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Opinion

Pain in Oncology, Reality and Paradox of Homeopathic Care

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Abstract:

***Background*:** Following fatigue, pain is one of the major complaints from cancer patients. Regular use of Class 1 analgesics may cause side effects and is not always sufficient to relieve pain. Homeopathy is the complementary and integrative medicine most frequently used in France in supportive care in oncology (SCO). What role, if any, may it play in the treatment of pain?

***Methods*:** Extraction and analysis of results concerning pain from three surveys on the main indications of homeopathy in SCO from doctors specializing in oncology (DSO), non-homeopathic general practitioners (NHGP), and homeopathic general practitioners (HGP). Two of the surveys were carried out in France and the third survey reviewed patients in a cancer ward in Vienna.

Results: Both NHGPs and DSOs are interested in homeopathic therapy primarily for the pain management of chemo-induced peripheral neuropathy (CIPN), but also for musculoskeletal pain. Compared to a control group, patients treated with homeopathy experienced more

pain relief (p <0.001). Paradoxically, the HGPs place the relevance of the homeopathic treatment of pain in only twelfth place.

***Conclusions*:** This work should encourage homeopathic physicians to realise that pain management using homeopathy, particularly as regards CIPNs, is effective and useful. The systematic evaluation of pain on the visual analogue scale (VAS) at each consultation and a good knowledge of the physiopathological mechanisms involved should help restore their confidence. The homeopathic prescription can be determined from the recommendations of the International Homeopathic Society of Supportive Care in Oncology (IHSSCO), or in more difficult cases, after an individualized consultation and repertorisation following the principles of similarity and globality of symptoms.

Keywords

Chemotherapy induced peripheral neuropathy; homeopathy; integrative oncology; musculoskeletal disorders; pain, supportive care

1. Introduction

Subsequent only to fatigue and sleep disorders, pain is the third complaint expressed by patients being treated for cancer, according to Cleeland et al. [1]. Class 1 analgesics are very frequently prescribed and consumed for this complaint. Their regular usage by oncology patients is often problematic due to their potential side effects [2].

As the integrative and complementary medicine most used in supportive care in oncology (SCO) in France [3, 4], homeopathy prescribed to patients being treated for cancer significantly reduced pain (p <0.001) compared with the control group receiving only conventional analgesics [5].

As a specialist in supportive care in oncology, I frequently use homeopathic medicine for this indication. With nearly 4000 support consultations per year [6], the positive feedback of patients confirms the strong medical benefit of homeopathy for pain management.

To further investigate the role of homeopathy, I have studied and compared the results of two surveys conducted in France as well as one survey among patients in a cancer ward in Vienna [5], on the helpfulness of homeopathy in SCO by combining the results of these different studies with my personal experience as a clinician, I sought to discover what concrete suggestions can be made concerning homeopathic analgesic prescriptions for SCO.

2. Important Note

I will speak here only of the pain caused by cancer treatments. The pain related to the cancer itself and its development most often require level 2 or 3 analgesics.

3. Results Concerning the Homeopathic Management of Pain

I had the opportunity to analyse two surveys regarding homeopathic SCO by French physicians: 150 medical specialists in oncology (radiotherapists, oncologists, and haematologists), 100 general practitioners without training in homeopathy, and 97 general practitioner homeopaths. I then

extracted from these surveys the data concerning the management of pain. My involvement with the research that supports this article followed a decision made in concertation with the homeopathic product manufacturer Boiron Laboratories to undertake the surveys. Boiron commissioned the survey research from two independent healthcare market research agencies, Axess Research and AplusA. The statistical analysis of the results was carried out by these agencies and I made my own analysis and interpretations of the outcomes concerning the management of pain by homeopathy in SCO because they raise questions which we will discuss here.

4. For Physicians Specializing in Oncology

Chemotherapy-induced peripheral neuropathy is manifested mainly by paraesthesia and pain in the extremities of hands and feet, such as tingling or stinging, aggravated by exposure to cold and pressure. They represent the fifth complaint for all cancers and the second in colon cancer due to the therapeutic use of oxaliplatin [1]. Among the various symptoms addressed, the treatment of peripheral neuropathies especially poses a problem for specialists in oncology that were questioned in the first study. Eighty percent of physicians are dissatisfied with currently available conventional treatments and 78% are interested in a homeopathic therapy for this indication.

Musculoskeletal pain (MSP) occurs mainly after anti-aromatase therapy. In this indication, 39% of cancer specialists say they are not satisfied with the available conventional treatments and 67% are interested in homeopathic treatment.

5. For Non-homeopathic General Practitioners (NHGP)

Frequently, pain is the reason for NHGP consultation as it ranks, in these two surveys, among23 symptoms studied, just after fatigue and before anxiety.

NHGPs, like oncologists, are dissatisfied with the conventional treatments available for peripheral neuropathic pain and rank this indication as being the most potential for homeopathic treatment in SCO.

With regards to musculoskeletal pain, the degree of satisfaction for the available conventional treatments is only moderate. However, the use of homeopathy seems to them to be less judicious for this type of pain.

6. For Homeopathic GPs (HGP)

Differing from their non-homeopathic colleagues, pain ranks sixth among symptoms addressed during consultations. Regarding their opinion on the relevance of homeopathic treatment of pain, they ranked it in twelfth position with a score of 6.1 / 10. Peripheral neuropathies are not ranked any better as they give the relevance of homeopathy in this indication a score of 5.8 / 10.

Musculoskeletal pain is a slightly more frequent reason for consultation with a score of 6.6 / 10 and a better potential with 6.6 / 10. The HGPs only rank them in 10th position for homeopathic indications in SCO.

7. For Patients

The Michael Frass et al. study shows that by improving the overall condition and quality of life of patients with individualized homeopathic treatment, it significantly improves many other symptoms, including pain. (Table 1).

Table 1 (with the permission of the author): Comparison of first vs. third visit with adjunctive homeopathy.

	Homeopathy group				Control group				Homeopathy vs Control			
	mean[+]	LCL	UCL	p	mean[+]	LCL	UCL	p	mean	LCL	UCL	p
Global health status[1]	10.6	5.3	15.9	<.001*	3.0	-2.5	8.4	0.288	7.7	2.3	13.0	0.005
Subjective wellbeing[1]	20.9	15.6	26.2	<.001*	6.1	0.3	11.9	0.039	14.7	8.5	21.0	<.001
Physical functioning[1]	7.0	1.8	12.2	0.008	-6.5	-11.0	-2.0	0.005*	13.5	8.6	18.4	<.001*
Role functioning[1]	17.0	9.3	24.7	<.001*	8.4	0.6	16.2	0.034	8.6	0.4	16.9	0.040
Cognitive functioning[1]	16.1	10.2	21.9	<.001*	2.4	-3.3	8.1	0.411	13.7	7.7	19.7	<.001*
Social functioning[1]	12.4	5.2	19.6	<.001*	-1.1	-7.8	5.6	0.738	13.6	6.7	20.4	<.001*
Emotional functioning[1]	15.3	8.7	21.8	<.001*	0.9	-5.2	7.1	0.767	14.3	8.0	20.7	<.001*
Fatigue[2]	-19.5	-25.8	-13.1	<.001*	-0.9	-6.9	5.1	0.766	-18.6	-24.7	-12.4	<.001*
Nausea and vomiting[2]	4.0	-1.6	9.7	0.163	8.9	3.9	13.9	<.001*	-4.9	-10.0	0.3	0.066
Pain[2]	-8.5	-15.6	-1.4	0.018	8.4	1.9	15.0	0.011	-17.0	-23.8	-10.1	<.001*

[+]Least squares group means vary with covariate and factor values; the values reported here are evaluated at a median age of 57, with a median baseline value of the respective outcome as well as without chemotherapy, metastases, or any other CAM treatment.

[1]positive change corresponds to improvement

[2]negative change corresponds to improvement

*significant after adjustment for multiple secondary outcomes using the method of Bonferroni-Holm

LCL = lower confidence limit; UCL = Upper confidence limit; confidence limits are the limits of a 95% confidence interval

8. Discussion and Suggestions

Pain is an analyzed via semiotics in homeopathy as it is an eminently personal and subjective symptom. It provides the homeopathic doctor with valuable information for choosing the

homeopathic medicine best suited to their patient. With nearly thousands of different varieties of pain sensations described in the original James Tylor Kent repertory [7], pain is certainly the most studied symptom in homeopathy. In addition to its semiological interest for the homeopathic physician, the study by Michael Frass et al. suggests the effectiveness of its prescription in SCO for the treatment of pain.

However, the results of the two studies involving doctors challenges us because it brings out an interesting paradox:

- On the one hand, oncologists and NHGPs have a high expectation for the homeopathic treatment of pain, a symptom for which these professionals feel relatively powerless to address in SCO.
- On the other hand, surprisingly, HGPs are only moderately confident in the pain management of patients, whether measured by the frequency of pain mentioned during consultation, or by the relevance of the homeopathic treatment.

9. How Can We Explain this Difference of Perception?

The first explanation is the absence of exact quantification of pain during general practitioner consultations. From one consultation to another, pain is always present and challenges the doctor. However, the previous treatment may have reduced the intensity and frequency of pain. The lack of precise quantification does not make it possible to evaluate the real effectiveness of the prescribed treatment and the degree of relief the patient experiences. The complaint remains the same, even when pain has reduced.

This repeated complaint can disturb the doctor's assessment of the effectiveness of the therapy. It should be recalled here that a reduction of two points on the visual analogue scale (VAS) of pain is sufficient for a conventional analgesic medicine to be considered effective in the treatment of pain.

We strongly encourage GPs and especially homeopaths to mention in their clinical observations the pain VAS of patients, obtained either with a ruler or analogically by simply asking the question: “From zero to 10, how much do you evaluate your pain: zero being the absence of pain, 10 being the maximum pain imaginable?” Monitoring the pain via the VAS curve gives the caregiver a clearer analysis of the clinical situation and the activity of the current treatment. The simple question: “Are you still in pain?” risks receiving a positive answer as long as cancer treatments responsible for the pain are ongoing. Discouraged, the doctor no longer asks the question, thus perhaps explaining the low frequency of the complaint of "pain" found in the questionnaire from HGPs.

A second possibility is the sometimes difficult choice of the best homeopathic medicine. This requires noticing all the homeopathic semiology and drawing a listing made complicated by the multiplicity of symptoms present during SCO. Faced with these difficulties, it might be useful to reflect on the physiopathology of this pain. Looking for the aetiology, also called causality, gives us valuable indications in the choice of homeopathic treatment [8].

The homeopathic physician should not confuse the pain associated with the cancerous disease itself and the pain related to the side effects of cancer treatments. In the first case, the homeopathic prescription will indeed be insufficient. Level III analgesics are necessary and effective.

10. Musculoskeletal Pain (MSP)

We can't help but take note of the hepatic, nephrological, or cardiac disturbances sometimes caused by regular use of class 1 analgesics in our consultations. A recent meta-analysis [9] concludes that there is no convincing evidence of paracetamol being different from placebo with regards to quality of life, use of rescue medication, or patient satisfaction or preference among cancer patients. Is it not possible that homeopathy could be an additional therapy available to the oncologist or supportive care physician in the management of pain and thus help to reduce iatrogenic risks?

Evaluation of the homeopathic management of MSP was carried out in the EPI3 pharmacoepidemiology study [10]. Of 1153 patients followed for one year by 825 GPs belonging to three different categories (one-third NHGPs, one-third mixed GPs, and one-third HGPs), the clinical benefits and evolution of musculoskeletal pain were compared in the three groups. Notably, patients treated by HGPs reported that they consumed 50% less nonsteroidal anti-inflammatory drugs and 25% fewer analgesics than those followed by NHGPs for chronic musculoskeletal pain. The authors note that this significant difference in chemical medication consumption was achieved without lessening efficacy and without loss of therapeutic opportunity over the 12 months of the follow-up.

In SCO, the most common reason for consultation for chronic MSP is pain secondary to taking anti-aromatase. This hormone-privation is prescribed as adjunctive therapy for hormone-sensitive breast cancer in menopausal women. When pain appears, it persists for as long as there is induced oestrogen deficiency, which is to say during the five to ten years of treatment. Homeopathy may sometimes appear to be insufficient to the prescribing physician, yet, when asked, patients are satisfied and come back regularly to continue the treatment of homeopathic support. The preliminary open study conducted in 2016 by Jean-Claude Karp et al. confirms the indication for homeopathic treatment in this situation [11]. It compared 20 patients starting anti-aromatase treatment with 20 patients starting the same treatment in combination with *Ruta graveolens* 5C and *Rhus toxicodendron* 9C, at 5 pellets each morning and evening for 3 months. A statistically significant decrease in joint pain occurred in the group treated with homeopathy ($p = 0.0001$). These positive preliminary results will make it possible to conduct studies on a larger number of patients. They should encourage homeopathic physicians to trust in the analgesic activity of these medicines.

In 2016, a learned society, the International Homeopathic Society for Supportive Care in Oncology (IHSSCO), was created to facilitate and develop the practice, teaching, research, and promotion of homeopathic therapy in the context of supportive care in oncology [12]. It recommended the same protocol developed by a consensus of experts published in 2017 [13], but modified it by decreasing the number of pellets taken at a time to facilitate compliance. It suggests the following for treatment of musculoskeletal pain: *Rhus toxicodendron* 9C and *Ruta graveolens* 5C, 3 pellets of each to dissolve in the mouth together morning, noon, and evening.

In our experience, if we want the analgesic action to persist beyond 3 months, it is necessary to treat the patient's terrain with a constitutional medication prescribed according to the principle of similarity and globality of symptoms. From the physiopathological point of view, it must be assumed that oestrogen deficiency is responsible for these joint symptoms. These joint pains especially affect the extremities (feet and hands) and they are ankylosis-type pain, improved by

movement and aggravated upon waking. If these symptoms first make us think of *Rhus toxicodendron*, the analysis also presents *Sepia officinalis* (Figure 1). Apart from the pain, the patients often express other symptoms such as low morale, low libido, cutaneous and vaginal dryness, and repeated urinary infections, all of which confirm the indication of *Sepia officinalis*, the homeopathic medicine specific to oestrogen deficiency.

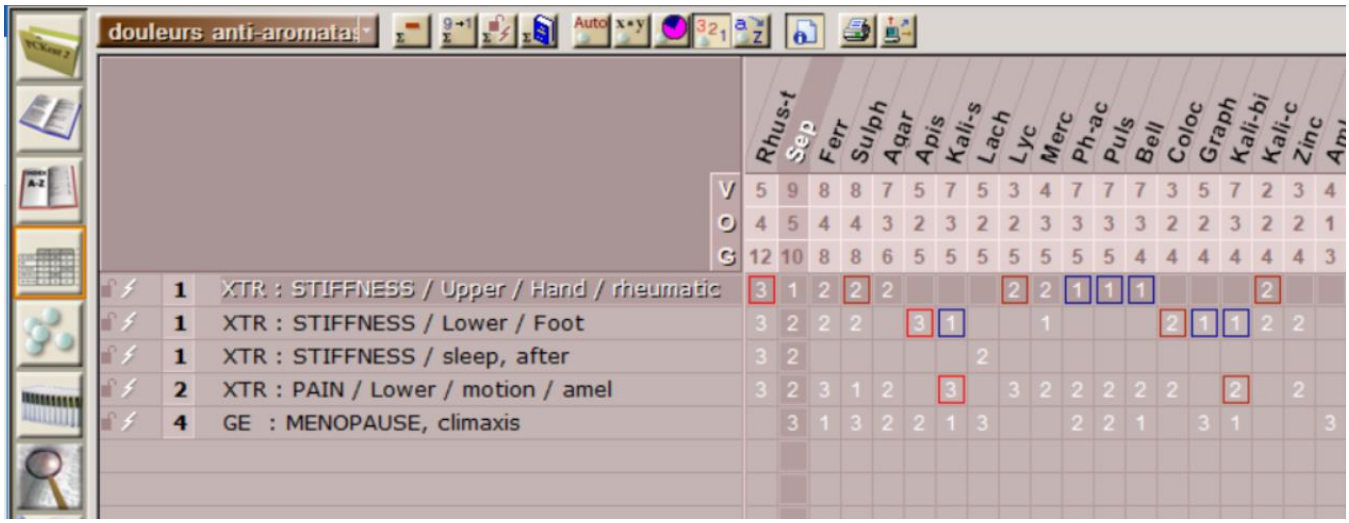

Figure 1 Repertory MSP secondary to antiaromatases on PCKent 2.2®. V=value, O=occurrence, G=Grade, XTR=extremity. GE=generality, Rhus-t=Rhus toxicodendron, Sep=Sepia officinalis, Ferr=Ferrum metallicum, Sulph=Sulphur, Agar=Agaricus muscarinus, Apis=Apis mellifica, Kali-s=Kalium sulphuricum, Lach=Lachesis mutus, Lyc=Lycopodium clavatum, Merc=Mercurius solubilis, Ph-ac=Phosphoricum acidum

The chronic and persistent nature of the pain, its aggravation by wet cold, and its iatrogenic origin indicate a sycotic reaction mode that can be treated if necessary with medicines like *Thuya occidentalis*, *Natrum sulfuricum,* and/or *Medorrhinum*.

Deformity of the hand joints and a previous history of radiotherapy may point towards the luetic reaction mode and lead to prescribing *Radium bromatum*, whose modes of improvement by movement and hot applications are the same as that of *Rhus toxicodendron*.

Other lesser-known local action medicines are: *Caulophyllum thalictroides* for intermittent and paroxysmal pain of the small hand and foot joints with articular stiffness or *Actaea spicata* for deformities and painful swelling of the first phalanges, which tend to be very sensitive to touch, but the pain is aggravated by movement. For the sake of completeness, *Polyganum aviculare* for pain in the second phalange of the fingers can also be used [14].

11. Chemo-induced Peripheral Neuropathies (CIPN)

With an incidence of 30–70%, CIPN is the second limiting factor for chemotherapy after haematological toxicity [15]. In 30% of cases, the improvement is incomplete after discontinuation of chemotherapy, making neuropathic pain a frequent reason for consultation in SCO.

CIPNs are mainly expressed by stinging pain and tingling of the hands and feet. The main agents responsible for peripheral neuropathies are platinum salts, taxanes such as paclitaxel and

docetaxel, vinca alkaloids bound to a monoclonal antibody, and bortezomib [16]. No neuroprotective treatment exists [17]. The only recommended preventive treatment is calcium and magnesium infusion prior to oxaliplatin [18]. There are no official recommendations for preventive treatment for other chemotherapies. Only dose reduction and spacing or discontinuation of chemotherapy are advised. Once established, the CIPNs are often resistant to conventional analgesics. This probably explains the high degree of dissatisfaction of oncologists and NHGPs and their significant demand for homeopathic management of these symptoms. Yet, homeopathic doctors are once again the least optimistic about the value of their treatment for this indication.

Our clinical experience shows that homeopathic treatment is especially effective in prevention at the beginning of the symptoms rather than in the treatment of well-established neuropathies. Therefore, it is important to anticipate the symptoms in homeopathic SCO and to start accompanying treatments from the first chemotherapy sessions.

The IHSSCO, in its recommendations by a professional consensus, proposes the following in prevention of peripheral neuropathies:

- *Nerve*s 8D or 4C, 1 ampoule in a little water, to keep a short time in the mouth before swallowing, morning and evening on D-1, D-0, D-1, D-2 and longer if tingling persists.
- *Phosphorus* 15C, 3 pellets in the evening on D-1, D-0, D-1, and D-2.
- *Oxalicum acidum* 9C, 3 pellets in the morning on D-1, D-0, D-1, and D-2 of associated oxaliplatin treatment.

From our experience and that of many of our colleagues, *Hypericum perforatum* is not very effective in the homeopathic treatment of CIPN pain. Although the physiopathological mechanisms responsible for iatrogenic neuropathies are still unclear, we are certain that they are not of traumatic origin, a major aetiological indication of *Hypericum perforatum*. Its frequent and automatic prescription by some colleagues may explain their therapeutic disappointments.

We carried out an online inventory for didactic purposes, looking for the most appropriate medication. Only the drugs present in the aetiological category "inflammation of the nerves" were selected. We identified the main symptoms described in the DN4 assessment questionnaire [19]. This theoretical exercise allowed us to identify five candidate medicines: *Natrum muriaticum*, *Phosphorus*, *Arsenicum album, Sulfur,* and *Aconitum napellus* from which we can choose according to the modalities and characteristics specific to each patient; this principle of individualization is necessary in homeopathy. We found that *Hypericum perforatum* only appears in 17th position.

The disruption of sodium, potassium, and calcium exchanges in the ion channels of the axonal membranes by chemotherapy (oxaliplatin in particular), is one of the mechanisms responsible for CIPNs. *Natrum muriaticum* soothes neuropathic pain and is at the top of the list of suggested medicines likely due to its ability to regulate cellular ion exchange at the sodium pump (Figure 2).

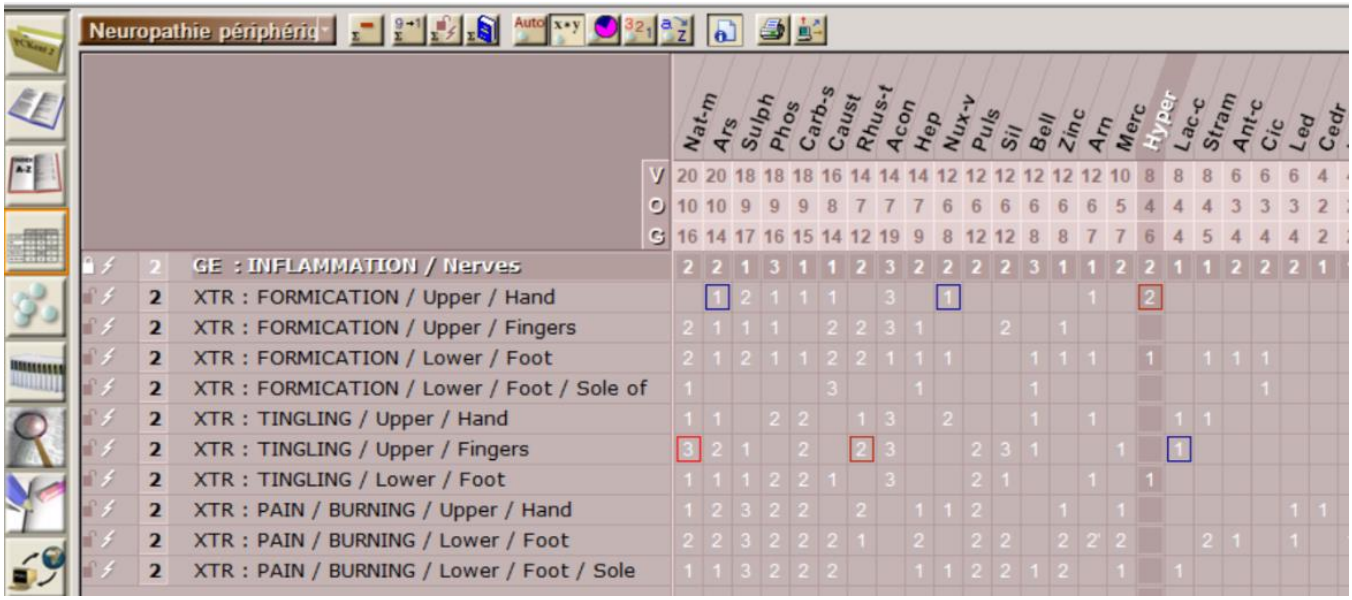

Figure 2 Repertory of painful symptoms of peripheral neuropathies according to DN4 questionnaire on PCKent 2.2®. V=value, O=occurrence, G=Grade, GE=generality, XTR=extremity, Nat-m=*Natrum muriaticum*, Ars=*Arsenicum album*, Sulph=*Sulfur*, Phos=*Phosphorus*, Carb-s=*Carboneum sulphuratum*, Caust=*Causticum*, Hyper=*Hypericum*

Another mechanism exhibited in the pathophysiology of CIPN is the inflammation of the spinal ganglia by a high presence of pro-inflammatory cytokines (IL1, IL6, and TNF-alpha) [20]. During chemotherapy, immune cells and cancer cells induce pro-inflammatory cytokines around nerve endings [21]. *Phosphorus* has been shown to exert an inhibitory effect *in vitro* on neutrophilic granulocytes. These play a fundamental role in acute inflammation, even at very high dilutions (10^{-15}) [22].

The anti-inflammatory action of *Phosphorus* (as described in the homeopathic literature) both on the peripheral nervous tissue and on the central nervous system can explain its clinical activity, which I personally observed in the control of peripheral neuropathies. IHSSCO routinely advises this medication preventively the day before, on the day of, and the day after each chemotherapy. It can also be used in the case of painful sequelae.

When painful manifestations are persistent, the aggravation modalities will be important to consider for the choice of treatment:

- For aggravation by cold we have two medicine choices. *Arsenicum album* is indicated in progressive bilateral, ascending sensory and motor paralysis of the hands and feet, which is preceded by numbness and tingling. The extremities are cold and the osteotendinous reflexes are diminished or even abolished. The musculature weakens and cramps are frequent, especially at night in bed. *Aconitum napellus* is indicated in neuropathic pain of recent appearance in conjunction with paraesthesia, frequently experienced as a tingling sensation then numbness after exposure to cold.
- For aggravation by heat, *Sulfur* helps when there is burning foot pain, aggravated by wearing shoes and relieved by walking barefoot on floor tiles or getting out of bed at night. This clinical situation occurs especially when neuropathies become chronic.

In fact, in the end, the choice of the correct remedy for the given indication depends on the overall picture the patient is presenting.

Organotherapy is a diluted and dynamized preparation of rabbit or pork organ extracts. It is used to restore and support the proper functioning of the patient's corresponding organ. Organotherapy is a supplement to homeopathic treatment to strengthen its action. The indication of the organotheray strain *Nerves*, is intriguing to us considering the pathophysiology of the neurological post-chemotherapy syndrome. Low organotherapy dilutions (4C) stimulate and high dilutions (30C) slow down the activity of the organ of the same name. This is why IHSSCO recommends *Nerves* 8D or 4C one to three times a day in the prevention and treatment of chemically-induced neuropathies. Given the very positive feedback of patients, some French oncologists have made it a routine prescription in neuropathies.

12. Conclusion

Pain is a very common side effect, and it often requires the use of class 1 analgesics whose relative effectiveness and potential toxicity make a regular prescription problematic. Homeopathic therapy with its medicinal status provides a guarantee of safety and the assurance of a prescription by a qualified doctor (in France). Considered relevant by oncologists as well as by NHGPs, homeopathic pain management represents a possible alternative to class 1 analgesics and anti-inflammatories. This work should encourage homeopathic physicians to re-evaluate pain management by utilizing the VAS at each consultation as well as discerning the pathophysiological mechanisms responsible for pain for the best-suited choice of their medicines. If the study and the listing of the totality of the symptoms is necessary for an individual prescription, the recommendations of the IHSSCO will be useful. Clinical studies evaluating the actual benefit of homeopathy in the management of pain secondary to cancer treatments are to be encouraged.

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Author Contributions

The author did all works.

Competing Interests

The author state that he participates in occasional interventions (expert reports, conferences, advisory and training activities) for Laboratoires BOIRON.

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