehne & Shlafer, 2010). The blood glucose is lowered by the insulin stimulating peripheral glucose uptake in muscle and fat tissue, as well as inhibiting hepatic glucose production (Lehne & Shlafer, 2010). Common side effects include symptomatic hypoglycaemia, systemic hypersensitivity, and injection site reactions (Kacerovsky-Bielesz et al., 2006).

There are many nursing implications and patient education that are essential for administering insulin glargine, especially since it is given subcutaneously. The nurse will monitor fasting blood glucose periodically and assess for signs and symptoms of hypoglycemia (Lehne & Shlafer, 2010). The nurse will educate the patient on proper injection sites, rotating injection sites, checking blood glucose, and signs of hypoglycemia and hyperglycemia (Lehne & Shlafer, 2010). The patient should be informed to ingest some form of sugar if hypoglycemia occurs and to seek medical attention (Lehne & Shlafer, 2010). The nurse will teach the patient how to administer subcutaneous injections, the importance of cleaning the vial cap and injection site with alcohol, and how to eliminate air bubbles from the syringe (Lehne & Shlafer, 2010). Lastly, the patient should be told to keep blood glucose between 80 and 120 mg/dl and report values outside the range (Lehne & Shlafer, 2010). Also, they should notify the physician of fever, infection, nausea, vomiting, and diarrhea which could indicate need for dosage adjustment (Lehne & Shlafer, 2010).

Venlafaxine (Effexor) is a serotonin norepinephrine reuptake inhibitor antidepressant, thus blocking the reuptake of norepinephrine and serotonin and weakly blocking the uptake of dopamine (Lehne, 2010b). The desired response of this drug in W.L.R. is to provide for the treatment of depression (Lehne, 2010b). W.L.R. current dosage is 150 mg tablet by mouth, once a day. The usual recommended dose in treating depression is 75 mg/day in two divided doses

(Lehne, 2010b). However, the dose can be increased up to 225 mg/day if needed based on individual patients (Lehne, 2010b). Common side effects of venlafaxine are nausea, headache, anorexia, nervousness, sweating, somnolence, insomnia, diastolic hypertension, and sexual dysfunction (Lehne, 2010b). The most life threatening adverse effects are suicide ideation and serotonin syndrome (Kozy & Varcarolis, 2010).

While a patient is using venlafaxine, the nurse will monitor for worsening signs of depression or suicidal ideation in the patient (Kozy & Varcarolis, 2010). The nurse should monitor blood pressure, heart rate, and weight periodically, as well as lab tests (Kozy & Varcarolis, 2010). The nurse should also provide education to the patient taking venlafaxine. The patient should be informed not to abruptly stop this medication or take concurrently with or recently discontinued MAOIs (Kozy & Varcarolis, 2010). The nurse will inform the patient to report worsening mental status, not to drive until response to drug is known, and to avoid alcohol while on venlafaxine (Kozy & Varcarolis, 2010).

After having discussed each of the medications W.L.R. is prescribed, it would be a good idea to take a look at the cost analysis for a one month's supply of medications. As evidenced by the table below, the generic costs are typically significantly less than the trade costs. However, the insulin glargine (Lantus) is currently only prescribed under the trade name, therefore, the cost for generic is the same as the trade for that drug. Overall, buying the generic of these medications would save a patient 12%. However, insurance saved W.L.R. a significant amount of the costs for the needed medications. The patients actual cost after insurance is approximately 4% of the trade costs.

Drug	Trade Cost	Generic Cost	Patient Pays
Amlodipine (Norvasc)	$130	$15	$1.50
Lisinopril (Zestril)	$77	$18	$3.00
Doxazosin (Cardura)	$60	$22	$3.00
Insulin glargine (Lantus)	$168	*$168	$13.50
Venlafaxin (Effexor)	$150	$142	$3.00
TOTAL	$585	$515	$24.00
*No generic available			

In conclusion, several medications were researched and related back to W.L.R. and his diagnoses. Blood pressure medications are commonly prescribed in combination with one another, which was the case for W.L.R. The insulin glargine prescribed is intended for bedtime use as it is a long acting insulin and the venlafaxin is for the treatment of his depression. Many nursing implications and patient education were addressed for this patient and his home health care. Although the cost of these medications can be extremely expensive on a monthly basis, W.L.R. fortunately has adequate insurance coverage to significantly decrease his medical expenses. This paper allowed for a substantial learning experience related to the mentioned diagnoses, medications, and implications. It further allowed for an appreciation of medication costs.

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