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Safety and efficacy of cryotherapy in the prevention and treatment of chemotherapy-induced peripheral neuropathy

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Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is a frequent complication of several chemotherapy agents routinely used in daily clinical practice [1]. It is important to prevent the onset of CIPN, since it can require chemotherapy dose reduction or early treatment discontinuation [2]. Furthermore, CIPN has a profound impact on the well-being of the patients and survivorship [3].

However, there is no effective CIPN prevention and treatment strategy; options are limited, and results are unsatisfactory [4]. The surface cooling technique during chemotherapy infusion, to reduce the blood flow in a certain area of the body by cold temperatures and limit the cytotoxic reach, has been used for some years to prevent chemotherapy-induced alopecia (cryotherapy), with satisfactory results and without raising concerns regarding the safety, and tolerability of the procedure. A few studies have been conducted to analyze the safety and efficacy of this strategy in CIPN prevention and treatment, and the results are controversial [5,6,7]. Therefore, more data are needed to clarify cryotherapy's role in this clinical context.

Materials & Methods

This is a retrospective analysis of 207 patients treated with potentially neurotoxic agents at a single Brazilian institution between December 2019 and January 2024.

Cryotherapy was administered by the Hilotherm Clinic Chemo HT02 device (Hilotherm GmbH - Oberwil bei Zug, Switzerland) [8]. The procedure consisted of patients using gloves and sock-like devices on their hands and feet throughout the chemotherapy infusion. The devices were pre-cooled to 10°C and then put on patients 30 minutes before starting, till one hour after the end of chemotherapy infusion.

A questionnaire, as proposed by Leonard et al. [9], was administered every cycle to assess the development and severity of CIPN symptoms. Palmar-plantar erythrodysesthesia (PPE) was classified according to the Common Terminology Criteria for Adverse Events, version 5.0 [10].

The quantitative variables have been described with median and interquartile range (percentile 25 and percentile 75). The qualitative variables have been described with the number (n) and percentages (%).

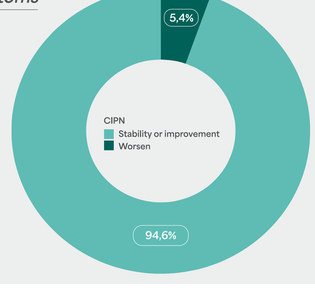
Objectives

To analyze the efficacy and safety of cryotherapy in the prevention and treatment of CIPN in patients treated with potentially neurotoxic agents in a single institution in Brazil.

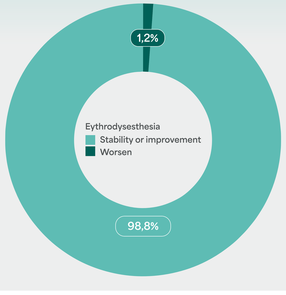
Results

Of the 207 patients analyzed, 117 (56.5%) underwent a taxane-based regimen and 90 (43.5%) received a platinum-based drug. The median duration of cryotherapy treatment was 1.4 months (interquartile range: 0.3 to 2.9). The chemotherapy was initiated with cryotherapy in 117 (56.5%) of patients. The median number of cryotherapy sessions was 4 (ranging from 1 to 31), and, when excluded patients who underwent only one session of cryotherapy (n=40), the median was 6 (range 2 to 31).
72 (34.8%) patients completed the cryotherapy. The treatment was ongoing in 14 (6.8%) of patients. The main reason for treatment discontinuation was patient decision (96 [46.4%]). In these patients that decided to left treatment, 32 (33.3%) did so after the first session of cryotherapy.
Of the 167 patients that underwent more than one session of cryotherapy, CIPN, PPE and onycholysis were stable or better than the baseline status for 94.6%, 98.8%, and 100% of them, respectively.
The percentage of patients with stable or improved CIPN than the baseline status was higher than 90% for most of the CIPN related symptoms.

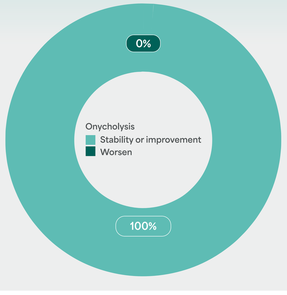
CIPN related symptoms



Eythrodysesthesia related symptoms



Onycholysis related symptoms



ANATOMIC REGION	SYMPTOM	How much of the symptoms did you have?		Did the symptoms affect your daily activities?	
		Worsen	Stability or improvement	Worsen	Stability or improvement
INFERIOR LIMBS	Tingling	34 (16.4)	173 (83.6)	18 (8.7)	189 (91.3)
	Numbness	27 (13)	180 (87)	17 (8.2)	190 (91.8)
	Difficulty of perceiving surfaces	15 (7.2)	192 (92.8)	9 (4.3)	198 (95.7)
	Difficulty feeling hot things	10 (4.8)	197 (95.2)	8 (3.9)	199 (96.1)
	Difficulty feeling cold things	9 (4.3)	198 (95.7)	9 (4.3)	198 (95.7)
	Exacerbated feeling to touch	16 (7.7)	191 (92.3)	13 (6.3)	194 (93.7)
	Burning pain or discomfort without the cold	17 (8.2)	190 (91.8)	7 (3.4)	200 (96.6)
	Burning pain or discomfort from cold	23 (11.1)	184 (88.9)	8 (3.9)	199 (96.1)
	Heavy legs	32 (15.5)	175 (84.5)	23 (11.1)	184 (88.9)
SUPERIOR LIMBS	Tingling	30 (14.5)	177 (85.5)	12 (5.8)	195 (94.2)
	Numbness	28 (13.5)	179 (86.5)	17 (8.2)	190 (91.8)
	Difficulty of perceiving surfaces	14 (6.8)	193 (93.2)	7 (3.4)	200 (96.6)
	Difficulty feeling hot things	10 (4.8)	197 (95.2)	8 (3.9)	199 (96.1)
	Difficulty feeling cold things	15 (7.2)	192 (92.8)	10 (4.8)	197 (95.2)
	Exacerbated feeling to touch	13 (6.3)	194 (93.7)	8 (3.9)	199 (96.1)
	Burning pain or discomfort without the cold	14 (6.8)	193 (93.2)	7 (3.4)	200 (96.6)
	Burning pain or discomfort from cold	15 (7.2)	192 (92.8)	12 (5.8)	195 (94.2)
	Difficulty to identify objects	11 (5.3)	196 (94.7)	9 (4.3)	198 (95.7)
	Involuntary movements	20 (9.7)	187 (90.3)	10 (4.8)	197 (95.2)
OROFACIAL	Jaw pain	11 (5.3)	196 (94.7)	9 (4.3)	198 (95.7)
	Droopy eyelids	15 (7.2)	192 (92.8)	9 (4.3)	198 (95.7)
	Discomfort in the throat	19 (9.2)	188 (90.8)	11 (5.3)	196 (94.7)
	Earache	17 (8.2)	190 (91.8)	8 (3.9)	199 (96.1)
	Orofacial Tingling in the mouth	13 (6.3)	194 (93.7)	6 (2.9)	201 (97.1)
	Difficulty to speak	11 (5.3)	196 (94.7)	8 (3.9)	199 (96.1)
	Burning or distress in the eye	19 (9.2)	188 (90.8)	12 (5.8)	195 (94.2)
	Loss of one of the views	12 (5.8)	195 (94.2)	1 (0.5)	206 (99.5)
	Sense of shock or back pain	18 (8.7)	189 (91.3)	11 (5.3)	196 (94.7)
	Breathing difficulty	13 (6.3)	194 (93.7)	11 (5.3)	196 (94.7)

Conclusions

Cryotherapy is a safe and tolerable strategy that can be used for patients undergoing chemotherapy with potentially neurotoxic agents. Our data suggests that this is an efficient approach to prevent and treat CIPN, however the results should be interpreted with caution since it is a retrospective study in a single center. Prospective randomized trials are needed to confirm the efficacy of cryotherapy in this context.

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