Diabetic Neuropathy – An Overview

Dr. Mark Hannon MD MSc FRCPI

Consultant Physician and Endocrinologist

Bantry General Hospital

Septebmer 20th 2017

Neuropathy in Diabetes

- Overall, one of the most common complications of DM
- Prevalence directly proportional to disease duration
- ~50% lifetime risk of neuropathy if one has DM
- Worse A1c, worse BP = more neuropathy

- Diabetic patients with foot problems occupy more hospital beds than do those with all other diabetic complications
- Average cost of DM foot adm in Beaumont Hospital = €33000

Type of DM Neuropathy

- Autonomic neuropathy
- Polyradiculopathy
- Mononeuropathy
- Symmetric peripheral neuropathy

Autonomic Neuropathy

- Cardiovascular autonomic neuropathy:
  - Persistent fixed sinus tachycardia
  - No HR variability during Valsalva manoeuvre – increased silent MI, sudden death
  - Orthostatic hypotension – BP drop > 20/10 within 3 mins
  - Posture induced tachycardia without a fall in blood pressure can result in significant postural symptoms of lightheadedness, dizziness and pre-syncope
  - Mean mortality 30% over 5 years – greatly increased from baseline
    - Macro and microvascular disease
    - Sudden cardiac death
    - Silent ischaemia
    - More stroke and renal complications
    - More sleep apnoea

Autonomic Neuropathy

- Cardiovascular autonomic neuropathy:
  - Tight control prevents progression
  - Fludrocortisone / midodrine / octreotide may help with symptomatic postural drop
  - Fludrocortisone worsens peripheral oedema, causes low K
  - Midodrine causes severe supine hypertension
  - Octreotide has multiple GI side effects

Autonomic Neuropathy

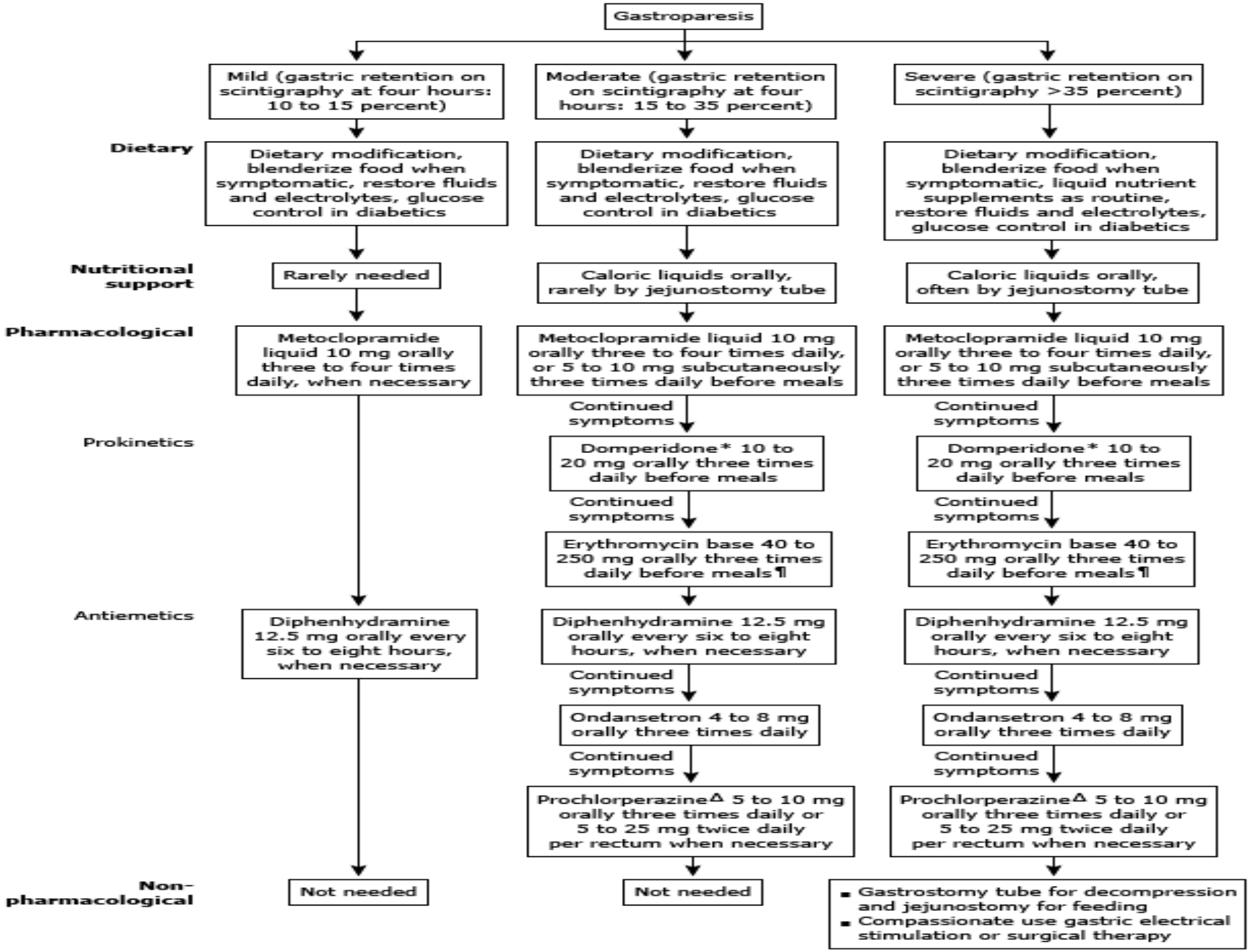
- Peripheral vasomotor neuropathy:
  - Loss of sweat function in a stocking and glove distribution which manifests as proximal hyperhidrosis
  - Changes in the texture of the skin, itching, oedema, venous prominence, callus formation, loss of nails, and sweating abnormalities of the feet
  - Symptoms such as aching, pulsation, tightness, cramping, dry skin, and pruritus
  - Peripheral oedema, which is often associated with both foot ulceration and poor wound healing
  - Development of Charcot arthropathy
  - Only treatment = better control

Autonomic Neuropathy

- GI autonomic neuropathy:
  - Severe reflux due to lower oesophageal sphincter relaxation
  - Symptoms of gastroparesis include nausea, vomiting, early satiety, bloating, and/or upper abdominal pain
  - Diarrhoea and steatorrhoea in advanced disease

Autonomic Neuropathy

- GI autonomic neuropathy:
  - High dose PPI may be needed long term
  - Remove GLP1 analogues
  - Metoclopramide = first line for gastroparesis
  - Others = domperidone, erythromycin
  - Gastric electrical stimulation
  - Surgery


Gastroparesis
Mild (gastric retention on scintigraphy at four hours: 10 to 15 percent)
Moderate (gastric retention on scintigraphy at four hours: 15 to 35 percent)
Severe (gastric retention on scintigraphy >35 percent)
Dietary
Dietary modification, blenderize food when symptomatic, restore fluids and electrolytes, glucose control in diabetics
Dietary modification, blenderize food when symptomatic, restore fluids and electrolytes, glucose control in diabetics
Dietary modification, blenderize food when symptomatic, liquid nutrient supplements as routine, restore fluids and electrolytes, glucose control in diabetics
Nutritional support
Rarely needed
Caloric liquids orally, rarely by jejunostomy tube
Caloric liquids orally, often by jejunostomy tube
Pharmacological
Metoclopramide liquid 10 mg orally three to four times daily, when necessary
Metoclopramide liquid 10 mg orally three to four times daily, or 5 to 10 mg subcutaneously three times daily before meals
Metoclopramide liquid 10 mg orally three to four times daily, or 5 to 10 mg subcutaneously three times daily before meals
Continued symptoms
Continued symptoms
Prokinetics
Domperidone* 10 to 20 mg orally three times daily before meals
Domperidone* 10 to 20 mg orally three times daily before meals
Continued symptoms
Continued symptoms
Erythromycin base 40 to 250 mg orally three times daily before meals¶
Erythromycin base 40 to 250 mg orally three times daily before meals¶
Antiemetics
Diphenhydramine 12.5 mg orally every six to eight hours, when necessary
Diphenhydramine 12.5 mg orally every six to eight hours, when necessary
Diphenhydramine 12.5 mg orally every six to eight hours, when necessary
Continued symptoms
Continued symptoms
Ondansetron 4 to 8 mg orally three times daily
Ondansetron 4 to 8 mg orally three times daily
Continued symptoms
Continued symptoms
Prochlorperazine△ 5 to 10 mg orally three times daily or 5 to 25 mg twice daily per rectum when necessary
Prochlorperazine△ 5 to 10 mg orally three times daily or 5 to 25 mg twice daily per rectum when necessary
Non-pharmacological
Not needed
Not needed
▪ Gastrostomy tube for decompression and jejunostomy for feeding
▪ Compassionate use gastric electrical stimulation or surgical therapy

Autonomic Neuropathy

- GU neuropathy:
  - Bladder dysfunction, retrograde ejaculation, erectile dysfunction, and dyspareunia
  - Erectile dysfunction is associated with the development of cardiovascular disease
  - Diabetic bladder dysfunction initially presents as a decrease in the ability to sense a full bladder, leading to frequency (mistaken for prostatism)
  - LUTS present in 20 percent of men with type 1 diabetes after 10 yrs, 30% of women have incontinence at 10 yrs
  - Retrograde ejaculation, cloudy urine, erectile dysfunction

Autonomic Neuropathy

- GU neuropathy:
  - Post void residual +/- urodynamics
  - Remove meds that impair detrusor activity (anticholinergic agents, tricyclic antidepressants and calcium channel antagonists) or agents that increase urethral sphincter tone (alpha bblockers)
  - ED – will need assessment of T (measure in early morning with SHBG, LH, FSH) in type 2 DM
  - PDE5 inhibitors if T normal

Polyradiculopathy

- Diabetic amyotrophy:
  - Not a pure lumbosacral plexopathy because it also affects the lumbosacral nerve roots and peripheral nerves
  - ? ischemic injury from a nonsystemic microvasculitis
  - Acute, asymmetric, focal onset of pain followed by weakness involving the proximal leg, with associated autonomic failure and weight loss
  - Progression occurs over months
  - Followed by partial recovery in most patients
  - Same process can occur in the contralateral leg, immediately following (within days) or much later than (months to years) the initial attack
  - EMG / MRI usually needed for dx

Polyradiculopathy

- Thoracic polyradiculopathy:
  - Less common
  - Affected patients present with severe abdominal pain, sometimes in a band-like pattern, and frequently have undergone extensive GI tests
  - Thoracic and upper limb involvement has also been observed as part of the syndrome of diabetic amyotrophy in a minority of patients
- Diabetic neuropathic cachexia:
  - Rare - unintended severe weight loss and depression
  - Most frequently occurs in men with type 2 diabetes on oral hypoglycemic agents who are middle-aged or older.
  - Most patients improve spontaneously within 12 to 24 months

Mononeuropathy

- Cranial mononeuropathy:
  - CN 3, 4 and 6 most commonly
  - Typically present with unilateral pain, ptosis, and diplopia, with sparing of pupillary function
  - Facial mononeuropathy (Bell's palsy) occurs more frequently in diabetic than in nondiabetic patients

Mononeuropathy

- Peripheral mononeuropathy:
  - Most common = median mononeuropathy at the wrist
  - Ulnar mononeuropathy, either at the elbow or, less commonly, at the wrist can also occur
  - Peroneal mononeuropathies with compression at the fibula are a well recognized complication of diabetes
  - Common peroneal palsy, for example, can result in foot drop
  - Isolated femoral mononeuropathies are rare in diabetes; many of these patients actually have a high lumbar radiculopathy (diabetic amyotrophy)

Mononeuropathy

- Mononeuritis multiplex:
  - Multiple mononeuropathies in the same patient are known as mononeuritis multiplex (or asymmetric polyneuropathy)
  - Overlapping presentation with vasculitis, which should also be considered in affected patients

Mononeuropathy

- Treatment Induced Neuropathy of Diabetes (TIND):
  - Also called insulin neuritis
  - Small fibre neuropathy that occurs in patients with chronic hyperglycaemia who experience rapid improvement in glyceamic control
  - Severe, treatment-resistant pain and autonomic dysfunction, along with worsening of retinopathy and nephropathy
  - Risk of developing TIND and the severity of neuropathic pain and autonomic dysfunction correlated with the magnitude of decrease in HbA1C.
  - Risk of TIND was increased with type 1 diabetes or a history of eating disorders, but it occurred with treatment using insulin or OHAs
  - Management = symptomatic
  - ? limit HbA1C reduction to < 2% (22 mmol/mol) over 3/12

Symmetric Peripheral Polyneuropathy

- Affects 10 to 18% at diagnosis!

- Primarily sensory

- Large fibres lost first – proprioception, vibration sense
- Then small fibres – touch
- Then motor weakness

Symmetrical Peripheral Polyneuropathy

- Progressive sensory loss predisposes to ulcer formation
- Chronic ulceration is multifactorial
  - Decreased sensation
  - Autonomic dysfunction + vascular insufficiency
- Imbalance between strength in toe extensors and flexors causing chronic metatarsal-phalangeal flexion (claw-toe deformity) which shifts weight to the metatarsal heads
- Collapse of the arch of the midfoot and bony prominences, leading to Charcot arthropathy, fragmentation and sclerosis of bone, new bone formation, subluxation, dislocation, and stress fractures

Symmetrical Peripheral Polyneuropathy

- American Academy of Neurology 2011 Guidelines:
- Pregabalin (300 to 600 mg daily) was regarded as **effective**
- A number of treatments were regarded as **probably effective:**
  - Gabapentin, 900 to 3600 mg daily
  - Sodium valproate, 500 to 1200 mg daily
  - Amitryptiline, 25 to 100 mg daily
  - Duloxetine, 60 to 120 mg daily
  - Venlafaxine, 75 to 225 mg daily
  - Dextrometorphan, 400 mg daily

Symmetric Peripheral Polyneuropathy

- ADA Management Algorithm 2005:
- Exclude nondiabetic aetiologies
- Stabilize glycaemic control (insulin not always required in type 2 diabetes)
- Tricyclic drugs (eg, amitryptiline / duloxetine)
- Anticonvulsants (eg, gabapentin / pregabalin)
- Opioid or opioid-like drugs (eg, tramadol or controlled release oxycodone)
- Consider pain clinic referral

Symptomatic Peripheral Polyneuropathy

- Optimal glucose control prevents diabetic neuropathy
- Optimal glucose control led to significant improvements in surrogate measures of neuropathy in patients with established neuropathy (Callaghan et al, Cochrane 2012)
- Optimal glycemic control is associated with improvement in symptoms for patients who develop acute painful diabetic neuropathy after a period of extreme hyperglycemia
- Established symptomatic diabetic neuropathy is generally not reversible even with intensive glucose control

Summary

- Neuropathy accounts for multiple presentations in DM patients
- Usually related to poor control and poor BP
- Often polysymptomatic and difficult to treat

- Prevention definitely better than cure!!

Thank you

- Questions?