3-30-2018

Diabetic Neuropathy

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Spring 2018

Title

Department Nursing

Degree Master of Science

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Abstract

In the United States alone, approximately 30.3 million people have diabetes (CDC, 2017; NIDDK, 2017). Of the complications associated with diabetes, diabetic neuropathy is the most common complication at about 90% and is a leading cause of morbidity in diabetic patients (Cohen, Shinkazh, Frank, Israel, & Fellner, 2015; Juster-Switlyk & Smith, 2016; Schreiber, Nones, Reis, Chichorro, & Cunha, 2015). A literature search was completed using the University of North Dakota's School of Medicine and Health Sciences Library to research the ways in which diabetic peripheral neuropathy is best treated and managed. As the prevalence of diabetes, and subsequently diabetic neuropathy, increases, it becomes increasingly important to study and understand the ability to manage and reduce diabetic neuropathy. Early diagnosis and management of diabetic neuropathy is important for reducing healthcare costs and prevention of other diabetic complications such as falls, foot ulcers, amputations, fractures, death, etc. (Khalil, Chambers, Khalil, & Ang, 2016). This paper reviews the case study of a patient experiencing peripheral diabetic neuropathy and highlights the ways in which providers can effectively manage and reduce diabetic neuropathy by providing patient education, implementing strict glycemic control, and using pharmacologic and non-pharmacologic measures.

Keywords: diabetic peripheral neuropathy, management, and neuropathic pain

Diabetic Neuropathy

A sixty-year-old Caucasian female presented for a diabetes recheck per recommendations from her diabetic educator last week. During the visit, the patient complained of numbness and tingling to her left great toe and first metatarsal. The patient reported that at that time, because the numbness and tingling were limited to a small area, it was not causing her any discomfort and was not affecting her quality of life. Her hemoglobin A1c level, hypercholesterolemia, blood pressure, alcohol use, and weight are all risk factors for the development of diabetic peripheral neuropathy (NIDDK, 2013).

Of the 30.3 million people with diabetes, 7.2 million are undiagnosed (CDC, 2017; NIDDK, 2017). Additionally, the prevalence of diabetes is increasing by 5% each year (CDC, 2017; NIDDK, 2017; Juster-Switlyk & Smith, 2016). With the prevalence of diabetes increasing every year, the prevalence of diabetic neuropathy is also increasing. Diabetic neuropathy can be diagnosed by noting a loss of vibratory and position sense, loss of sensation, and/or a loss or reduction of the Achilles tendon reflex (Feldman, 2017). However, in order to rule out other etiologies, laboratory tests should be completed (Epocrates, 2018). Laboratory testing for patients with neuropathies should include thyroid function, vitamin B12, immunoglobulin electrophoresis, electrolytes, complete blood count (CBC), and erythrocyte sedimentation rate (Epocrates, 2018). Determining whether a complaint of numbness and/or tingling is truly a result of peripheral neuropathy or is a CNS lesion can be done using a 128-Hz tuning fork (Azhary, Farooq, Bhanushali, Majid, & Kassab, 2010). When utilizing the tuning fork to test vibratory sensations, a loss of sensation is indicative of peripheral neuropathy. The clinical manifestations of diabetic neuropathy include loss of pain sensation, tingling, burning, “electric shocks”, allodynia, hyperalgesia, and a sensation of “pins and needles” (Juster-Switlyk & Smith, 2016).

Additional signs and symptoms can include falling due to lack of coordination, muscle weakness, a variety of sensations in the area, and patients may complain of pain that is gradually spreading from the feet, upwards to the legs, and even the arms (MayoClinic, 2017). Typically, neuropathy is first noted in the toes, as with the patient described in this case study (Feldman, 2017). Characteristically, the neuropathy is noted symmetrically, on both sides of the body (Feldman, 2017).

Knowing when to initiate active treatment and the best way to reduce and manage peripheral neuropathy can be difficult; however, it is important in helping reduce complications and morbidity in diabetic patients. Diabetic peripheral neuropathy is known to currently be reduced and/or managed with patient education, glycemic control, pharmacologic agents, and non-pharmacologic measures.

Case Report

A sixty-year-old Caucasian female patient presented to the clinic for a diabetes recheck per the recommendation of the diabetes educator last week. The patient reported a past medical history significant for diabetes mellitus type II, hypertension, and hyperlipidemia. The patient reported an increase in fatigue, a weight gain of about twenty pounds in the past two years, and an increase in urinary frequency. She stated that she was currently checking her blood sugar about twice per week which ranges from 150-200 mg/dL. The patient was currently taking metformin 500 mg twice daily, aspirin 81 mg daily, lisinopril 20 mg daily, atorvastatin 20 mg daily, and a daily multivitamin; she reported compliance with taking her medications as prescribed. She denied pain at that time. She was up to date on her influenza vaccination but denied having had the pneumonia vaccination. She denied smoking or illicit drug use. She reported drinking two beers on two to three nights per week. She currently works as a pharmacy

technician and stated that her job can be stressful at times but was manageable.

Vitals signs at the time of the visit were blood pressure: 148/98, pulse: 80, respirations: 20, and temperature: 98.6. No weight was obtained during the visit, but some central obesity was noted. The physical exam was fairly unremarkable. Pertinent findings did include the blood pressure of 148/98 as The Eighth Joint National Committee (JNC 8) recommends a blood pressure of no more than 140/90 in patients with diabetes. The patient also had a monofilament score of 8/10 to her left foot; loss of sensation was noted to her left foot first metatarsal and great toe. Patient reported that this was sometimes distracting and odd feeling but denied that it was affecting her quality of life in any way.

A hemoglobin A1c, lipid panel, and comprehensive metabolic panel were requested by the provider and reviewed on this visit. The A1c resulted as 7.8%. The lipid panel showed an abnormal total cholesterol of 220 mg/dL, triglycerides of 186 mg/dL, and high-density lipoproteins (HDL) of 36 mg/dL. The comprehensive metabolic panel was unremarkable.

The treatment plan for this patient included improved management of diabetes mellitus type II, hypertension, and hyperlipidemia. Glimepiride 1 mg every day was added to her already ordered metformin 500 mg twice daily to assist in managing her diabetes. It was requested that she check her blood sugars daily at random times and to record the results with a plan to follow-up in one month. The goal was to decrease her hemoglobin A1c to less than 7%. The plan also included monitoring of the patient's left foot neuropathy as it was currently limited to the left first metatarsal and great toe and was not inhibiting patient's activities or quality of life, nor was it causing her any pain. Based on the American College of Cardiology (n.d.) ASCVD (Atherosclerotic Cardiovascular Disease) risk estimator, the patient had a current 15.6% ten-year ASCVD risk. Therefore, it became especially important to manage this patient's blood pressure

and cholesterol as they were modifiable factors for this patient. Regarding the patient's blood pressure, she denied checking her blood pressure at home. It was requested that she purchase a home blood pressure cuff and check and record her blood pressures every other day for one month in addition to continuing her already ordered lisinopril 20 mg daily. The goal was to decrease her blood pressure to less than 140/90, per JNC 8 guidelines. Lastly, atorvastatin 20 mg was increased to 30 mg with a goal of reducing her cholesterol and triglycerides to less than 200 and 150, respectively. Patient education included the importance of moderate exercise daily for at least thirty minutes to help reduce weight, improve blood sugar control, and improve blood pressure control. The patient was also educated on the importance of wearing well-fitting footwear, not walking barefoot, and completing daily bilateral foot checks to prevent diabetic foot wounds. The patient was encouraged to receive her pneumonia vaccine, complete a dual-energy X-ray absorptiometry (DEXA) scan, and colonoscopy as she denied having completed these health maintenance procedures.

Literature Review

Diabetic neuropathy is the most common complication of diabetes mellitus and is important to diagnose and manage early to avoid further diabetic complications (Juster-Switlyk & Smith, 2016; Khalil et al., 2016). The patient previously described had a diagnosis of type II diabetes and was experiencing the clinical manifestations of diabetic neuropathy. The neuropathy was likely the consequence of unmanaged glycemic control, hypertension, dyslipidemia, and the length of time the patient has had diabetes (Cohen et al., 2015). The goals of managing diabetic peripheral neuropathy include pain control, an improvement in glucose control, restoring the patient's functioning, and providing patient education (Cohen et al., 2015). A literature review regarding diabetic peripheral neuropathy showed that it can be prevented, managed and/or

treated with patient education, glycemic control, pharmacologic measures, and non-pharmacologic measures. The prevalence of diabetes mellitus is increasing drastically, therefore increasing the prevalence of peripheral neuropathy. As a result, it is becoming increasingly important for providers to be knowledgeable about prevention and management of diabetic peripheral neuropathy in order to delay and avoid further associated complications.

Patient Education

Patient education is valued as it is important for the patient to understand the cause of neuropathy as well as the management in order to improve compliance (Javed, Petropoulos, Alam, & Malik, 2015). Patient education regarding the symptoms and risks associated with diabetic peripheral neuropathy is the provider's responsibility for primary prevention of complications such as falls, amputations, foot ulcers, fractures, or even death (Cohen et al., 2015; Juster-Switlyk & Smith, 2016). Education as simple as encouraging the patient to wear the appropriate footwear, completing foot examinations, the importance of having podiatry care, falls prevention, and making lifestyle changes is important in both the prevention of and management of neuropathy (Cohen et al., 2015; Javed, Alam, & Malik, 2015a). It is also vital that the patient is educated in order to improve glycemic control, an important part of both prevention and management (Javed et al., 2015c).

Glycemic Control

There are many theories that suggest why hyperglycemia may cause neuropathy. Still, the pathophysiology of the development of neuropathy still remains largely unknown (Schreiber et al., 2015). Glycemic control is considered a prophylactic therapy for diabetic peripheral neuropathy (Schreiber et al., 2015). It is now understood that glycemic control reduces the risk of peripheral neuropathy in those with type I diabetes, more so than with type II diabetes (Juster-

Switlyk & Smith, 2016). Good glycemic control, with a hemoglobin A1c of less than 7% in patients with type I diabetes can potentially decrease the incidence of peripheral neuropathy by 60-70% whereas in type II diabetes the incidence is only decreased by 5-7%. However, even those with good glycemic control with a hemoglobin A1c of less than 5.4%, are still at risk (Juster-Switlyk & Smith, 2016). While glycemic control does not decrease the incidence of neuropathy as strongly in type II diabetes, it is still considered a modifiable factor and does improve vibration detection and motor nerve conduction (Callaghan, Little, Feldman, & Hughes, 2012). Oral sensitizing medications can be utilized in patients with type II diabetes to manage glycemic control and have been found to decrease neuropathy (Cohen et al., 2015).

Results of the Diabetes Control and Complications Trial indicated that thirteen to fourteen years after the end of the initial study, tight glycemic control continued to reduce the risk of diabetic peripheral neuropathy (Javed et al., 2015b; Martin, Albers, Pop-Busui, & DCCT/EDIC Research Group, 2014). Risks associated with tight glycemic control in both types of diabetes include hypoglycemic events, impaired consciousness, weight gain, and death. This makes it important for the provider to weigh the risks and benefits for each patient as well as indicates the need for further research to determine the optimum glycemic target (Callaghan et al., 2012). In patients who experience painful neuropathy, tight glycemic control is found to no longer be effective in reducing or preventing neuropathy and symptomatic control with pharmacotherapy becomes necessary (Cohen et al., 2015; Javed et al., 2015b).

Pharmacologic Measures

Pharmacologic measures are mainly focused on symptom management and are unable to treat the cause of painful peripheral neuropathy (Schreiber et al., 2012). Research tended to agree that anticonvulsants and tricyclic antidepressants remain the first line treatment of neuropathic

pain and are the most efficacious (Schreiber et al., 2015; Javed et al., 2015b; Javed et al., 2015c; Votrubec & Thong, 2013; Khalil, 2016). The antidepressants amitriptyline, venlafaxine, and duloxetine are typically used first over other antidepressants. There is a lack of evidence to show that any of the previously mentioned antidepressants are any more effective than the others (Cohen et al., 2015). The American Academy of Neurology (AAN) has provided a set of guidelines for the treatment of neuropathic pain. The guidelines set forth are reflected in research recommendations which recommends the use of the anticonvulsant, pregabalin, as first line treatment over other anticonvulsants such as Gabapentin and sodium valproate (Cohen et al., 2015; AAN, 2011).

Non-steroidal anti-inflammatory drugs (NSAIDs) have not been shown to be valuable in diabetic peripheral neuropathy and are not recommended due to their adverse effects in diabetic patients, such as gastrointestinal hemorrhage or exacerbation of renal dysfunction (Javed et al., 2015b; Javed et al., 2015c; Cohen et al., 2015). Opioids can be utilized; however, this class of medications should only be used as a second or third line option and considered when other therapies have not proven to be effective (Cohen et al., 2015). The risks of long-term use of opioids for peripheral neuropathy is controversial due to the many adverse effects, in addition to the high rate of abuse and risk of dependence (Javed et al., 2015b).

Topical agents can also be considered for the treatment of pain. Topical agents utilized may include capsaicin, topical nitrate, 5% lidocaine, and intradermal botulinum toxin type A (Javed et al., 2015b). There is little evidence to prove the use and efficacy of topical treatments due to a lack of studies (Peltier & Callaghan, 2014). Capsaicin has been found to be somewhat intolerable due to initial pain when applied. Lidocaine is typically only effective for local, rather than disperse pain (Peltier & Callaghan, 2014). Intradermal botulinum toxin type A has been

shown to reduce pain and improve sleep; studies have shown its efficacy when compared to a placebo (Javed et al., 2015b; Waldfogel et al, 2017). While topical agents are not considered first line, their benefit may be in patients who have multiple co-morbid conditions, as they have few drug-drug interactions (Peltier & Callaghan, 2014).

Non-Pharmacologic Measures

Non-pharmacologic measures can also be considered in the management of painful diabetic peripheral neuropathy. These measures are mainly considered when other treatments are inadequate or cannot be used (Javed et al., 2015b). These treatments can consist of electrical stimulation, acupuncture, exercise, and education regarding continued glycemic control. Electrical stimulation has inconsistent study results with some saying that it is likely effective and others denying its efficacy (Javed et al., 2015b; Peltier & Callaghan, 2014). Thus far, acupuncture has not shown to be successful in studies that have been completed (Javed et al., 2015c).

Exercise has been newly studied for its role in diabetic neuropathy. Exercising routinely can potentially prevent or delay some causes of peripheral neuropathy (Dobson, McMillan, & Li, 2014). According to Dobson et al. (2014), "…benefits of exercise training include improvements in nerve function, reductions in neuropathic pain, reductions in other types of sensory dysfunction (e.g., numbness) and improvements in both static and dynamic functional mobility in those with peripheral neuropathy" (para. 25). Thus far, routine strength-stability and aerobic exercise has been studied. While positive results have been found in sensory benefits, neuropathic pain, and the known general benefits of exercise, more studies are needed (Dobson et al., 2014). Juster-Switlyk and Smith (2016) also discussed how diet and exercise have been shown to reduce pain and reduce the risk of falls. While exercise may have been found to be

efficacious in the prevention of neuropathy, more studies are needed to assess its efficacy in patients who have already developed the complication (Javed et al., 2015b).

Conclusion

Diabetic peripheral neuropathy is growing in prevalence due to an increase in the prevalence of diabetes. Several complications such as foot ulcers, amputations, falls, fractures, death, etc. can result if the neuropathy is left untreated. Patient education and glycemic control are important in helping prevent or delay neuropathy. When pain occurs with the neuropathy there are several pharmacologic and non-pharmacologic treatment options, all with varying efficacy. Reducing and managing the complications of diabetes is both the patient's and provider's responsibility. It is the patient's responsibility to be proactive in participating in the education and instruction she has received from her provider and to return for follow-up appointments to ensure that her glycemic control, hypertension, and hyperlipidemia can be managed appropriately. Meanwhile, it is the provider's responsibility to take this patient's diagnosis and subsequent neuropathy seriously in order to prevent further complications. Currently, patient education regarding diabetes management and self-care measures and glycemic management are the only known measures to prevent diabetic peripheral neuropathy; however, new research is showing that exercise may also be effective in prevention. It seems appropriate for the patient in this case to work on diet and exercise and to be vigilant with her instruction to reduce her hemoglobin A1c, blood pressure, and cholesterol in order to help prevent and delay worsening neuropathy. For painful diabetic neuropathy, pharmacologic and non-pharmacologic agents can be used. First line agents include tricyclic antidepressants and anticonvulsants. Of the medication classes discussed, duloxetine, pregabalin, and tapentadol are the only medications that have been approved for the use of diabetic peripheral neuropathy by

the food and drug administration (FDA), all others are prescribed off-label but have shown to be efficacious nonetheless (Cohen et al., 2015). Proper management of diabetic peripheral neuropathy can help in preventing further diabetic complications, indicating the importance of provider knowledge in the treatment of diabetic peripheral neuropathy.

Learning Points

- It is the provider's responsibility to provide the patient with the necessary education to be active and compliant in managing their disease, as well as prevent complications.
- Early diagnosis and management of peripheral neuropathy is essential in preventing additional diabetic complications and reducing healthcare costs. Further complications can include falls, amputations, foot ulcers, fractures, death, etc.
- Glycemic control should be utilized for prophylaxis of diabetic peripheral neuropathy. Glycemic control is more efficacious in type I diabetes than type II; nevertheless, it is beneficial to both types. The risks and benefits of tight glycemic control must be weighed for each patient to help avoid adverse events. It is no longer effective to maintain tight glycemic control for peripheral neuropathy once the neuropathy has become painful.
- Painful neuropathy can be treated with tricyclic antidepressants and anticonvulsants as first line therapy. If needed, opioids and topical agents can be utilized as second and third line therapy.
- Non-pharmacologic measures can be considered for use in the management of painful diabetic peripheral neuropathy. Electrical stimulation has shown inconsistent study results. Acupuncture has not shown efficacy in completed studies. Exercise has shown the most benefits in preventing or delaying the onset of neuropathy, but more studies are needed regarding exercise in the treatment or management of developed neuropathy.

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