Screening, diagnosis and management of diabetic sensorimotor polyneuropathy in clinical practice: International expert consensus recommendations

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At a glance:

- Diagnosis of diabetic sensorimotor polyneuropathy (DSPN) in clinical practice, relies on the assessment of neuropathic symptoms and signs (deficits).
- The three cornerstones of DSPN treatment include: (1) Lifestyle modification, optimal blood glucose control and management of cardiovascular risk factors, (2) pharmacotherapy targeted at the underlying pathogenetic mechanisms (e.g. α-lipoic acid and benfotiamine) and (3) symptomatic treatment of neuropathic pain.
- Expert consensus recommendations and comprehensive algorithms for screening, diagnosis, and treatment of DSPN in clinical practice were derived from a Delphi process.

Introduction & Background

DSPN affects about one third of people with diabetes. It increases morbidity, mortality and reduces the quality of life. Neuropathic pain and foot ulcers result in increased healthcare costs. As DSPN is often inadequately diagnosed and treated, effective strategies to improve this situation are needed. Recommendations are mainly derived from systematic reviews, which are frequently inconclusive. Hence, the report originating from an International Consensus Conference aims to provide comprehensive recommendations and algorithms suitable for the screening, diagnosis and treatment of DSPN in clinical practice.

Consensus finding process

A panel consisting of 15 international experts in the field of diabetic neuropathy, shared their personal clinical experi-

ence and routine in the diagnosis and treatment of DSPN and reviewed recent literature and current guidelines to formulate consensus recommendations and to define algorithms for screening, diagnosis and treatment of DSPN for clinical practice.

A hierarchical approach was used, considering evidence from systematic reviews, meta-analyses and individual RCTs, and allowing the use of participating experts' own clinical experience when evidence from clinical trials was lacking. The Delphi method, a structured communication technique, was used to reach consensus on the different topics.

Screening and diagnosis

Most frequently there is parallel damage of small and large nerve fibers in patients with DSPN and, hence, testing of both aspects with appropriate bedside tests is equally important. A consensus was reached on the fact that "Bilateral impairment of vibration sensation with tuning fork (large fiber) and/or pinprick test (small fiber) may be appropriate as minimal criteria for diagnosis of DSPN in clinical practice" (consensus statement 3.1). Validated scores may be used to assess neuropathic symptoms and signs. For differential diagnosis of DSPN, other causes of polyneuropathy need to be considered and assessed by patient history and/or laboratory measures. The algorithm visualizing the consensus on screening and diagnosis of DSPN in clinical practice is shown in Figure 1.

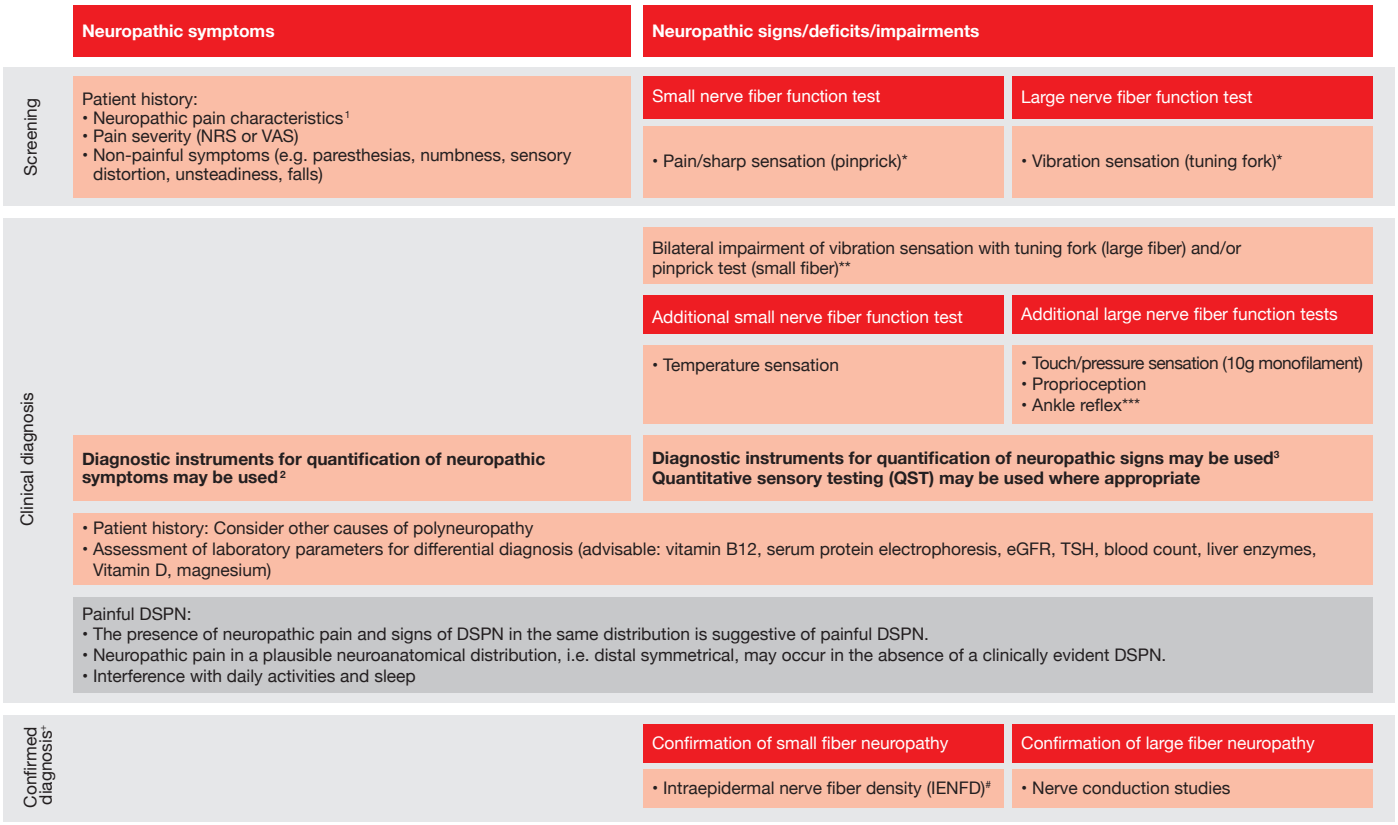

Figure 1 | Screening and diagnosing DSPN in clinical practice

* For screening purposes the application of one single test may be appropriate. A single abnormal screening test bilaterally suggests the presence of DSPN and may require a more extended diagnostic workup; ** minimal criteria for diagnosis of DSPN in clinical practice; *** CAVEAT: healthy elderly might show absent reflexes; + Confirmed diagnosis of DSPN based on Toronto Consensus criteria, consider referral to neurologist where appropriate; # Usually restricted to rare difficult cases in whom the diagnosis is uncertain; [1] The "Douleur Neuropathique en 4 Questions" (DN4-Interview) may be used to screen for neuropathic pain characteristics; [2] Includes e.g. the Neuropathy Symptom Score (NSS), Total Symptom Score (TSS) or Neuropathy Total Symptom Score-6 (NTSS-6); [3] Includes e.g. the Neuropathy Disability Score (NDS), Michigan Neuropathy Screening Instrument Examination part (MNSI-E), Modified Toronto Clinical Neuropathy Score (mTCNS) or Utah Early Neuropathy Scale (UENS). DSPN: Diabetic Sensorimotor Polyneuropathy; eGFR: estimated glomerular filtration rate; NRS: Numeric Rating Scale; VAS: Visual Analogue Scale; TSH: Thyroid-stimulating hormone.

Management

(1) Causal treatment

In type 1 diabetes patients, intensive insulin therapy has been shown to be effective in preventing and delaying progression of DSPN. However, in type 2 diabetes patients such evidence is lacking. Nonetheless, it is generally accepted that glucose control should be optimized in both type 1 and type 2 diabetes patients as a basic measure in the management of DSPN (see consensus recommendation of an algorithm for the choice of treatment options in Figure 2).

(2) Pathogenetically-oriented treatment

The antioxidant alpha-lipoic acid and the thiamine derivative (prodrug) benfotiamine are mainly relevant in the treatment targeted at the underlying pathogenetic mechanisms of DSPN as these are licensed as drugs and approved for treatment of DSPN in several countries worldwide. Both alpha-lipoic acid and benfotiamine, display favorable safety profiles also during long-term treatment. Alpha-lipoic acid may also be used to treat neuropathic deficits (see Figure 2).

(3) Symptomatic treatment of neuropathic pain

Gabapentinoids (pregabalin and gabapentin) and antidepressants (duloxetine and amitriptyline) were considered 1st line, tramadol 2nd line and strong opioids 3rd line analgesic treatments for painful DSPN. As evidence from clinical trials indicates only a maximum response of 50% for any monotherapy, analgesic combinations may be useful (see consensus recommendation of an algorithm on analgesic pharmacotherapy in Figure 3). Non-pharmacological treatment options may also be considered.

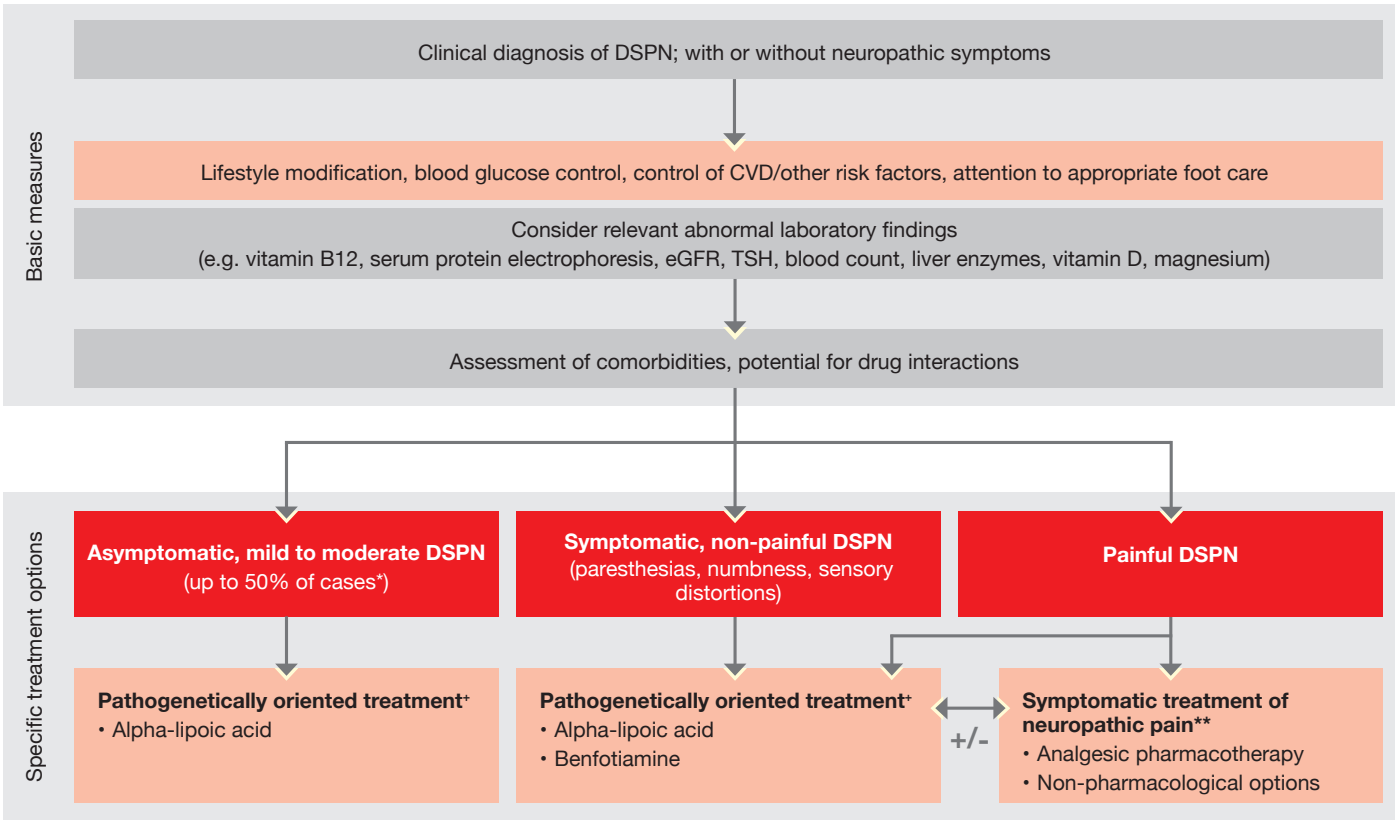

Figure 2 | Choice of treatment options for DSPN in clinical practice

+ If available. Also improves deficits/impairment/signs; *according to Pop-Busui et al.; ** for more details see Figure 3; CVD: cardiovascular disease; DSPN: diabetic sensorimotor polyneuropathy; eGFR: estimated glomerular filtration rate; TSH: thyroid-stimulating hormone.

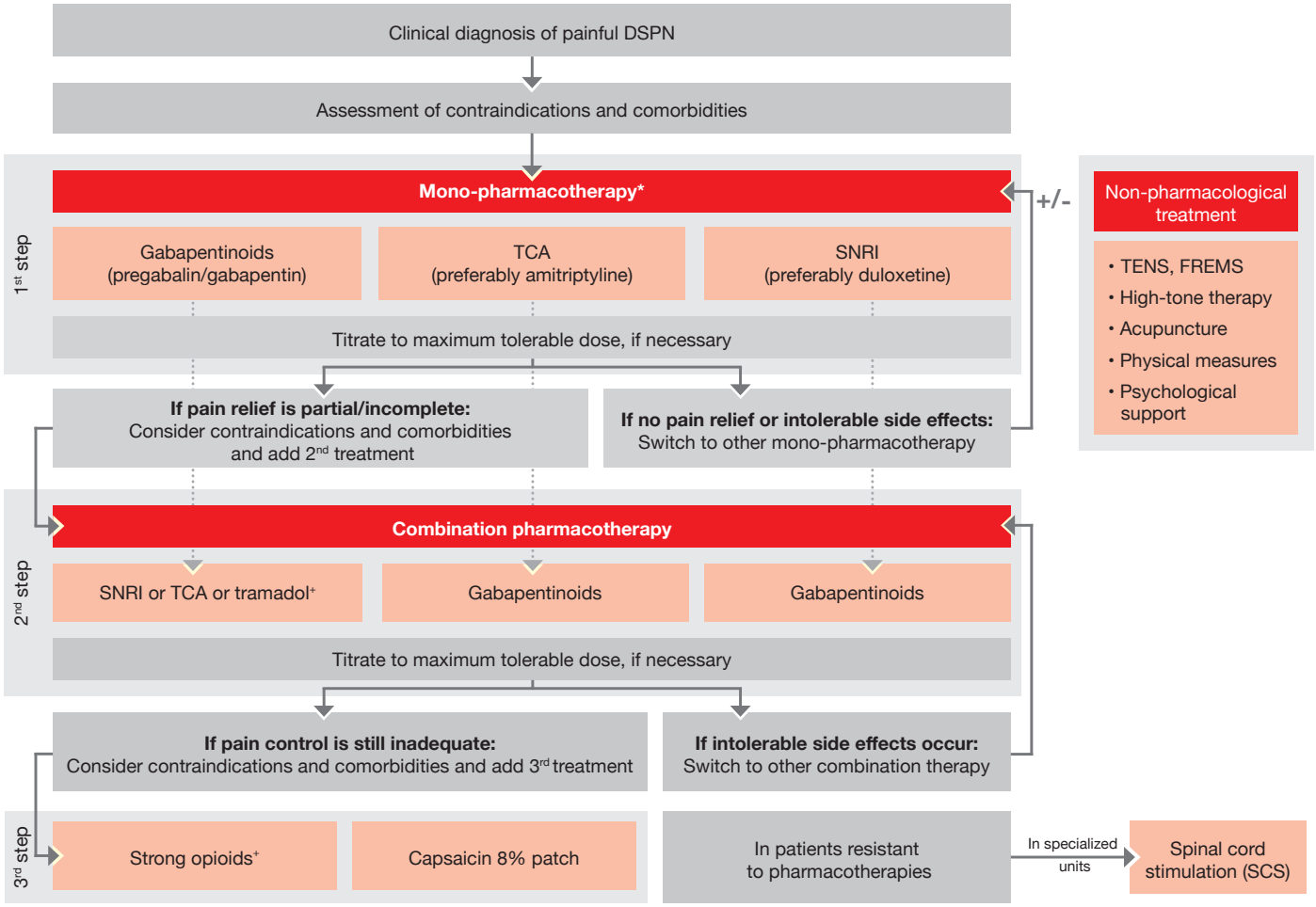

Figure 3 | Algorithm for analgesic pharmacotherapy and non-pharmacological treatment options in painful DSPN in clinical practice

* Pathogenetically oriented treatment approaches may also be considered; DSPN: diabetic sensorimotor polyneuropathy; TCA: tricyclic antidepressants; SNRI: serotonin-norepinephrine reuptake inhibitors; TENS: transcutaneous electrical nerve stimulation; FREMS: frequency-modulated electromagnetic neural stimulation; + for short term use only, whenever possible

Conclusions

DSPN is still poorly diagnosed and treated although it represents an important public health challenge. Therefore, it is essential to consider and implement strategies for early detection and prevention of the disease in national diabetes plans. Optimizing the therapeutic strategies against DSPN constitutes an unmet medical need. Hence, harmonized and up-to-date therapeutic algorithms may promote appropriate and effective treatments in daily routine.

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