


Management of neuropathic pain: A graph theory-based presentation of literature review

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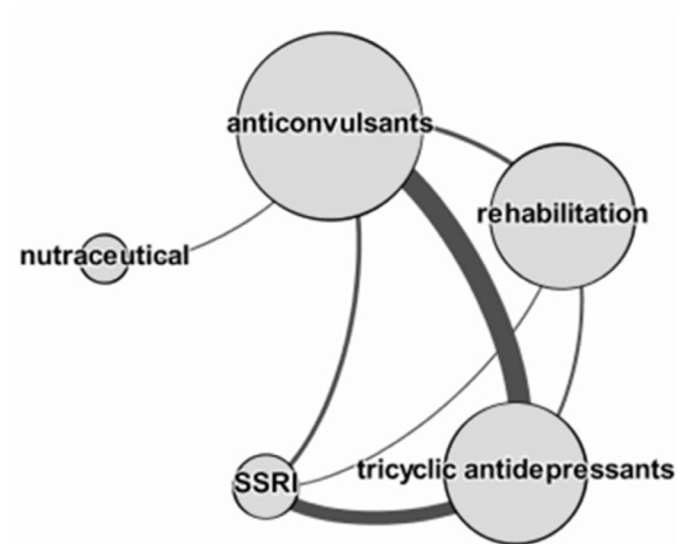
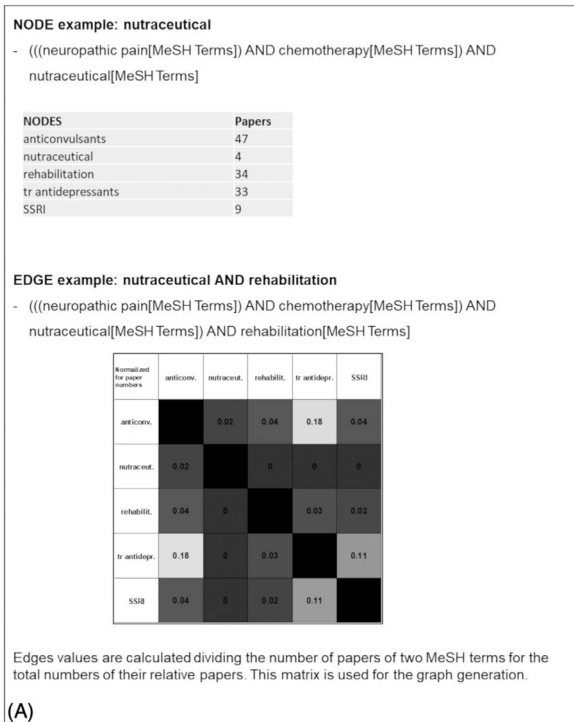
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Neurotoxicity and neuropathic pain are relative common side effects of antineoplastic chemotherapies.¹ The use of specific drugs to treat and, desirably, to prevent these effects is extremely important in order to offer an acceptable quality of life for the patients.¹ Recently, Aghili and colleagues showed gabapentin, an anticonvulsant drug, may give potential benefits in the prevention of neuropathic symptoms and signs and nerve function impairment.² In particular, this drug may even reduce the worsening of nerve conduction. Indeed, the clinical patterns simply represent a part of the multiple faces of neuropathies. The demonstration of positive influences in electrophysiological nerve responses improves the significance of the specific drug effects. In order to better define the usefulness of gabapentin, further studies should be conducted with this multifaceted approach, even considering other objective outcome measurements, like nerve ultrasound. In fact, in cases of different neuropathies, this tool provides useful data for diagnosis completion and decision management.³

Through the work by Aghili and colleagues, besides the relevant translations in clinical practice, we can infer the importance of literature review to design a proficient research study.² Generally, the knowledge of the status of the art about a disease is a fundamental component of scientific work. In their paper, the authors correctly based their hypotheses and discussions on other studies and especially on the guidelines developed by the American Society of Clinical Oncology (ASCO).¹ However, the number of publications is incessantly growing with a continuous expansion of information about a matter. The trick in the literature reviews is due to the difficulties in acquiring a comprehensive summary of this high number of scientific data, especially when they are controversial. Furthermore, when the researchers perform a literature review, showing the results in simple way is often hard: the found papers and their relationships seem similar to an intricate maze. Recently, some authors have suggested

the application of graph theory to display the literature network about a specific topic.⁴ A graph is a structure made up of nodes and edges. Each node is a unit linked to one or more other nodes through connections, represented by the edges. For example, a node can represent a person or a scientific topic and the edges his/her/its relationships with other similar entities. Furthermore, in this graphical translation, these elements can vary their dimensions, on the basis of the weight of the information they represent. The graphs are used in big data analyses and in several fields like Medicine, Sociology, Economy and so on. The advantages of their use are not simply related to a direct graphical representation of a network, but also to the possibilities to calculate different parameters able to describe the network.⁴ Hence, the characteristics of a graph allow increasing the usability and the study of scientific literature.

We present an example of this graph theory-based model of literature review about the management of neuropathic pain. We performed a research on PubMed database using the Medical Subject Headings (MeSH) terms 'neuropathic pain' and 'chemotherapy', associated with the Boolean operator 'AND'. We considered the results of the last 10 years with no other filter restriction, finding 1,135 papers. Then, we added the following MeSH terms, considering the interventions listed in the ASCO guidelines: "anticonvulsants", "antidepressants, tricyclic", "inhibitors, serotonin reuptake", "nutraceutical" (for the dietary supplements), "rehabilitation".¹ These last terms became our graph nodes. We decided to use general labels of therapies (eg 'anticonvulsants' for carbamazepine and similar). Finally, on the basis of our experience, we used the term 'rehabilitation' for its clinical impact in the management of pain and, consequently, in patient's quality of life. Initially, each MeSH term of intervention was separately added to 'neuropathic pain' and 'chemotherapy' with the Boolean operator 'AND', in order



(B)

FIGURE 1 A, Examples of the literature research to obtain numbers about the nodes (number of papers about a therapy) and the edges (number of papers in which two therapies are together assessed). The matrix below is a table, where the strength of connections (co-examination of all considered therapies) is visible. The grey shade is related to this strength. B, The graph build with the proposed method. The largeness of the node is related to the number of papers about a specific therapy, while the size of the edge to the amount of the papers exploring two therapies at the same time

to find the number of papers related to each node (Figure 1A). The dimension of each node represented this number. In our graph model, the edges indicated the strength of connection between two medical interventions, meaning the number of papers simultaneously containing two therapies. In this way, we evaluated how much they were integrated in the literature. For this assessment, we again performed the last search, but coupling the MeSH terms of intervention, thus obtaining ten combinations (Figure 1A). In this way, a final graph was built, by the free software Gephi 0.9.2 (Figure 1B).⁴ The graph shows anticonvulsants are the most presented drugs in the literature and they represent the only family of therapies related to all the others. Interestingly, nutraceuticals are scarcely mentioned and only combined with anticonvulsants. Finally, the strongest therapy combination concerns anticonvulsants and antidepressants. In this suggested graph, 'graph density', a number explained how much the graph is complete, hence, how much the possibilities of therapy combinations are explored, is equal to 0.7 (1.0 should represent the exact completeness). This is just a simple example, explaining the potentialities of this approach, directly showing the results of the selected variables. In case of massive graph, with many variables gathered from the literature research, this presentation and the related calculations could help in guiding further studies. In future, its application in the literature review might support research activity, revealing hidden information useful for increase knowledge about patients' management and for personalized medicine.⁵

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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