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Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers:

An American Society of Clinical Oncology Clinical Practice Guideline

Introduction

- CIPN is a common treatment-related side effect
- It has the potential to result in chemotherapy dose reductions and/or early discontinuation.
- The overall incidence of CIPN is ~38% in patients treated with multiple agents
- This percentage varies depending on regimens, duration of exposure and assessment methods.
- Chemotherapy combinations with higher incidences include those that involve platinum drugs, vinca alkaloids, bortezomib and/or taxanes

Guideline Development Process

- An Expert Panel, led by 2 co-chairs, with multidisciplinary representation in medical oncology, community oncology, nursing, pain research, genetics, neurology, pharmacology, patient representation, and guideline methodology was convened
- Expert Panel members contributed to the development of the guideline, provided critical review, interpretation, and finalized the guideline recommendations based upon consideration of evidence.
- ASCO guidelines are based on systematic reviews and are reviewed and approved by the ASCO Clinical Practice Guideline Committee prior to publication.

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Systematic Review Methods

- Articles were included in systematic review if they:
  - focused on chemotherapy-induced neuropathy
  - included cancer survivors
  - considered neuropathy as an important outcome
  - were RCTs (Phase II and III)
  - reported on any of the following outcomes: incidence and severity of neuropathy, neurophysiological changes, symptom relief, patient-reported outcomes, or QOL.
- Articles were excluded if they:
  - only included patients <18 years of age
  - included <10 participants
  - were animal studies or non-English publications
  - focused on RT related or stem cell transplant related neuropathy

Systematic Review Results

- 48 RCTs met eligibility criteria and comprised the evidentiary base for the recommendations.
- A total of 42 studies covered 19 different interventions for the *prevention* of CIPN.
- *Treatment* of established CIPN was considered in 6 RCTS investigating 6 different agents.

Final Recommendations:
Prevention

- There are no established agents recommended for the prevention of CIPN in cancer patients undergoing treatment with neurotoxic agents.
- This is based on the paucity of high-quality, consistent evidence and a balance of benefits versus harms.

Final Recommendations:
Prevention (continued)

- Clinicians should not offer the following agents for the prevention of CIPN to cancer patients undergoing treatment with neurotoxic agents:
  - acetyl-L-carnitine (ALC)
  - amifostine
  - amitriptyline
  - CaMg for patients receiving oxaliplatin-based chemotherapy
  - diethyldithio-carbamate (DDTC)
  - glutathione (GSH) for patients receiving paclitaxel/carboplatin chemotherapy
  - nimodipine
  - Org 2766
  - all-*trans* retinoic acid
  - rhuLIF
  - vitamin E

Final Recommendations: *Prevention (continued)*

- Venlafaxine is not recommended for routine use in clinical practice. While the venlafaxine data supports its potential utility, the data were not strong enough to recommend its use in clinical practice, until additional supporting data become available.

- No recommendations can be made on the use of N-acetylcysteine, carbamazepine, glutamate, glutathione for patients receiving cisplatin or oxaliplatin-based chemotherapy, goshajinkigan (GJG), omega-3 fatty acids, or oxycarbazepine for the prevention of CIPN at this time.

Final Recommendations:
Treatment

- For cancer patients experiencing CIPN, clinicians may offer duloxetine.

- No recommendations can be made on the use of:
  - Acetyl-L-carnitine, noting that a positive phase III abstract supported its value, but this work has not yet been published in a peer-reviewed journal and a prevention trial suggested that this agent was associated with worse outcomes.

Final Recommendations:
Treatment (Continued)

- No recommendations can be made on the use of:
  - Tricyclic antidepressants; however, based on the limited options that are available for this prominent clinical problem and the demonstrated efficacy of these drugs for other neuropathic pain conditions, it is reasonable to try a tricyclic antidepressant (e.g., nortriptyline or desipramine) in patients suffering from CIPN following a discussion with the patients about the limited scientific evidence for CIPN, potential harms, benefits, cost, and patient preferences.

Final Recommendations: *Treatment (Continued)*

- No recommendations can be made on the use of:
  - Gabapentin, noting that the available data were limited regarding its efficacy for treating CIPN. However, the panel felt that this agent is reasonable to try for selected patients with CIPN pain given that only a single negative randomized trial for this agent was completed, given the established efficacy of gabapentin and pregabalin for other forms of neuropathic pain, and given the limited CIPN treatment options. Patients should be informed about the limited scientific evidence for CIPN, potential harms, benefits, and costs.

Final Recommendations: *Treatment (Continued)*

- No recommendations can be made on the use of:
  - A topical gel treatment containing baclofen (10 mg), amitriptyline HCL (40 mg), and ketamine (20 mg), noting that a single trial supported that this product did decrease CIPN symptoms. Given the available data, the panel felt that this agent is reasonable to try for selected patients with CIPN pain. Patients should be informed about the limited scientific evidence for the treatment of CIPN, potential harms, benefits, and costs.

Additional Resources

- Additional Information including data supplements, evidence tables, and clinical tools and resources can be found at www.asco.org/guidelines/neuropathy.
- Patient information is also available at www.cancer.net.

ASCO Panel Members

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