Pharmacological and Nonpharmacological therapies in the Management of Diabetic Peripheral Neuropathy in Type 2 Diabetes :A Comprehensive Review

Snehil Dixit*, Alahmari[1], Faisal Asiri[2]

[1,2]Assistant Professor, Department of Medical Rehabilitation Sciences, College of Applied Medical Sciences, King Khalid University, Abha, Kingdom of Saudi Arabia.

ABSTRACT

Diabetes is a form of chronic illness usually requiring glycemic monitoring, self-management education and support to prevent acute complications and to reduce the risk of long-term complications. Diabetic peripheral neuropathy (DPN) implies damage or loss of function of the peripheral nerves. Though there are a number of theories trying to postulate the exact mechanism for DPN, still there remains a dearth in literature as to the exact cause for DPN. Two main problems can result from loss or damage to the sensory nerve fibers. The first problem is loss of the sensation for pain. This increases the likelihood of ulcers in diabetic population. The second problem is a small fiber dysfunction seen in DPN which exhibits itself clinically as heightened sensation of pain and burning sensations that can be quite uncomfortable for the patient suffering from type 2 diabetes. This review discusses about the available pharmacological and non-pharmacological therapies for glycemic control and management of painful (small fiber dysfunction) neuropathy in type 2 diabetes.

Key Words: Drug therapy, pharmacological therapy, pathogenesis, Diabetic peripheral neuropathy, exercise, diet.

Key Message: Diabetic Peripheral Neuropathy is a debilitating disease in type 2 disease. A need for early comprehensive management is emphasized using both pharmacological and non-pharmacological therapy to reduce the complications in Diabetic Peripheral Neuropathy.

INTRODUCTION

Background

The world health organization has described diabetes mellitus as "Metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs".[1] Diabetes is a form of chronic illness usually requiring glycemic monitoring, self-management education and support to prevent acute complications and to reduce the risk of long-term complications.[2,3]

***Corresponding address**
Prof. Snehil Dixit
Assistant Professor, Department of Medical Rehabilitation Sciences, College of Applied Medical Sciences, King Khalid University, Abha, Kingdom of Saudi Arabia, Email : snehildixit83@gmail.com

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Diabetes was first described in Egyptian culture in 15th century as "too great emptying of urine". Hindu physicians in the Ayurveda developed the first clinical test for diabetes. They observed that flies and ants were attracted to the sweet tasting urine of people afflicted with certain diseases. Indian physicians around the same time identified the disease and classified it as 'madhumeha' or honey urine as they observed that the urine would attract ants.

In diabetes long standing metabolic derangement is associated with functional and structural changes in many organs, particularly those of vascular system, which leads to clinical 'complications' of diabetes. These characteristics may affect eyes, kidneys and nervous system.[1] Such pathophysiological complications in type 2 diabetes are affecting middle aged and younger population worldwide at a rapid rate, leading to increase in epidemiology of type

2 diabetes world wide.

This review discusses about the available pharmacological and non-pharmacological therapies for the management of type 2 diabetes and diabetic peripheral neuropathy which is commonly seen in type 2 diabetes.

Aetiopathogenesis

Hyperglycemia plays an important role in the pathogenesis of diabetic neuropathy (Figure 1) . Other metabolic consequences like increased polyol pathway activity, myo-inositol depletion and Na+/K+ - ATPase activity (Figure 1) also contributes to the pathogenesis of diabetic neuropathies.[4]

Polyol pathway

In the presence of excess hyperglycaemia, there is an intracellular accumulation of glucose. This excess glucose

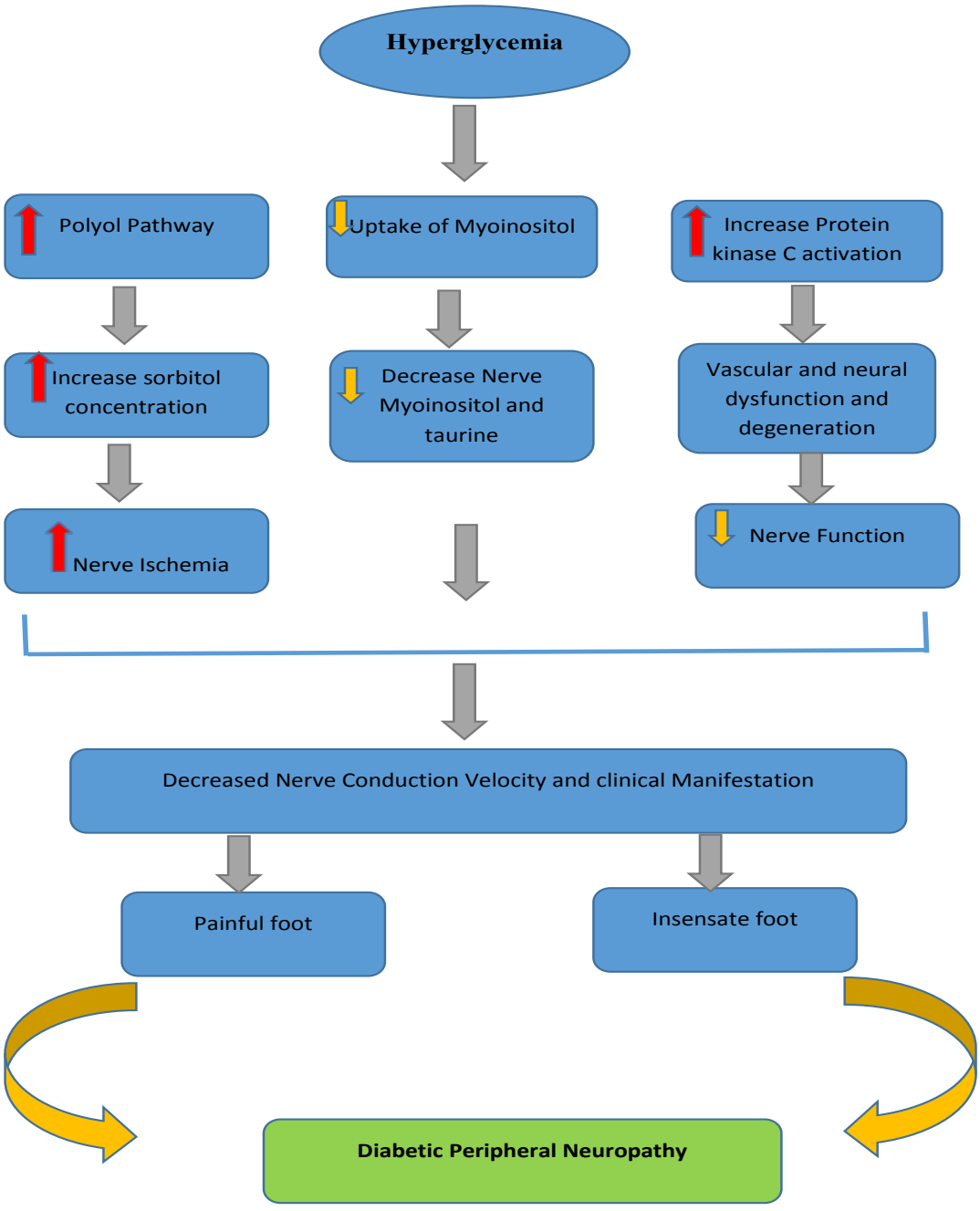

Figure 1: Diagram depicting postulated pathways leading to diabetic peripheral neuropathy

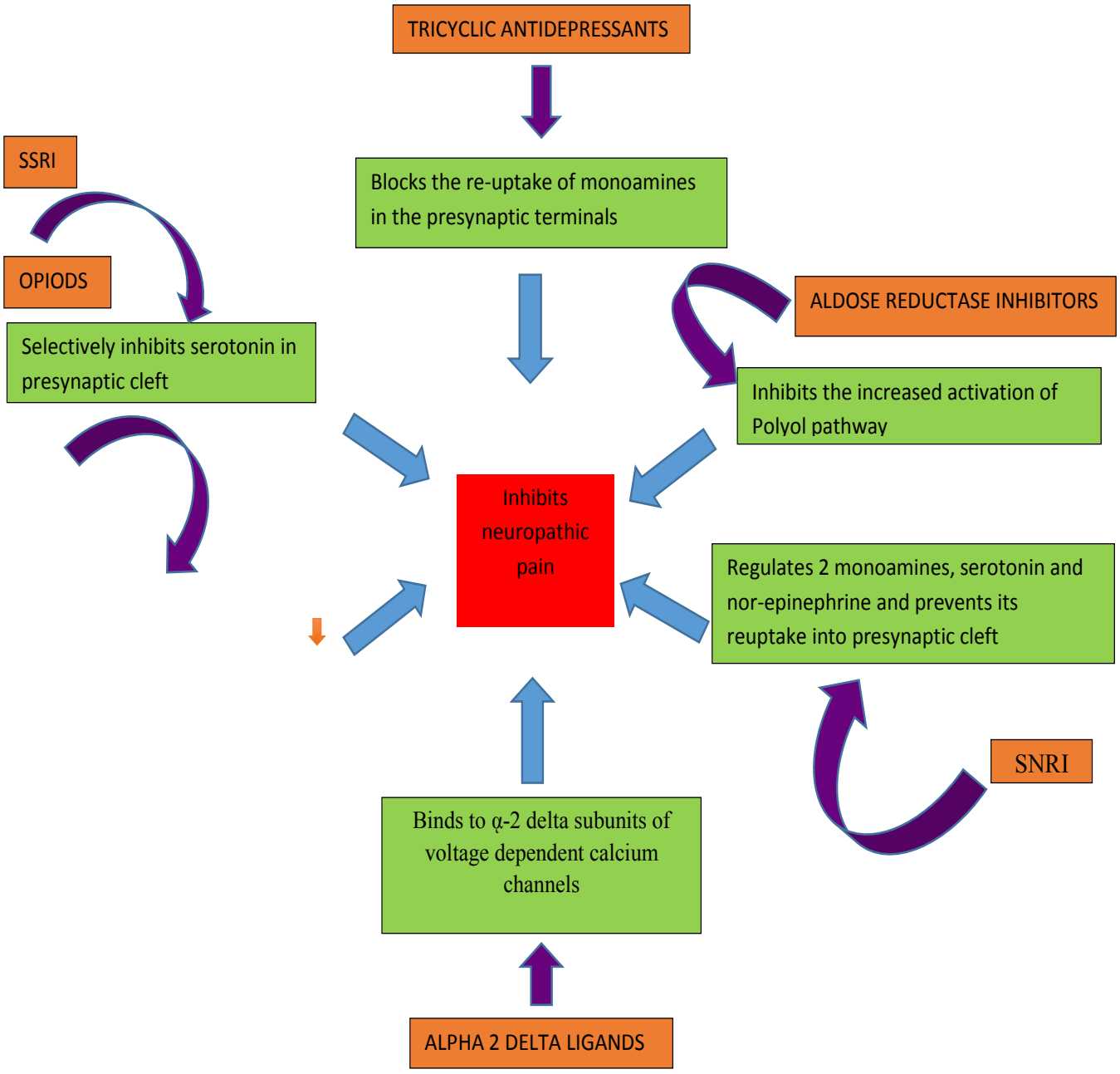

Figure 2: Schematic diagram representing the mode of action of various drugs on neuropathic pain

gets converted into sugar alcohol i.e. sorbitol by enzyme aldose reductase. Sorbitol accumulation has deleterious effect on nerve conduction velocity. This is attributed to schwann cell damage caused by an increase in osmolarity due to sorbitol and fructose.[4,5]

Myo-inositol metabolism

Myo-inositol is an important constituent of phospholipids and cell membranes. It is found in higher concentration in peripheral nerves. Hyperglycemia causes increased intracellular concentrations of glucose, resulting in increased activity of polyol pathway leading to depletion of myo-inositol concentrations that inhibits Na/K ATPase tissue activity. Reduced activity of Na/K ATPase activity results in diminished myo-inositol uptake in the nerve.[4]

Protein kinase C pathway activation (PKC)

Hyperglycemia increases the formation of diacylglycerol, which in turns activates PKC. In addition hyperglycemia activates polyol pathway which causes depletion of myoinositol. PKC mediates a vascular response to hyperglycemia that involves both endothelium and

smooth muscles. PKC regulates the vascular permeability, contractility, basement membrane synthesis and cellular proliferation. Inhibition of PKC due to euglycemia plays a pivotal role in decrease of vascular permeability and deregulation of basement membrane synthesis of the endothelium.[4]

Advanced glycation end products (AGE)

non-enzymatic addition of glucose of glucose to proteins is called glycation. Glucose forms a chemically reversible product with protein called as Schiff base. The degree to which glycation occurs depends on blood plasma glucose concentration.[4]

Hexosamine pathway

is activated when excess intermediates are formed from increased glycolytic activity. These intermediates alter gene function and protein expression that contribute to diabetic microvascular complications.[5]

Clinical Presentation

Symptoms of DPN vary from patients to patients, but common complaints are numbness, tingling and pain beginning in the toes and soles of the feet, ankles and lower shins. Patients often enlist another description of pain as dead feeling in the feet, burning sensation in the feet, pins and needles in the feet (Paresthesias). In addition to these pains superimposed shock like, electric or ice-pick pain frequently complicates the lives of patients with diabetic neuropathy. Other descriptors used by patients include jabbing, throbbing, icy cold, cramping, intense itching. Sensory symptoms are usually worse at night when the patient is trying to sleep. Often, patients with diabetic neuropathy state that movement, walking or standing lessens the pain. Balance problem is also increasingly common among people with neuropathy, usually dynamic or static balance is affected in diabetic peripheral neuropathy.[6]

Pharmacological therapies in DPN

DPN implies damage or loss of function of the peripheral nerves. Though there are number of theories trying to postulates the exact mechanism for DPN, still there remains a dearth in literature as to the exact cause for DPN. But it is clear that high glucose levels in the body changes the metabolism of nerve cells. Two main problems can result from loss or damage to the sensory nerve fibers. The first problem is loss of the sensation for pain. This increases the likelihood of ulcers in the diabetic population. The second problem is a small fiber dysfunction seen in DPN which exhibits itself clinically as heightened sensation of pain and burning sensations that can be quite uncomfortable for the patient suffering from type 2 diabetes.[5,6]

Good glycemic control usually halts or delays the onset of DPN but once a person gets diagnosed with DPN treatment options seems to be limited for the control of symptoms.

Various pharmacolcogical therapies have been proposed that might have a curative effect on the neuropathic pain that is usually perceived in diabetic peripheral neuropathy (Figure 2).

Antidepressants

Is a common form of drugs used for neuropathic pain.

Tricyclic antidepressants (TCAs): TCAs, such as desipramine and nortriptyline have proven to have beneficial effects. Yet, the most common adverse effects with tricyclic antidepressant use are the anticholinergic effects, which include dry mouth, blurred vision, constipation, urinary retention and cognitive impairment. Other serious side effects associated with these agents relate to cardiovascular toxicity and include orthostatic hypotension, tachycardia and changes in atrioventicular conduction.[7]

Selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs)

In a Cochrane review (Saarto & Wiffen, 2006) of antidepressant use in the management of neuropathic pain, the SSRIs, such as citalopram, paroxetine, sertraline and fluoxetine, were shown to have a little benefit.[7]

Duloxetine

Duloxetine hydrochloride is a reuptake inhibitor of 5-hydroxytryptamine and norepinephrine used to treat depression, generalized anxiety disorder, neuropathic pain, and stress incontinence in women. Duloxetine is also equally effective for the treatment of DPN and fibromyalgia.[7]

Anticonvulsants

It is noticed apart from seizure management this group of drug is also effective in the management of pain.

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Alpha2-Delta Ligands

A systematic review stated that 15 studies of gabapentin including 1468 participants including trials of acute pain, post-herpetic neuralgia (two studies), diabetic neuropathy (seven studies), a cancer related neuropathic pain (one study) phantom limb pain (one study), Guillain Barré syndrome (one study) , spinal chord injury pain (one study) and various neuropathic pains (one study). The pooled data indicates that forty two percent of participants improved on gabapentin compared to 19% on placebo.[8]

There have been seven randomized controlled trials of gabapentin in diabetic neuropathy. Four were placebo-controlled and three had active comparators. Three of the four placebo-controlled trials showed a statistically significant difference in pain, which was generally defined as at least a 50% reduction in pain. The fourth trial showed no benefit, but used the lowest dose of all the trials at 900 mg per day. Two studies compared gabapentin to amitriptyline, showing that gabapentin is as effective as amitriptyline.[9]

The most common adverse effects noted to be associated with gabapentin use are related to the central nervous system. These include somnolence, ataxia and dizziness. Patients may also notice problems with gait or balance and experience gastrointestinal upset. Even though of the adverse events reported the systematic review by Wiffen et al reported that the adverse events leading to withdrawal from a trial was not significant. Though there were minor harms reported still withdrawal following the trial were insignificant. Hence it appears that gabapentin is effective in neuropathic pain.[8]

Pregabalin is a new alpha 2-delta ligand on the market and is the first agent to have been approved for the primary indication of neuropathic pain.[7]

Opioids

Usually opioids are considered to be the last line of drugs for the treatment of DPN. In a multicenter, randomized, double-blind, placebo-controlled, parallel-group study which lasted for 6 weeks and included 159 subjects with moderate to severe pain due to diabetic neuropathy assigned to treatment and placebo groups. The treatment group recieved one 10-mg tablet of controlled-release (CR) oxycodone (n = 82) and placebo group received identical placebo (n = 77) every 12 hours respectively. CR oxycodone was effective for the treatment of moderate to severe pain due to diabetic neuropathy. Adverse events were reported. The authors stated that CR oxycodone[10] with dosage of 10 to 60 mg can be safe and effective in the management of pain.

Though these benefits comes at the cost of adverse effects that are also seen on administration like constipation, nausea, vomiting and sedation are the most common ones and can greatly impact a patient's productivity throughout the day. Physical dependence will also develop with chronic use and, therefore, it is important to reduce the dose of the agent slowly, if discontinuation is necessary, to avoid any symptoms of withdrawal.[7]

Mexiletine

Mexiletine is a local anesthetic, taken by mouth, which is similar to lidocaine and has been studied in symptomatic management of neuropathic pain. Adverse effects of the drug includes gastrointestinal upset, sleep disturbance, headache, shakiness, dizziness, tiredness and, in rare cases, tachycardia.[7]

Insulin and oral hypoglycemic agents (OHA)

The largest study, Accord 2010, demonstrated a 0.70% per year risk reduction and a 5% relative risk reduction at a median of 3.7 years of follow-up (non-significant) in those receiving intensive therapy (3 or more insulin injections/day) but neither showed a statistically significant difference in favor of either groups. The second largest study, by Duckworth et al, revealed a 0.29% per year risk reduction and a 4% relative risk reduction at a median follow-up of 5.6 years and these results were also not statistically significant.[11] Support for a positive effect of intensive therapy comes from the UKPDS Study Group 1998 that defined neuropathy based on a biothesiometer measurement. They followed 3867 participants for as many as 15 years of follow-up and found that there was a modest risk reduction in favor of intensive treatment.[11] Overall, the available evidences partially supports the use of Insulin therapy for the improvement in neuropathy outcomes in participants with enhanced glycemic control.

According to the systematic review by Callaghan et al., the authors reported that even the patients underwent enhanced glycemic control with insulin therapy the chances to develop clinical neuropathy was high, though a small improvement in motor conduction was found by few studies still, there was a large increased risk of adverse events with enhanced glucose control in both types of diabetes. In type 2 diabetes specifically there was

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significant increase in the risk of death in the trial targeting glycosylated hemoglobin (HbA1c) of less than 6%.[11]

A systematic review analysed twenty RCTs (mean trial duration 10 months) including 1,811 participants, with mean age 59.8 years and mean duration of diabetes of 9.6 years. Majority of the trial included were of low methodological quality, none of the studies assessed diabetes-related morbidity, mortality or total mortality. On the final analysis of the 13 trials it was revealed that Insulin-OHA combination therapy had statistically significant benefits on glycaemic control over insulin monotherapy. The Combination therapy with bedtime insulin resulted in statistically significantly less weight gain compared to insulin monotherapy. However they found even when the patients had good control of their hyperglycemia in diabetes there were no significant differences in quality of life related issues.[12]

Insulin dosage

The studies included in the trials titrated insulin to a predetermined glycaemic targets based on fasting and post prandial glucose levels or diurnal mean glucose values. Median fasting glucose target was less than 7.0 mmol/l (range: less than 5.6 to less than 10.1 mmol/l). Riddle et al 1992 commenced insulin at 30 units/day and increased the dose weekly by 20 units for mean fasting capillary glucose more than 10 mmol/l, by 15 units for 7.8 to 10 mmol/l, by 10 units 6.7 to 7.8 mmol/l and by 5 units for mean capillary glucose 5.6 to 6.7 mmol/l. A reduction in insulin dose of 5 to 10 units was permitted for recurrent symptomatic or biochemical hypoglycaemia (less than 3.3 mmol/l). Riddle et al 1998 commenced insulin at 10 units/day and increased the dose weekly by 10 units until fasting glucose was less than 7.8 mmol/l for two consecutive days, then by 5 units weekly until fasting glucose was less than 6.7 mmol/l, aiming for a target fasting glucose 5.5 to 6.7 mmol/l. Yki-Jarvinen 1999 used a patient-led insulin self-titration regimen based on daily fasting glucose measurements. Chow 1995 limited the maximum daily dose of insulin for combination therapy and insulin monotherapy regimens to 26 and 84 units (or less than 1 unit/kg bodyweight) respectively. Furthermore, there appears a variance in application of Insulin therapy in the management of hyperglycemia of type 2 diabetes as the therapy centers or is patient oriented, inorder to achieve a enhanced glycemic control.[12]

Very few studies in this review reported adverse effects of oral agents or insulin therapy. Moreover very few trials in the review reported regarding patient oriented outcome measures over longer duration of the trial.

Though for painful neuropathy drugs like TCA, anticonvulsants, opioids appear to be the mainstay of treatment for curing the symptoms of painful neuropathy, still their scope of practice clinically is very limited. In a systematic review of TCAs, anticonvulsants, opioids, and capsaicin cream, the evidence suggested that they are effective for management of acute pain in diabetic neuropathy in adults, although in most of the studies due to the side effects of the drugs treatment was discontinued.[7]

Molecules in the treatment of DPN pain

Botulinum toxin

Botulinum toxin (BTX), a neurotoxic protein is synthesized by the bacterium Clostridium botulinum, and there are seven different serotypes designated as A-G. various preclinical studies have confirmed that BTX-A can obstruct the secretion of substance P and calcitonin gene-related peptide in the cultures of neurons, these findings may also indicate the ability of BTX to directly suppresses nociceptors causing symptoms of pain.[13] A clinical trial investigated the analgesic effect of BTX-A in 29 patients with focal painful neuropathies and mechanical allodynia found BTX-A to be eefective in the managmenet of pain.[14] Studies have also found that subcutaneous administration of BTX-A, significantly reduces pain, compared with lidocaine and placebo.[15] Though there are studies indicating

Table 1: Classification of Exercise Intensity, Based on Exercise Lasting up to 60 Minutes

Cardiorespiratory or Endurance-Type Training				
Intensity	**VO_2R (%), HRR (%)**	**% HR max**	**RPE**	**Resistance-Type Training*: Maximal Voluntary Contraction, % (1RM)**
Very light	< 20	< 30	< 10	< 30
Light	20–39	35–54	10–11	30–49
Moderate	40–59	55–69	12–13	50–69
Hard	60–84	70–89	14–16	70–84
Very hard	≥ 85	≥ 90	17–19	≥85
Maximal	100	100	20	100

‡VO_2R indicates an oxygen uptake reserve; HRR, heart rate reserve; HR max, maximum heart rate; RPE, rating of perceived exertion; and 1RM, maximum weight that can be lifted in 1 repetition. †Adapted from the American College of Sports Medicine Position Stand [20]

the efficacy of BTX, still studies with larger sample size needs to be performed to evaluate the efficacy of BTX for clinical use.

High-concentration capsaicin Patch

Capsaicin is a highly selective activating ligand for transient receptor potential vanilloid 1 receptor (TRPV1).[16] Discomfort is a common problem often reported with the application of capsaicin, hence a high-concentration capsaicin patch (capsaicin, 8%) was developed for use in neuropathic pain treatment. In a RCT of 402 postherpetic neuralgia (PHN) patients, application of 8% Capsaicin had an ameliorative effect on pain symptoms between the second and the tenth week post application.[17] Researches on long-term benefits usually 48 weeks have found that repeated treatments with high-concentration patch over 48 weeks are generally efficacious, safe and well tolerated in PHN patients.[18]

Lacosamide

Lacosamide, synthesized as an anticonvulsive drug, also show antinociceptive effects. Several clinical trials have confirmed its analgesia effect for painful DPN treatment.[19] Studies have demonstrated long-term safety and efficacy of lacosamide in DPN patients.

Non pharmacological management of diabetes and diabetic neuropathy

Aerobic exercise in type 2 diabetes

Estimates of global diabetes prevalence suggests that as much as 7.1% of the global adult population is afflicted with diabetes.[20] A current guidelines from scientific bodies have recognized aerobic exercise or strength training as an important modality to achieve glycemic control, modulating body composition and risk factors[21-23] in type 2 diabetes.

A combined effect of all the therapies have been outlined in Figure 3 that might be helpful in attaining glycemic control hence delaying the progression of the complications as commonly seen with type 2 diabetes.

Effect of intensive glycemic control on neuropathy

The changing lifestyle, physical inactivity and dietary habits clearly signify that there is a shift in global epidemiology of type 2 diabetes, and its complications like neuropathy, retinopathy and nephropathy, myocardial infarction and stroke or mortality are on verge to rise in Indian population. A systematic review performed in 2012 which included randomized controlled trial (RCT) highlighted the positive effects of aggressive glycemic goals through the use of diet and exercise, oral hypoglycemic agents, insulin, or oral hypoglycemic agents plus insulin on neuropathy. Lifestyle interventions and medications significantly brought down the relative risk of foot ulceration in type 2 and type 1 diabetes. The authors concluded that enhanced glucose control significantly reduces nerve conduction and vibration threshold abnormalities. But the draw back in the high quality trial was that they were pragmatic in nature and aggressive therapies which included interventions like medications, diet, exercises (resistance and aerobic) were heterogeneous in nature, hence it is difficult to analyze the type of intervention that really made a difference in terms of relative risk, risk difference, and mean difference between the conventional and treatment groups.[11]

Aerobic exercise training in DPN

Aerobic exercise training in DPN, can help to modulate neuropathic symptoms. In a study which included fives patients with type II diabetes mellitus predominantly distal sensory polyneuropathies who underwent 8-week program of a supervised moderate exercise program (40-75% of maximal ventilator oxygen uptake reserve (VO2)) found that exercise can be performed safely in type II DPN and in addition to that exercises can also produce enhancement in nerve functions in DPN.[24] Another study evaluated seventeen patients with diagnosed DPN revealed that aerobic exercises can lead to improvements in neuropathic and cutaneous nerve fiber branching following supervised exercise in patients with diabetic peripheral neuropathy.[25] A snapshot for classification of the Intensity of exercise have been provided in Table 1.

Frequency

Aerobic exercise should be performed minimum of 3 days/ week with interval not greater than 2 consecutive days between the exercise bouts. The Joint Position Stand by ADA and ACSM (American College of Sports Medicine) for exercise training recommends 5 days of the exercise / week of moderate intensity in type 2 diabetes in adults.[26]

Intensity

Aerobic exercises should be moderately intense at 40%-60% of VO2 max or 40%-60 % of heart rate reserve has been proved to be beneficial in controlling blood glucose and increasing insulin sensitivity in type 2 diabetes. For most of the people brisk walking may appear as moderately intense exercise which might be useful in controlling blood

glucose levels. Added benefits are seen with vigorous exercises more than 60 % of VO_2 max.[26] A metanalysis shows that individual who exercised at higher intensity seems to have better control of blood glucose than individual who performed greater volume of exercises.[27] Though higher intensity of exercise might not be tolerated by individuals of all the age-group affected by type 2 diabetes. Hence moderate intensity exercises play a pivotal role in the management of type 2 diabetes.

Duration

The duration of the exercise prescription can be divided into the duration of each exercise session, as well as the period of training required to have a desired effect.[22]

Session Duration

Patients with type 2 diabetes should accumulate a minimum of 150 minutes of moderate-intensity exercise or 90 minutes of vigorous-intensity exercise each week [Evidence Level I (A)].[22] The duration of each individual session can vary, although the aim should be a minimum of 10 minutes per session.

Program Duration

Exercises have beneficial effects even on shorter duration of exercise regime. Exercises help in improvement of arterial stiffness and insulin resistance only after 3 weeks of aerobic training, despite the lack of measurable changes in anthropometric factors (body mass index or body fat). However the duration of exercise program may not be associated with changes in body mass index but at the same time it may be associated with decrease in insulin resistance, blood glucose control and lowering CVD risk seen in type 2 diabetes.[22]

Mode

Both aerobic and resistance training have important roles in Type 2 diabetes. The combination of both forms of training was twice as effective for improving glycemic control (10). Any form of aerobic exercise (including brisk walking) that uses large muscle groups and causes sustained increases in HR is likely to be beneficial.[26]

Rate of progression

At present, no study on individuals with type 2 diabetes has compared rates of progression in exercise intensity or volume. Gradual progression of both is advisable to minimize the risk of injury, particularly if health complications are present, and to enhance compliance.[26]

Aerobic exercises in chronic peripheral neuropathies

There still remains dearth in literature regarding the role of aerobic exercises in modifying the natural progression of peripheral neuropathy. The studies reported are of poor methodological quality[28] and are inconclusive about the effect of aerobic exercise on DPN. The only study that has documented the effect of home based exercises on DPN was by Ruhland et al which lacked blinding and allocation concealment. Another study by Smith et al which followed up patients for a year found that diet plus exercise can result in partial cutaneous innervations.[29] Unfortunately the study design was case control and had a poor methodological approach in the study.

Resistance exercises

Aerobic exercises have proved there efficacy in the managmenet of neuropathic symptoms (Figure 3) (Table 1).[24,25] There is only one study that used combination of aerobic and resistance training in the management of DPN.[25]

Resistance training is also growing therapeutic tool which has the potential to improve muscular strength , endurance, enhance flexibility, enhance body composition, and decrease risk factors for cardiovascular disease which are commonly encountered. A minimum of 8–10 exercises involving the major muscle groups should be performed with a minimum of one set of 10–15 repetitions to near fatigue. Increased intensity of exercise, additional sets, or combinations of volume and intensity may produce greater benefits and may be appropriate for certain individuals in type 2 diabetes.

Therefore its is important that all individuals with type 2 diabetes All persons with type 2 diabetes should be carefully screened before beginning this type of training and should receive proper supervision and monitoring. Caution should be used in cases of advanced retinal and cardiovascular complications.[22,23,26,27] Resistance training has been shown to induce a hypertrophic response and a muscle-fiber type shift in exercising muscles, which allows for a potential increase in wholebody glucose utilization. A consequent increase in GLUT4 proteins may in turn improve glycemic control. An increased capillary to- muscle ratio further favors improved glucose control. The use of resistance training to improve glycemic control in type 2 diabetes is supported by the American College of Sports Medicine and ADA position statements.[26,30] Furthermore, the potential benefits of increases in muscle mass on body composition

Figure 3: Schematic representation of various non-pharmacological methods in the management of DPN

Figure 4 : Schematic diagram emphasizing on dietary components

and other CVD risk factors have also been reported. Unlike aerobic training, higher intensities of resistance training (3 sets of 8 to 10 repetitions at 75% to 85% of 1 repetition maximum) have not only shown benefits but also have been well tolerated by patients with type 2 diabetes.[22,26,30] However, for some patients, lower exercise intensities may be more appropriate.

Effect of Diet

Lifestyle modifications forms the cornerstone in the management of blood glucose levels and prevention of other complications like hypertension, higher levels of low density lipoproteins (LDL) or total cholesterol in the body (Figure 4). Meta-analysis of RCT on the use of dietary fibers in type 2 diabetes showed beneficial effects of dietary fibers on glycosylated hemoglobin with an overall mean decrease in HbA1c of 0.26%.[31] A RCT investigating the effect of diet and physical activity on blood pressure and glucose concentrations (HbA1c) concluded that an intensive diet intervention soon after diagnosis can improve glycemic control at 6 months. Moreover, they found physical activity seems to have no added benefits in early lifestyle intervention.[32]

Carbohydrate diet to prevent neuropathy in type 2 diabetes

The carbohydrates are usually defined as sugars, starch and fibers. A number of factors influence glycemic responses to foods, including the amount of carbohydrate, type of sugar, nature of the starch, cooking and food processing, and food form, as well as other food components. Though low glycemic index diet may reduce post-prandial hyperglycemia but the sustainability of these diets in long terms have not been established. Moreover, effect of carbohydrate diets on glycaemia and lipids appear to be modest only, with the long term effect of such interventions are questionable, as most of the studies are flawed and subject to criticism for the design.[32]

Fiber

Fiber diet in type 2 diabetes plays a vital role in the control of hyperglycemia. A variety of fiber-containing foods, such as whole grains, fruits, and vegetables, because they provide vitamins, minerals, fiber, and other substances are important for good health. Recent studies have reported mixed effect of fibers on diabetes and lipid control. Ingestion of fibers in diet in large amount is a cornerstone in the management of hyperglycemia and hyperinsulinemia, and elevated plasma lipids.[32]

Though diet plays a modest role in the control of hyperglycemia but still there is a need to individualize the benefits of nutritional therapy for people with diabetes, with consideration of individual's food and eating habits, metabolic profile, treatment goals, and desired outcomes.[32]

Yoga to prevent neuropathic complications in type 2 diabetes

Art of yoga is an ancient science of Indian mythology. Yoga programs usually train large muscle groups that results in increase in maximal oxygen uptake, decrement of sub maximal heart rate and augmentation of stroke volume. They also results in metabolic changes, such as reduction of blood lipid levels and decrease in blood lactate concentration during sub-maximal work.[33] A systematic review on impact of yoga on type 2 diabetes concluded that there is a need of well-designed randomized controlled trials to assess the long term effectiveness of yoga on type 2 diabetes. They further suggested that in future, trials of good methodological quality should be used with yoga as primary intervention for examining its effect on glycemia in type 2 diabetes. Apart from studying the long-term impact of yoga there also appears a need to report a standardized mode or protocol for reporting data in trials involving yoga as a primary intervention.[33] Yoga therapy can be an importrnat tool to have an ameliorative influence on neuropathic symptoms in type 2 diabetes, still there is a need to know the efficacy of yoga therapy to prevent DPN in type 2 diabetes patients, a well designed trial should be conducted to evaluate the benefits associated with yoga therapy.

CONCLUSION

In conclusion though for painful neuropathy drugs like TCA, anticonvulsants, opioids appear to be the mainstay of treatment for curing the symptoms of painful neuropathy, still their scope of practice clinically is may be limited, on the contrary newer molecules in the management of neuropathic pain may offer important scope in the managmenet of neuropathic pain. There is also a need to explore the effect of non-pharmacological therapies in the management of diabetic peripheral neuropathy in type 2 diabetes. Moreover there appears to be an overall need to evaluate the effects on quality of life shall, which still remains to be explored or investigated in the management of diabetic peripheral neuropathy.

SD is the guarantor of this work and has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. SD

researched data.SD,SK,SU and AM wrote the manuscript. SD,SK,BA,SU Reviewed/edited the manuscript.

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