Review Article

A review on Diabetic Neuropathy: Complications and treatment

Vandana Pokhriyal*, Preeti Kothiyal, Neeraj Kumar, Sudhakar Kaushik

Division of Pharmaceutical Sciences, Shri Guru Ram Rai Institute of Technology and Science, Dehradun, Uttarakhand, India

Received: 31 May 2018 Revised: 26 June 2018 Accepted: 27 June 2018

Abstract

Diabetes Mellitus is the commonly prevalent and diverse metabolic disorder caused by occurrence of hyperglycemia with disturbance of carbohydrate metabolism, fat & protein metabolism. Diabetic Neuropathy is the most common and debilitating complication of diabetes mellitus and results in pain and decreased motility. Long term hyperglycaemia elicits enhanced Polyol pathway, increased non-enzymatic glycation of various structural proteins, which moreover increased oxidative stress as well as altered the protein kinase C (PKC) activity and poly ADP-ribose polymerase (PARP) activation that are all inter-related for the cause and development of neuropathy. Microvascular complication Diabetic neuropathy leads various complications such as loss of sensation, foot ulcer, urinary tract infection, gangrene, sexual dysfunction. Treatment of Neuropathy consist two beneficial approaches: pathogenic treatment and symptomatic treatment. Diabetic neuropathy symptomatic treatment involves the use of tricyclic antidepressant, serotonin norepinephrine reuptake inhibitor, selective serotonin reuptake inhibitor, Opioids and topical medication while pathogenic treatment include glycemic control, pancreas transplant, Alpha lipoic acid(antioxidant). Main goal of the treatment is to prevent neuropathic pain and complication associated with neuropathy.

***Keywords*:** Diabetes, neuropathy, hyperglycemia, foot ulcer

Introduction

Diabetes, moreover referred to as diabetes mellitus, is a type in which body is not competent to accurately normalize blood sugar level. Diabetes Mellitus is the commonly prevalent and diverse metabolic disorder caused by occurrence of hyperglycemia with disturbance of carbohydrate metabolism, fat & protein metabolism. It is the leading cause of morbidity and is the 5th leading cause of death in the United States. Diabetes is a bulge of continual diseases characterized by hyperglycemia. Over time, having too much glucose in blood can cause serious problems. It can damage eyes, kidneys, and nerves and also cause heart disease, stroke and even the need to remove a limb. Gestational diabetes is a condition when pregnant women suffer from diabetes. The destructive call sound effects of hyperglycemia are separated into Microvasular (such as diabetic neuropathy, nephropathy & retinopathy) and Macrovasular (such as Coronary artery disease, Peripheral disease & stroke) complications. At a current time, Diabetes Mellitus branded as disabling disorders. The frequency quotient is 7% in one day of newly diagnosed diabetes and 50% in stretched posture diabetes history tolerant aged on top than 25 year. Among them 12% patients suffer from Diabetic neuropathy. Predictions for the next 20 years show that diabetes prevalence will continue to rise, reaching epidemic proportions by 2030 (Wild et al., 2004; Cnop et al., 2005; Michael and Flowcer, 2008).

Address for Corresponding Author:
Vandana Pokhriyal
Division of Pharmaceutical Sciences, Shri Guru Ram Rai Institute of Technology and Science, Patel Nagar, Dehradun 248001, India
Email: pvandu95@gmail.com

Diabetic Neuropathy

Diabetic neuropathy (DN) is a most common complication of diabetes mellitus, caused by low response of blood flow and hyperglycemia leading to Nerve damage. Diabetic Neuropathy affect nearly 66% of type1 and 59% of typeII diabetic patient and 20% of all diabetic patients suffer from chronic neuropathic pain (NP). International Association for the study of pain (IASP) defined Diabetic Neuropathy-"Pain initiated or caused by a primary lesion or dysfunction in the nervous system". Diabetic neuropathy characterizes a dynamic fluctuation between neuronal falling apart and regeneration. Neuropathies are a family of nerve disorders caused by diabetes. It is regular and unbearable Microvascular complication of both type 1 and type 2 diabetes. Up to 50% of every single one patient with diabetes

DOI: https://doi.org/10.31024/ajpp.2018.4.4.6

arise neuropathy and the popularity of heartrending neuropathy ranges from 10 to 20% of patients with diabetes. Diabetic patient over time can develop, nerve impairment throughout the body. Path physiology of Neuropathy including elevated hexosamine shunt, aldose reductase activation, decreased nerve myoinositol content, activation of protein kinase C, activation of poly ADP-ribose polymerase, impaired insulin/C peptide action, and formation of advanced glycation end products (AGEs).Nerve destruction produce symptoms such as pain, tingling, or numbness-loss of feeling-in the hands, arms, feet and legs. The maximum rate of neuropathy in those cases in which, people had diabetes for at least 25 year(James et al., 2008).

Classification of DN

Diabetic neuropathy is not a solo being but a quantity of atypical syndromes, ranging from subclinical to clinical manifestation depending on the curriculum of nerve fibers involved. It has been efficiently predictable that the secret code and symptoms of DN & treatment depending upon the types of neuropathy and the nerves affected (Bansal et al., 2006; Kehal et al., 2013). DN can be classified as:

- Peripheral neuropathy
- Autonomic neuropathy
- Proximal neuropathy
- Focal neuropathy

Peripheral Neuropathy

Peripheral neuropathy, additionally called distal symmetric neuropathy or sensorimotor neuropathy. It is the large amount common form of DN in which the distal parts of the extremities are exaggerated consequential in sensory loss. It involves equally in minor as well as greater fibers and has insidious inception. Moreover, it involves the impairment of nerves in legs, hands and arms. Feet and legs are likely to be affected before hands and arms. The symptoms of peripheral neuropathy can be manifested by changed heat perception, hyperaesthesia, par aesthesia, numbness, hyperalgesia, allodynia, loss of balance, tingling, pickling sensation or burning feeling, muscle weakness, foot injury, bone and joint pain and loss in lower limb. Effected parts are: Toes, feet, legs, hands, arms (Watkins et al., 1984; Tesfaye et al., 1996).

Autonomic Neuropathy

Autonomic neuropathy is an acute and habitually (frequently) overlooked element of diabetic neuropathy. Any organ of the body connected by autonomic nerves if exaggerated leads to the changed functions of digestive system, heart, sweat glands, sexual organs, bowel and bladder function, perspiration and urinary system. It has been acknowledged that about 65% of type 2 diabetic patients state autonomic neuropathy. Further, the increasing rate stern develop of autonomic neuropathy affects the survival and leads to loss of life. Heart and blood vessels, digestive system, urinary tract, sex organs, sweat glands, eyes, lungs mainly affected (Rebrina, 2013).

Proximal Neuropathy

Proximal neuropathy is also called lumbosacral plexus neuropathy, femoral neuropathy, or diabetic amyotrophy, starts with soreness in the thighs, hips, buttocks, or legs, frequently on one part of the body. It predominantly affects the elderly males (> 50 year) having type 2 diabetes mellitus. They may be symmetrical or asymmetrical, with or without sensory thrashing. It predominately affects fore (quadriceps) and adductor compartments of thigh. Weakness of quadriceps is consequently dangerous that the knee regularly set way, and patients may fall. In addition, patients on hand with this group of DN generally obtain stumbling block in climbing the stairs due to pain. Effected parts are: Thighs, hips, buttocks, legs (Barohn et al., 1990).

Focal Neuropathy

Focal neuropathy appears rapidly and affects special nerve which is above all linked with head, torso or leg. Focal neuropathy may make happen lack of ability to focus the eye, double vision, aching behind one eye, paralysis on one side of face which know as Bell's palsy syndrome, Pain sensation in the lower back or pelvis, hurting in the adjoin of a thigh, pain in the chest, stomach, or side, pain on the outside of the shin or inside of the foot, chest or abdominal pain that is occasionally flawed for heart disease, a heart attack, or appendicitis. It is most common type of sorrowful and unpredictable neuropathy and occurs generally in adults with diabetes. However, it tends to convalesce by itself over weeks or months and does not cause long-term impairment. The main subtypes which are implicated in Focal neuropathy are: Cranial neuropathy, Truncal neuropathy, snare neuropathy. Eyes, facial muscles, ears, pelvis and lower back, chest, abdomen, thighs, legs, feet (Medicin, 2007).

Complications

Loss of limb

In diabetic neuropathy nerve impairment causes lack of sensation in feet, scratch &sores. This may go unobserved and eventually become harshly infected or ulcerated. It is a condition in which skin & soft tissue brokendown. The risk of infection is high because diabetes reduces blood flow in feet. It is a circumstance in which skin & soft tissue brokendown. The possibility of infection is high for the reason that diabetes reduces blood flow in feet. Infection extends to the bone and cause tissue death (gangrene) which

may be difficult to cure and treat for that amputation of toe, foot or lower leg require (Spero, 2015).

Charcot joint

Joint mainly in foot become injured because of nerve impairment, it is known as Charcot joint. Charcot joint Manifested by loss of sensation, as well as swelling, instability or sometime detoriates in the joint itself. Suitable medical care and treatment healing and prevent future damage (Abott and Vileikyte, 1998).

Urinary tract infection and urinary incontinence

Damage to the nerves that control bladder can cause severe effect in urinary system. This nerve damage allows bacteria to multiply in bladder and kidneys, leading to urinary tract infections. It can also cause loss of feel when urinate & disability to control the muscles that release urine (Cornblath and Davia, 2004).

Hypoglycemia unawareness

When blood sugar level is low- below 70 milligram per decilitre (mg\dl) or 3.9 milimoles per liter (mmol/L) this conditions expand symptoms such as Shakiness, instability, sweating, starvation heartbeat. People with autonomic neuropathy, if symptoms may not occur, it make hypoglycemia difficult to recognize. Problems other than neuropathy can also cause hypoglycemia unawareness (Roshna and Thaifa, 2007).

Low blood pressure

Diabetic neuropathy damage nerve that control circulation can affect body's ability to adjust blood pressure. This cause sharp drop in pressure when we stand after sitting which is also known as orthostatic hypotension, this may led to dizziness and fainting. Diabetic neuropathy cause destruction of nerve that direct motion and involve body's power to correct blood pressure. This foundation punctually bead in pressurize what time we stand up after meeting which is additionally established as orthostatic hypotension, this may led to vertigo and fainting.

Digestive problems

In digestive system nerve destruction may lead to improper bouts of constipation & diarrhoea and also cause nausea, vomiting, bloating and loss of appetite. Diabetic neuropathy causes Gastroparasis, a condition in which stomach empties excessively low point or not at all. It can interfere with absorption, digestion and raise many type of digestive problems, which effect blood sugar level and nutrition of our body.

Gastroparasis

Neuropathy affect the stomach nerve (also called as vagus nerve) which cause diabetic gastroparasis. It is a neuropathy complication interferes with digestive system leads to the digestive complication.

Sexual dysfunction

A most important impact of diabetic nerve damage manifests as sexual dysfunction. Nerves are injured by hyperglycemia and low blood flow. Sexual neuropathy in men causing erectile dysfunction, lack of desire, or incapability to orgasm. In women, nerve impairment can cause diminish lubrication, pleasure, orgasm and relaxation. It can also affect sex life.

Decreased and increase sweating

In Diabetic neuropathy sometime excessive sweating may seemed especially at night while eating. Body sweat gland play important role to regulate body temperature if they don't work properly, body is incapable to regulate its temperature mannerly. A reduced or completely lack of perspiration (anhidrosis) can be life threatening.

Diabetic foot ulcer

Neuropathy damage nerve in foot which cause an open wound and sore on the skin that's slow to heal is known as foot ulcer. This mostly occurs in people with peripheral neuropathy. Blister is formed in ulcer due to improper fitting shoes and careless towards foot. If we walk continue without care & protect of blister, it may turn into an ulcer. Prohibitive blood sugar level be able to impaired blood vessels, caused incorrect blood supply befall restricted. A low blood supply to the skin in the feet shows that it collect less amount of infection fighting cells , which means wound healing time get longer, be capable of go ahead to gangrene. People with chronic conditions, such as diabetes, are particularly susceptible to foot ulcers. People with persistent conditions, such as diabetes, are intensely susceptible to foot ulcers. In fact, about 15 percent of every single one patient with diabetes will cause a foot ulcer at any state of their lives. Healthy care of foot put the brakes on foot ulcers before it develop(Khwja and Neera, 2007).

Gangrene

Peripheral neuropathy exploit a wound infection on the feet, there is a possibility lead to gangrene (death of the infected part of skin or underlying tissue). In gangrene it required surgery to eliminate the damaged tissue (known debridement) and antibiotic to take care of any underlying infection. In serious cases patient toe & feet may necessitate to be amputated. Diabetes person must take extra care of feet and get regular check-up by foot specialist (Podiatrist). Gangrene also occurs inside the body, damaging organs and muscles & outside the body fingers toe and limbs are most often affected (Khan et al., 2015).

There are two main types of gangrene:

Dry gangrene: More common in people with blood vessel

disease, diabetes, and autoimmune diseases, dry gangrene usually affects the hands and feet. It develops when blood flow to the affected area is impaired, usually as a result of poor circulation. In this type, the tissue dries up and may be brown to purplish-blue to black in color.

Wet gangrene: Wet gangrene almost always involves an infection. Injury from burns or trauma where a body part is crushed or squeezed can rapidly cut off blood supply to the affected area, causing tissue death and increased risk of infection. The tissue swells and blisters and is called "wet" because of pus& it spread quickly throughout the body.

Cardiovascular Autonomic Neuropathy

Cardio vascular autonomic neuropathy is a potentially severe complication of diabetic polyneuropathy. It appears when peripheral nerves damage and disrupts the autonomic function that control blood circulation and heartbeat (Mohd, 2012).

The two major noticeable symptoms of CAN are:

- An incapability to exercise
- Orthostatic hypotension-(Feeling of dizziness and faint when you stand up due to low blood pressure)

Treatments

After diagnosis of Diabetic Neuropathy, there are two beneficial approaches: Pathogenic approaches-Treatment targets the underlying path physiological processes to prevent nerve fibre loss and Symptomatic approaches- Treatment aim to alleviate the painful symptoms of PDN to normalize physical and psychological functioning (Javes et al., 2015; carolina et al., 2006).

Pathogenetic treatments

A number of pathogenetic treatments have been evaluated in diabetic neuropathy.

Glucose control: Data from the Diabetes Control and Complications Trial (DCCT) emphasized a role for intensive glucose control through insulin in both the primary and secondary prevention of Peripheral diabetic neuropathy. The best way to treat diabetic neuropathy (also called diabetic nerve pain) is to keep tight control on blood glucose levels. Irregular blood glucose levels cause diabetic neuropathy, so it makes sense that control blood glucose in an acceptable range can help to avoid nerve damage or stop it from getting worse. How blood glucose should be control: eat right, exercise, take your diabetes medication, and monitor your blood sugar (blood glucose) levels throughout the day(Albers et al., 2010; Daniel et al., 2014).

Pancreas transplantion: The only known therapy to restore insulin secretion in response to feedback mechanisms in patients with diabetes is pancreas transplantation. The role of pancreas transplantation in the management of diabetic neuropathy is limited by the availability of suitable organs, the complications of surgery and the consequences of long-term immune suppression. Islet-cell transplantation is being considered as a less invasive option in patients with type 1 diabetes and marked improvements in neurophysiology have been reported in these patients, although skin biopsy results showed no improvement (Fioretto et al., 1998; Agudo et al., 2002).

Alpha Lipoic Acid: An increased free-radical production along with defective antioxidant mechanisms can generate oxidative stress that has been linked to the development of diabetic neuropathy. Alpha-Lipoic acid (ALA) is an antioxidant. It has been found to be well tolerated, however it must be delivered intravenously for symptom relief in neuropathy. This is a natural cofactor of dehydrogenase complex and is a redox modulating agent. It has been effective in both somatic and autonomic diabetic neuropathy(Zegiler et al., 1995).

Aldose Reductase Inhibitor: Aldose reductase is an imperative enzyme in the Polyol pathway concerned in the metabolism of blood glucose. Thus, it has been proposed to prevent distal symmetric peripheral neuropathy. ARIs reduce the flux of glucose through Polyol pathways, inhibiting accumulation of sorbitol and fructose, and preventing reduction of redox potential (Oates, 2002; Bensted and Chalk, 2007).

Sympatomatic treatment

Most guidelines suggest usually using tricyclic agents (TCAs), serotonin–norepinephrine reuptake inhibitors (SNRIs) or γ-amino butyric acid (GABA) analogues (gabapentin or Pregabalin) as first-line agents followed by opioids and topical treatments (Schreieber et al., 2015; Mojtaba, 2014).

Tricyclic agents: The TCAs have multimodal actions. These include blocking of serotonin and noradrenaline reuptake from synaptic clefts and varying degrees of anticholinergic receptor inhibition. Some agents, such as amitriptyline, have also been found to have a role in sodium channel blockade. There are several tricyclic antidepressants available for the treatment of chronic pain, including amitriptyline, nortriptyline, and desipramine. Tricyclic antidepressant drugs are effective for patients with painful diabetic neuropathy. The dose of tricyclic antidepressants used to treat diabetic neuropathy is typically much lower than that used to treat depression (Wong et al., 2007).

Seretonin Norepinephrine Reuptake Inhibitors: Serotonin norepinephrine reuptake inhibitors (SNRIs) are a class of antidepressant drugs which used for treatment of

neuropathic pain. SNRIs are monoamine reuptake inhibitors: specifically, they are inhibitors of the reuptake of serotonin and norepinephrine. These neurotransmitters are known to play an important role in mood. Inhibition of serotonin and norepinephrine reuptake leading to enhanced descending inhibition of centrally sensitized pain**.** They may have a better adverse event profile compared with TCAs. Examples of SNRIs include venlafaxine and duloxetine. The SNRIs duloxetine was the first drug to be approved for DPN by the US Food and Drug Administration in 2004. Some of the adverse events seen with the SNRIs include nausea, vomiting, headache, sweating, and increase in blood pressure, dizziness, and insomnia (Marks and Shah, 2009).

Anticonvulsant: Anticonvulsant drugs have a long history of effectiveness in the treatment of neuropathic pain. Gabapentin second line anticonvulsant drug has the most clearly demonstrated analgesic effect for the treatment of neuropathic pain, specifically for treatment of painful diabetic neuropathy. It increases brain GABA levels, binds to the alpha2-delta subunit of voltage-gated calcium channels, and inhibits branched chain amino acid transferase. Pregabalin (Lyrica) is approved for the treatment of pain due to generalized diabetic peripheral neuropathy and may be considered as a first-line agent in diabetic peripheral neuropathic pain (Theinel, 2004).

N-Methyl-D-Asparate Receptor Antagonist: The N-methyl-D-Aspartate (NMDA) receptor has been proposed as a primary target for the treatment of neuropathic pain Activation of the NMDA receptor is associated with abnormalities in the sensory (peripheral and central) system, resulting in neuronal excitation and abnormal pain manifestations (spontaneous pain, allodynia, hyperalgesia) . Blocking of these receptors by antagonists may possibly impede or reverse the pain pathology, leading to a reduction of Spain. N-methyl-D-aspartate receptor antagonists are generally used for the management of postoperative pain. Dextromethorphan has been found to be effective in alleviating the painful symptoms of diabetic neuropathy when used on its own or in combination with memantine. Ketamine is, an N-methyl-D-aspartate receptor antagonist, widely used as an anesthetic agent. Clinical evidence has proven that NMDA receptor antagonists reduce pain caused by nerve injury (Christene, 2000)**.**

Opoid Analgesic: Opoids are recommended as a second or third line class of analgesic that may provide acceptable analgesic relief from chronic neuropathic pain. Among various property Opoids have specific property to provide analgesic effect in various neuropathic pain states through inhibit the voltage gated sodium channel, which contribute in raising pain. It is becoming appreciated that various different mu-opioid receptor agonists may differ significantly in their ability/potency to inhibit voltage-gated sodium channels as well as the individual sodium channel type that they inhibit. Tapentadol extended-release (ER) (Nucynta) is only Opoids which is approved by FDA for diabetic peripheral neuropathy (Gilmbel, 2003).

Non-Steroidal Anti-Inflammatory Agents: NSAIDs have a two-fold effect—they work as painkillers and they fight inflammation. They work by blocking the body from creating prostaglandins, which are chemicals that cause inflammation and pain**.** In patients with acute painful neuropathy, simple analgesics such as nonsteroidal anti-inflammatory drugs [NSAIDs] and acetaminophen may provide pain control. They also may be used as first-line therapy in painful peripheral neuropathy. Ibuprofen and sulindac have been studied to demonstrate their effectiveness in controlling pain (Katherine and Galluzzi, 2005).

Topical medication: Topical medication has the potential to pain relief, satisfactory efficacy and better compliance without any systemic toxicity. They are more commonly used for the treatment of localised Neuropathic pain when oral drug therapy failed has or stopped due to side effect. Capsaicin is an alkaloid derived from chili peppers that desensitizes afferent sensory nerves, resulting in pain relief. In 2009, the FDA approved a high-concentration transdermal capsaicin 8% patch (Qutenza, Acorda Therapeutics) for long-term pain relief after shingles attacks. Even a small decrease in pain can dramatically increase quality of life and the risk of significant adverse effects appears low(Capoacin, 1992).

Other treatments

Foot care

Foot problems, including sores that don't heal, ulcers and even amputation, are a common complication of diabetic neuropathy. But you can prevent many of these problems by having a comprehensive foot exam at least once a year, having your doctor check your feet at each office visit and taking good care of your feet at home (Aljasir, 2010).

To protect the health of your feet:

- Check your feet every day.
- Look for blisters, cuts, bruises, cracked and cracking skin, reddishness and swelling.
- Keep your feet uncontaminated and dry.
- Wash your feet every day with lukewarm water.

Healthy food

Meal have a balanced diet which includes stain of good healthy foods— especially fruits, vegetables and whole grains — and limit portion sizes to help achieve or maintain a healthy weight (Aljasir, 2010).

Exercise

Daily activity protects your heart and improves blood flow. It

also plays a major role in keeping your blood sugar and blood pressure under control. The American Diabetes Association generally recommends about 30 minutes of moderate exercise in a day especially in morning is best for health. If you have severe neuropathy and low sensation in your legs, your doctor may recommend that you participate in non-weight-bearing activities, such as bicycling or swimming (Whyte, 2013).

Stop smoking

Diabetes patient use tobacco in any form, it more likely than are nonsmokers with diabetes to die of heart attack or stroke. Person more likely to develop blood circulation problems in body. If you use tobacco, talk to your doctor about finding ways to quit (Justin and Sherman, 2005).

Risk factor (Tammy et al., 2010)

Duration of diabetes

Diabetes duration is a key and well-recognized attempt issue of diabetic neuropathy and its complication. A prolonged duration of diabetes and poor glycemic control is concerned with high degree of production of glycosylation end products, metabolic derangements, endothelial injury, and oxidative products .A lower prevalence of polyneuropathy in those with duration of DM < 5 years and highest in those with duration of DM > 15 years (Nisar et al., 2015; Tammy et al., 2010).

Hyperglycemia

Hyperglycemia is the other most important threat issue of DN. Its paramount response has been recognizable in equally type 1D and type 2 diabetes. It has been calculated that every 1% increment in HbA1c is associated with approximately 10-15% higher frequency of DN. Therefore, the effectiveness of glycemic control mainly related to incidence and sequence of Diabetic neuropathy (Bansal et al., 2006).

Alcohol abuse

Regular consumption of even moderate amounts of alcohol (i.e., two to four drinks per day), however, clearly interferes with diabetic blood sugar control and increases the risk of many type of diabetic complications such as; peripheral neuropathy, proximal & autonomic neuropathy. Unnecessary drinking of alcohol severely affects the nervous system, causing lack of feeling of the hands and feet. Alcohol abuse also causes a condition known as hyperalgesia in which the already damaged nerves become even more sensitive to pain (Nicholas, 1998).

Repetitive Stress

An incidence that puts stress on one nerve for long periods of time increases the chances for development of peripheral neuropathy. Some time playing certain sports or musical instruments or even using powerful vibrating tools & crutches puts deep pressure on peripheral nerves and leads to nerve irritation (Sandireddy and Yeera, 2014).

Hypertension

Hypertension strongly associated with diabetic neuropathy and the observed sensory loss may be aggravated by hypertension-induced nerve ischemia and hypoxia. Elevated blood pressure many time become a risking cause for nerve tissue damage in body (Forrest and Maser, 1997).

Obesity

Risk of developing neuropathy increase if body mass index become greater than 24.obesity have a considerable impact on development and progression of Microvascular diabetic neuropathy. It is known that obesity correlates with detoriation of metabolic control (Tomic, 2003).

Vitamin deficiency

Deficiency of vitamin especially vitaminB1 (thiamine) and B12 makes peripheral neuropathy more likely. Vitamin B12 (Cobalamin) is a water soluble vitamin that plays a very fundamental role in DNA synthesis, optimal haemopoesis and neurological function. In case of pernicious anaemia, in which body can't absorb B12 properly, often leads to peripheral neuropathy (Kibirige and Mwebaze, 2013).

Conclusion

Several distinct subtype of neuropathy stay alive but diabetic neuropathy is largely regular complication allied with both type1 and type2 diabetes. It can lead to substantial discomfort, pain and in more advance cases nonhealing foot ulceration, amputations and loss of sensation. It can be able to lead generous discomfort, pain and in more advance cases nonhealing foot ulceration, amputations and loss of feeling. This review article explored the various types of complication and treatment associated with diabetic neuropathy. Pathogenic and Symptomatic treatments have been proposed to manage neuropathic pain. The main risk factor for DN is hyperglycemia. People with diabetes are more likely to develop symptoms relating to peripheral neuropathy as the excess glucose in the blood. Duration of the disease and degree of glycemic control also contribute in developing peripheral neuropathy.

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