Diabetic neuropathy

≈ 50% of patients with DM develop neuropathic symptoms or show slowing of nerve conduction velocities on electrodiagnostic testing. Neuropathy may sometimes be the initial manifestation of diabetes. Diabetic neuropathy is reduced by tight control of blood glucose.

Syndromes

Disagreement exists over the number of distinct clinical syndromes; there is probably a continuum and they likely occur in various combinations. Some of the more readily identified syndromes include:

1. primary sensory polyneuropathy: symmetric, affecting feet and legs more than hands. Chronic, slowly-progressive. Often with accelerated loss of distal vibratory sense (normal loss with aging is ≈ 1% per year after age 40). Presents as pain, paresthesias, and dysesthesias. Soles of feet may be tender to pressure. Meralgia paresthetica may be first manifestation

2. Diabetic autonomic neuropathy: involving bladder, bowel, and circulatory reflexes (resulting in ortho- static hypotension). May produce impotence, impaired micturition, diarrhea, constipation, impaired pupillary light response

3. diabetic plexus neuropathy or proximal neuropathy: possibly secondary to vascular injury to nerves (similar to a diabetic mononeuritis):

a) one that occurs in patients >50 years old with mild diabetes type II that is often confused with femoral neuropathy. Causes severe pain in the hip, anterior thigh, knee, and sometimes medial calf. Weakness of the quadriceps, iliopsoas, and occasionally thigh adductors. Loss of knee jerk. Possible sensory loss over medial thigh and lower leg. Pain usually improves in weeks, the weakness in months

b) diabetic amyotrophy: occurs in similar patient population often with recently diagnosed DM. Alternative names include: Bruns-Garland syndrome, ischemic mononeuropathy multiplex…. Abrupt onset of asymmetric pain (usually deep aching/burning with superimposed lancinating paroxysms, most severe at night) in back, hip, buttocks, thigh, or leg. Progressive weakness in proximal or proximal and distal muscles, often preceded by weight loss. Patellar reflexes are absent or reduced. Sensory loss is minimal. Proximal muscles (especially thigh) may atrophy. EMG findings consistent with demyelination invariably accompanied by axonal degeneration, with involvement of paraspinals and no evidence of myopathy. Symptoms may progress steadily or stepwise for weeks or even up to 18 months, and then gradually resolve. Opposite extremity may become involved during the course or may occur months or years later. Sural nerve biopsy may suggest demyelination c) diabetic proximal neuropathy (DPN): fairly similar findings to diabetic amyotrophy except for subacute onset of symmetric LE involvement that usually start with weakness may be a variant.

Treatment

Treatment of Bruns-Garland syndrome is primarily expectant, although immunotherapy (steroids, immune globulin, or plasma exchange) may be considered in severe or progressive cases (efficacy is unproven) [1)].

For sensory polyneuropathy, good control of blood sugar contributes to reduction of symptoms. Adjunctive agents that have been used include:

1. mexiletine (Mexitil®): start at 150 mg q 8 hrs, and titrate to symptoms to a maximum of 10 mg/kg/d

2. amitriptyline (Elavil®) and fluphenazine (Prolixin®): : start with 25 mg amitriptyline PO q hs and 1 mg fluphenazine PO TID; and work up to 75 mg amitriptyline PO q hs17 (≈ 100 mg qd ami- triptyline alone may also be effective). Usefulness has been challenged, but many studies do show benefit.

Side effects: that may limit use include sedation, confusion, fatigue, malaise, hypomania, rash, urinary retention, and orthostatic hypotension

3. desipramine (Norpramin®): more selective blocker of norepinephrine reuptake (which seems more e ective for this condition than serotonin reuptake blockers). Effectiveness at mean doses of 110 mg/day ≈ same as amitriptyline and therefore may be useful for patients unable to tolerate amitriptyline.

Side effects: include insomnia (may be minimized by AM dosing), orthostatic hypo-tension,rash,bundle branch block,tremor,pyrexia.Supplied : 10,25,50,75,100 &150mg tablets

4. capsaicin (Zostrix®): effective in some.

5. paroxetine (Paxil®): a selective serotonin reuptake inhibitor (SSRI) antidepressant. : 20 mg PO q AM. If necessary, increase by 10 mg/d q week up to a maximum of 50 mg/day (except in elderly, debilitated, or renal or hepatic failure where maximum is 40 mg/day). Supplied : 20 mg (scored) &30 mg tablets

6. gabapentin (Neurontin®) doses of 1800–3600 mg/d produces at least moderate pain relief from painful diabetic neuropathy in 60%of patientsand was ≈ as efficacious as amitriptyline. Dosage must be reduced with renal insuffuciency.

7. see Pregabalin for Diabetic Neuropathy

Tapentadol extended release was approved in 2012 for the treatment of Diabetic neuropathy (DN) [2]. More recently, tapentadol extended release has been demonstrated to be effective in the management of painful diabetic neuropathy, an often debilitating condition affecting approximately one-third of all patients with diabetes [3] [4].

To investigate the mechanisms underlying the efficacy of surgical treatment for painful diabetic peripheral neuropathy. Rats were initially divided into 3 groups (I, control rats, II, streptozotocin-induced diabetic rats, III, streptozotocin-induced diabetic rats with latex tube encircling the sciatic nerve without compression). When mechanical allodynia (MA) became stable in the third week, one third of group III rats were sacrificed and the remainder were further divided into subgroups depending on whether the latex tube was removed. Except for some rats in group III, all rats were sacrificed in the fifth week. Morphometric analysis of nerve fibers was performed. Expression level of GABAB receptor protein in spinal dorsal horn was determined. Changes of GABAB receptor within areas of primary afferents central terminal were identified. Chronic nerve compression caused by the

interaction of diabetic nerves swelling and the encircling latex tube increased the incidence of MA in diabetic rats, and nerve decompression could ameliorate MA. In diabetic rats with MA, demyelination of myelinated fibers was noted and reduction of GABAB receptor was mainly detected in the area of myelinated afferent central terminals. MA in DPN should be partially attributed to compression impairment of myelinated afferents, supporting the rationale for surgical decompression [5)].

Canagliflozin did not affect the risk of neuropathy events in the CREDENCE trial. Future large randomized studies with prespecified neuropathy endpoints are required to determine the impact of sodium glucose cotransporter 2 inhibitors on diabetic neuropathy [6)]

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