Antineoplastic-induced alopecia: An integrative review of the use of hair cryotherapy as a prevention strategy

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ABSTRACT

INTRODUCTION: The present study is an integrative literature review on the use of capillary cryotherapy to prevent chemotherapy-induced alopecia. Alopecia is one of the most feared adverse reactions by most patients diagnosed with cancer, having a higher impact on females because it is an aspect that is related to femininity. Hair loss affects not only the patients' physical state, but especially the psychological state, decreasing self-esteem and impairing the quality of life of these patients. The method consists of cooling the scalp through the use of frozen caps that must be changed every 30 minutes or through a cooling system that maintains a constant temperature of the cap, not being necessary for change. OBJECTIVE: This study aims to identify the effectiveness of capillary cryotherapy, in the prevention of chemotherapy-induced alopecia in patients undergoing cancer treatment. METHOD: The data collection method was performed based on the theoretical framework of Whittemore and Knafl, which consists of six stages: identification and elaboration of the research problem, search in the literature, evaluation of the data found, data analysis and presentation of the results. To elaborate the research problem, the PICO strategy was used and defined as: Is capillary cryotherapy effective to prevent chemotherapy-induced alopecia in cancer patients? Data were collected from June to August 2022. The search was conducted on the main research platforms such as the National Library of Medicine (MEDLINE), PUBMED, periodic CAPES, GOOGLE ACADEMIC and Virtual Health Library (VHL) from 2012 to 2022. RESULTS: A total of 3795 articles were found, but 3701 were excluded after reading the titles and abstracts because they did not attend the theme proposed by the study, remaining only 94 articles. However, only 15 remained for analysis, since 34 articles were not entirety available, 12 did not address the subject, 31 were duplicated and 2 were dissertations. The results were presented and detailed by constructing a flowchart based on the recommendations of the PRISMA method. To evaluate these articles, we elaborated the construction of a chart that addresses the name of the article, author, language and year, type of study and main results of each article. Then, the articles were discussed in three categories: Greater efficacy of capillary cryotherapy with the use of taxanes; Methods of using hair cryotherapy; and adverse effects of capillary cryotherapy. CONCLUSION: It is concluded that capillary cryotherapy is effective in preventing chemotherapy-induced alopecia, but to obtain positive results, a series of recommendations and care should be followed. Many factors can interfere with its effectiveness, especially the protocol that the patient uses for treatment. It is noticed that, when associated with chemotherapy based on taxanes, its use presents better results compared to anthracyclines. Nevertheless, concerns about the appearance of scalp metastases and cold-

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associated burns are highlighted. Albeit, we emphasize the importance of the nursing professional in this process, because he is responsible for welcoming, preparing and guiding the patient on the care and use of the cap. For this, the professional must be qualified and able to clarify doubts and perform the technique correctly.

Keywords: Cryotherapy, Alopecia, Antineoplastic Agents.

INTRODUCTION

Cancer is a serious disease considered a public health problem, characterized as the disordered growth of cells from a certain organ with a great capacity to invade adjacent organs and tissues (Silva *et al*., 2020).

According to information from INCA (2022), the development of cancer can occur due to several causes, divided into internal and external causes. Internal causes are related to immunological changes, hormonal changes, or genetic mutations. External causes, on the other hand, are related to the interference of the environment with our body, which is responsible for 80% to 90% of the causes of cancer. External causes include changes in the environment caused by human beings and behaviors of lifestyle habits.

Cancer is one of the leading causes of death in the world. According to information from the Pan American Health Organization (PAHO), one out of every six deaths is due to cancer. It is estimated that by 2030 the number of cancer deaths will increase by 2.1 million (Pan American Health Organization, 2022).

Over the years, policies and programs have been developed with the aim of better serving this population, giving them more security and quality in the care provided.

In 2005, the National Oncology Care Policy was instituted in Brazil through Ordinance No. 2,439 of December 8, 2005, which deals with the rights of cancer patients in relation to health services in order to promote an improvement in the quality of life of this population, as well as to encourage the development of health promotion and disease prevention actions through mechanisms for monitoring risk factors for cancer (Brazil, 2005).

In 2021, through Law No. 14,238 of November 19, 2021, the Statute of the Person with Cancer was developed, which aims to guarantee the rights of people with cancer, develop strategies for early diagnosis, guarantee these patients the right to appropriate treatment, guarantee the patient access to all information about the disease, qualify professionals to care for cancer patients, reduce mortality, and improve the quality of life of this population, among others (Brasil, 2021).

When a person is diagnosed with cancer, it is as if they are reaching the end of their life at that moment, see the stigma that the word itself brings. Karkow *et al.,* (2015) report in their study that cancer is culturally seen as a threat to life, being feared by society, and can affect a family significantly. It highlights that receiving a cancer diagnosis can affect not only the patient's life, but their entire circle of life, since they will experience all the suffering during the diagnosis and treatment of this patient. Therefore, in the same way that family and friends are important support for coping with this disease, they also need to be cared for.

In the female universe, breast cancer is the most prevalent, followed by colon and rectum and cervix. It is estimated that in 2020, there were a total of 66,280 new cases of breast cancer in women and a total of 17,825 deaths (INCA, 2022).

Breast cancer is already considered a public health problem in Brazil due to its high incidence and mortality rates, and it is also the cancer that most affects women worldwide (Medeiros *et al.*, 2019).

In this sense, the importance of early detection of breast cancer is highlighted, an action that should be stimulated by health services and especially by Primary Health Care (PHC), which is the gateway to such services.

According to the Primary Care Booklet for the control of cervical and breast cancers, nurses play an elementary role through nursing consultations, screening and control of patients, clinical breast examination (MCE), and request and evaluation of mammograms, according to established protocols and guidelines (Brazil, 2013).

The discovery of the diagnosis of breast cancer generates a lot of fear, uncertainties and anguish for women, since with it comes a series of physical and psychological changes that most of the time affect their quality of life.

After receiving the diagnosis of cancer, there are numerous challenges faced by the patient, including the adverse effects of treatment, whether with chemotherapy, immunotherapy, hormone therapy, radiotherapy or surgeries.

Chemotherapy consists of the administration of chemical substances in the body in order to combat the proliferation of cancer cells, but in addition to the diseased cells, this treatment also affects healthy cells causing a series of side effects in the patient such as nausea, vomiting, diarrhea, constipation, neutropenia, fever, fatigue, alopecia and among others (Baitelo; Kings; Gradim, 2015).

According to Silva *et al.*, (2020), 65% of patients undergoing chemotherapy treatment have alopecia as a side effect, which is the most feared by the female population because it affects their self-esteem and influences the way society sees them. This author also points out that numerous methods have been developed to prevent chemotherapy-induced alopecia (IQR), but the scalp cooling technique has been the most effective and is the most used worldwide.

Thus, IQA is one of the main concerns pointed out by women undergoing chemotherapy treatment, for this reason this study seeks to answer the following research question: Is hair cryotherapy effective to prevent chemotherapy-induced alopecia in cancer patients?

To answer this question, the objective was: To identify the efficacy of capillary cryotherapy in the prevention of chemotherapy-induced alopecia in patients undergoing cancer treatment.

METHODOLOGY

The present study is an integrative literature review based on the theoretical framework of Whittemore and Knafl (2005). The authors divide this process into six stages: identification and elaboration of the research problem, literature search, evaluation of the data found, data analysis, and presentation of the results.

The definition of the research problem was carried out through the PICO strategy (Population, Intervention, Comparison and Outcome). The population was defined as "Patients undergoing cancer treatment", the intervention "Use of capillary cryotherapy", the comparison "Patients who did not use it" and the outcome decreased alopecia. Thus, the research problem was presented as follows: Is hair cryotherapy effective to prevent chemotherapy-induced alopecia in cancer patients?

The search for studies took place between the months of June and August 2022, in electronic databases such as the National Library of Medicine (MEDLINE), PUBMED, CAPES periodicals, GOOGLE SCHOLAR and virtual health library (VHL) with the help of the librarian of the Federal University of the Southern Border (UFFS) on the Chapecó campus.

For the process of searching for the articles, we opted for the definition of descriptors in health sciences (DeCS) and synonyms combined with the Boolean operator AND, and these combinations were used in Portuguese and English to search for the articles.

Table 1 – Descriptors.

Descriptors used
Crioterapia capilar AND alopecia AND quimioterapia
Hair cryotherapy AND chemotherapy
Crioterapia capilar AND alopecia AND paclitaxel
Crioterapia capilar AND alopecia AND doxorrubicina
Crioterapia capilar AND alopecia AND docetaxel
Hair Cryotherapy AND Cancer
Hair cryotherapy AND chemotherapy
Hair cryotherapy AND câncer
Hair cryotherapy AND cancer AND chemotherapy
Hair cryotherapy AND cancer AND paclitaxel
Hair cryotherapy AND cancer AND doxorubicin

Source: Author (2023).

Scientific articles in English, Portuguese and Spanish that deal with the use of hair cryotherapy for the prevention of chemotherapy-induced alopecia, published in journals from 2012 to

2022, were chosen as inclusion criteria. Exclusion criteria were: duplicate articles in different databases, articles unavailable for full reading, and articles that addressed the use of cryotherapy for other purposes.

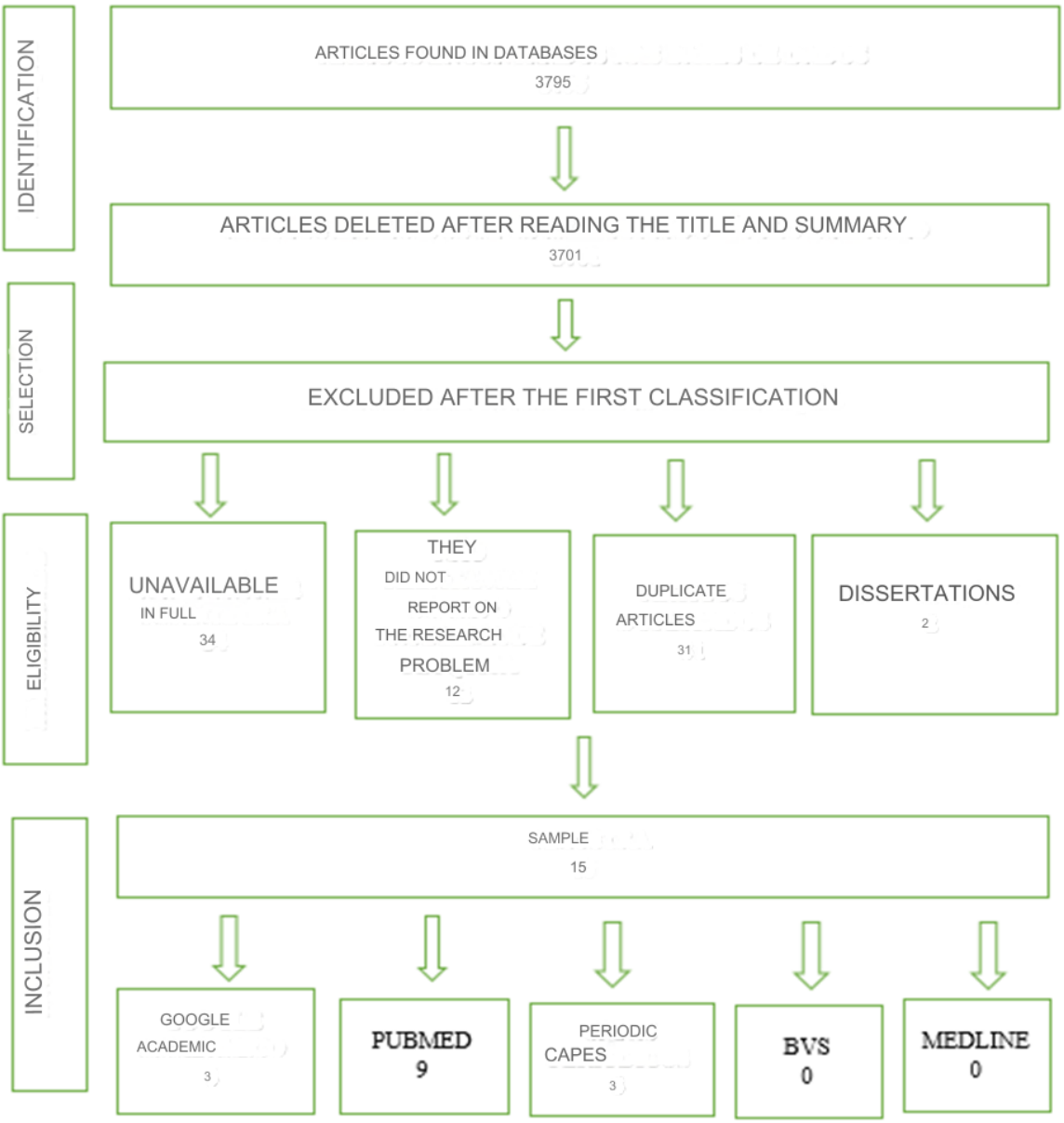
Subsequently, a table was formulated on the *Word*® platform with the following information: database, descriptors, number of articles found and number of articles found between the years 2012 and 2022, after which the search began in each of the databases. In this phase, 3795 articles were found.

After this first exclusion criterion, a second table was constructed, this time in *Excel*®, divided according to the database with the following information: title of the articles, name of the authors, website of the article, type of study and results found. The title and abstract of the articles were read and at this stage 3701 documents were excluded, leaving 94 articles to be read in full. Of the excluded articles, most dealt with the use of cryotherapy for other purposes such as mucositis, alopecia errata, peripheral neuropathy, use in animals, among others.

Subsequently, the articles were searched and read in full and a new table was prepared with the articles consistent with the objective of the research. Of the 94 articles found, 15 were included in the study and 79 were excluded. Of these, 34 were not available in full, as they needed to be paid to have access, 12 did not report on the subject proposed by the study, 31 articles were duplicates, and 2 were dissertations. Of the articles included, three were found in Google Scholar, nine in PUBMED and three in CAPES PERIÓDICO.

Based on the results found, it was decided to construct a flowchart based on the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Figure 1 – Flowchart.



Source: Author (2023).

RESULTS AND DISCUSSION

Based on the sample found, four articles are in the Portuguese language, one in Spanish and 10 in English. As for the type of study, three are presented as literature review, two systematic reviews, two literature reviews, two randomized trials and two observational studies, one cohort study, one logistic regression analysis study, one case report study and one prospective study.

Regarding the year of the study, there was a prevalence of the year 2020 with five studies, followed by 2017 with three studies, 2018 with two studies, 2012 with two studies, 2015 with one study, 2021 with one study, and 2022 with one study.

Chart 2 – List of articles found.

No.	TITLE	AUTHOR	LANGUAGE/YEAR	STUDY	RESULT
1	Hair cryotherapy as a strategy to reduce alopecia induced by oncological chemotherapy: a systematic review	Débora Esteves Monteiro	Portuguese/ 2021	Systematic review	Recommended for all types of solid tumors when using medications that cause hair loss. But it is allowed to be used only for breast cancer. Positive result in prevention, but attention should be paid to the pre-placement and post-removal care. Best result in taxanes
2	Scalp Cooling as a Method of Preventing Chemotherapy-Induced Alopecia	Antônia Cleia Silva de Souza, Lorena de Oliveira Viana, Elias Rocha de Azevedo Filho, Alberto César da Silva Lopes, Wanderlan Cabral Neves, Pablo Randel Rodrigues Gomes, Marcondes Edson Ferreira Mendes	Portuguese/ 2020	Exploratory literature review	It should be used in solid tumors. Positive results of up to 92% efficacy in taxane-based medications and up to 50% in doxorubicin and epirubicin. The English PAXMAN machine was used, which maintains a temperature of -2 to -4°. Beginning 30 minutes before medication and staying up to 90 minutes after. Concern about the risk of scalp metastasis.
3	A Clinical and Biological Guide to Understanding Chemotherapy-Induced Alopecia and Its Prevention	Christopher John Dunnill, Wafaa Al-Tameemi, Andrew Collett, Iain Stuart Haslam, Nikolaos Theodoros Georgopoulos	English/2017	Literature review	50% efficacy, with influence on the length of stay after the end of the medication infusion, proper fitting of the cap, preparation of the hair before applying the cap as well as moistening the hair. Efficacy depends on the dose and type of medication, one study addressed that ethnicity, age, and gender also have an impact on effectiveness. Less efficacy in TAC protocol (doxorubicin, docetaxel, and cyclophosphamide.

					Start of cooling 30min before infusion. Efficacy of prevention with a residence time of 45 min after the end of the infusion. Concerns about the appearance of scalp metastases.
4	Association Between Use of a Scalp Cooling Device and Alopecia After Chemotherapy for Breast Cancer	Esperança S Rugo, Paula Klein, Susan Anitra Melin, Sara A Hurvitz, Michelle E Melisco, Anne Moore, Parque Glen, Jules Mitchel, Erika Bågeman, Ralph B D'Agostino Jr, Elizabeth S Ver Hoeve, Laura Esserman, Tessa Cigler.	English/2017	Prospective cohort study	Study conducted with women with stage I and II breast cancer who received adjuvant and neoadjuvant chemotherapy, excluding anthracycline and taxane sequential or combined. Increased efficacy in taxane treatment regimen. Cooling started 30 min before medication, during and maintained for 90 to 120 min after the end of chemotherapy. Patients experienced adverse effects of cryotherapy such as headache. None of the patients had scalp metastasis. Cooling was effective with a result of 50% or less hair loss.
5	Randomized Controlled Trial of Scalp Cooling for the Prevention of Chemotherapy-Induced Alopecia".	J Bajpai, S Kagwade, A Chandrasekaran, S Dandekar, S Kannan, Y Kembhavi, J Ghosh, S D Banwani, S Gupta.	English/2020	Randomized controlled trial	It rules out the possibility of scalp metastases. Used PAXMAN system. Cooled 30 min before, during, and 90 min after end of medication. Effective in about less than 50% hair loss. It has the main adverse effect of headache.
6	Safety and Efficacy of the Scalp Cooling System in the Prevention of Chemotherapy-Induced Alopecia - A Prospective Single-Center Study	Shruti Kate, Roshankumar Patil, Dina Pathan, Rohini Vyakane, Sheela Joseph, Vibin Baby, Yasam Venkata Ramesh, Raj Nagarkar.	English/2020	Prospective observational study	30% efficiency using PAXMAN device. Cooled 30 min before, during, and 90 min after end of medication. Positive result more effective in patients using taxanes

					compared to those using anthracycline. Study conducted with various types of cancers. Most effective in men. Ethnicity interferes with effectiveness.
7	Effect of a Scalp Cooling Device on Alopecia in Women Undergoing Chemotherapy for Breast Cancer: The SCALP Randomized Clinical Trial	Julie Nangia, Tao Wang, Cynthia Osborne, Polly Niravath, Kristen Otte, Steven Papish, Frankie Holmes, Jaime Abraão, Mario Lacouture, Jay Courtright, Richard Paxman, Mari Rude, Susan Hilsenbeck, C Kent Osborne, Mothaffar Rimawi	English/2017	Multicenter randomized clinical trial	More than 50% efficacy, good tolerance. More efficiency in taxanes. Rare appearance of scalp metastases. For the study it was used based on the PAXMAN device. Cap was applied 30 min before medication and remained 90 min after.
8	Scalp Cooling for Hair Preservation and Associated Features in 1411 Chemotherapy Patients - Results from the Dutch Scalp Cooling Registry	Corina J van den Hurk, Mijke Peerbooms , Lonneke V van de Poll-French , Johan W Nortier , Jan Willem W Coebergh , Raça Wim P.	English/2012	Logistic regression analysis.	It is effective, but it depends a lot on the type of drug that is used. Taxane shows better results. It depends a lot on the time the cap remains after the end of the infusion, hair type. Great results in men. Wetting the hair does not interfere with the result. Paxman system used. It was applied 38 min before the infusion and remained for 90 min after the end of the infusion. Less effective when associated with the TAC protocol. Worst result in Asians and the elderly. Chemically treated hair, hair length did not interfere with the result.
9	Considerations for the Use of Scalp Cooling Devices in Black Patients	Erinolaoluwa F Araoye, Vered Stearns, Cristal Aguh.	English/2020	Case report	It reports on the lower efficacy in patients with curly hair due to the difficulty of adhering the cap to the head. It brings aspects that help in the effectiveness of the cap

					in patients with curly hair
10	Pathogenesis and treatment options for chemotherapy-induced alopecia: a systematic review	Belen Rubio-Gonzalez MD, Margit Juhas MD, Jamie Fortman MSc, Natasha Atanaskova Masinkowska MD, PN.	English/2018	Systematic review	It discusses the medications that cause ASD and the effectiveness of scalp cooling. Proven efficacy with the PAXMAN device. Indicated only for patients with solid cancer, due to the possibility of scalp metastases. Hair loss of less than 50%.
11	Short post-infusion scalp cooling time in the prevention of docetaxel-induced alopecia	C.J.G. van den Hurk, W.P.M. Breed and J.W.R. Nortier	English/2012	Observational study	Proven efficacy with the PAXMAN device. The cap was applied 30 min before the infusion, during and 45 to 90 min after the end of the infusion. Most effective result in 45 min time.
12	Chemotherapy, alopecia, and scalp cooling systems	D yellow, D for Boni, m neck.	Spanish/2022	Literature review	Used in solid tumors, especially breast cancer. Start 30 - 45 min before medication, during and 90 min after. The PAXMAN method resulted in less than 50% alopecia in patients, while the DIGNICAP system was 39.3% effective.
13	Scalp hypothermia as a preventive measure for chemotherapy-induced alopecia: a review of controlled clinical trials	VV Shah, TC Wikramanayake, GM Del Canto, C van den Hurk, S Wu, ME Lacouture, JJ Jimenez.	English/2018	Bibliographic research	It proves the effectiveness of hair cryotherapy, especially when used for taxanes. Lower efficacy when associated with taxanes and anthracyclines. He reports that this efficacy depends a lot on the drug and the dose used. It reports on the appearance of metastases on the scalp after the use of hair cryotherapy. Greater effectiveness when the temperature is maintained at 18 degrees during infusion.

					Care should be taken at home, such as avoiding washing your hair in warm water and avoiding drying your hair.
14	Efficacy of Scalp Cooling in the Prevention of Chemotherapy-Induced Alopecia in Breast Cancer Patients Receiving Adjuvant Docetaxel and Cyclophosphamide Chemotherapy	Caesar Cigler Devora Isseroff Bárbara Pederlein Sarah Schneider Ellen Chuang Linda Vahdat Anne Moore	English/2015	Prospective study	For this study, the Penguin Cold Caps device was used in 20 women who received treatment with docetaxel and cyclophosphamide protocol, which demonstrated efficacy in the prevention of chemotherapy-induced alopecia. She reports on the risk of metastasis due to the fact that chemotherapy does not reach the scalp. 90% of the participants did not report the need to wear a head covering. It reports that scalp cooling is effective depending on the protocol.
15	Scalp Cooling in the Prevention of Chemotherapy-Induced Alopecia: Overview	Giselle de Barros Silva, Kathryn Ciccolinib, Aline Donatic, Corina van den Hurkd.	Portuguese/2020	Literature review	It addresses that the permanence time of the post-infusion cap can interfere with the success of cryotherapy and that its result depends on the protocol being used. With the best result the time of 45-90min. Reports better results with protocol taxanes 81% - 94%. She reported concern about the incidence of metastasis in the scalp. Adverse events such as nausea, dizziness, headache and scalp burning.

Source: Author (2023).

After reading, three categories were elaborated: Greater efficacy of hair cryotherapy with the use of taxanes; Methods of using hair cryotherapy; and Adverse effects of hair cryotherapy.

INCREASED EFFICACY OF HAIR CRYOTHERAPY WITH THE USE OF TAXANES

Based on the articles that make up the study sample, it was highlighted that most of them addressed that the effectiveness of hair cryotherapy depends largely on the chemotherapy protocol that the patient receives. Articles No. 01, 02, 03, 06, 07, 08, 13 and 15 reported better efficacy in protocols composed of taxanes (paclitaxel and docetaxel).

Study number 1 was conducted with women diagnosed with breast cancer using chemotherapy treatments with anthracyclines and paclitaxel, docetaxel and cyclophosphamide, with greater efficacy in patients who used taxanes compared to those who used anthracyclines.

Study number 6, also conducted with women with breast cancer, addressed a 59% efficacy rate in women who underwent scalp cooling under treatment with a taxane-based protocol compared to 16% who used anthracyclines. In a randomized study discussed in the article, 6 it showed a 77% rate of hair preservation in women who underwent treatment with taxanes, compared to 33% who used anthracyclines.

Alopecia is the most feared side effect by most women undergoing cancer treatment, for many it is more traumatic than receiving the diagnosis of the disease, going through the mastectomy process or living with the disease itself (Mairink *et al.,* 2020).

According to Reis and Gradim (2018, p. 448), alopecia is described as "the loss of hair and any other body hair such as eyebrows, axillary hair, pubic hair and/or leg and arm hair".

For women, hair loss is closely related to femininity and its loss, in addition to causing changes in their physical state, can also affect their emotional state, which can be the most difficult stage to be faced during treatment (Monteiro, 2021; Silva, 2020).

Hair loss happens due to the strong aggression that the hair suffers during the infusions of chemotherapy drugs. Atrophy of the hair follicle occurs, causing weakening and subsequent hair loss. This decrease may occur between two and three weeks after the beginning of the treatment, and may last until its end (Baitelo; Kings; Gradim, 2015). The return of hair growth may take three to six months after the end of treatment and permanent alopecia may rarely occur (Kruze; Abraham, 2018).

Chemotherapy treatment consists of the administration of antineoplastic medications in the body, which can be isolated or combined. There are numerous chemotherapeutic drugs that cause alopecia, among them we can highlight doxorubicin, epirubicin, docetaxel, paclitaxel, etoposide, cyclophosphamide and ifosfamide. (Konen *et al.*, 2013; Souza *et al.*, 2020),

Given the impact that alopecia has on the lives of cancer patients, several studies have already been carried out in order to find a way to minimize this suffering. According to Silva *et al.,* (2020), hair cosmetics have been developed that help with hair growth, but not in the prevention of IQR, but they still need more evidence. The scalp cooling technique has been used since 1970 and has been

proving its effectiveness every day. This technique is used through the application of cryogel pouches, caps, and cooling machines.

For Martinez *et al.*, (2018), alopecia is a factor that significantly affects the quality of life of patients undergoing cancer treatment, especially women. Based on his study, about 8% of the female population abandons treatment or does not even start when they discover that the process has alopecia as one of its adverse effects. This study also addresses that the patient is affected emotionally regardless of the degree of alopecia, whether it is 1 with loss of up to 50% of hair or 2 with significant loss of more than 50%.

The quality of life of the patient who is undergoing cancer treatment is drastically affected during this cycle, and having to live with and deal with alopecia is not easy.

Some patients suffer so much that they end up isolating themselves from the world, family and friends and often end up falling into depression because they do not accept the appearance and the diagnosis. On the other hand, the world is cruel to these people, because we live in a place where a standard of beauty is still imposed and the bald woman is seen with pity, because this is the main characteristic of the patient undergoing chemotherapy treatment.

Although many ways of treating alopecia with the use of topical creams have been developed, this method has not shown much proof of its effectiveness. On the other hand, the use of hair cryotherapy has been gaining more and more space, however the success of the treatment depends on many factors, such as the chemotherapy protocol in use, and the method of application of the cap. Better results are seen in taxane-based treatments of about 50% compared to the use of anthracyclines, which showed results of 16% efficacy (Kang *et al*., 2019).

As it is an important concern in the population undergoing chemotherapy, especially in the female population, the presence of permanent alopecia in patients after treatment has been studied.

Normally, the hair grows back about 3 to 6 months after the end of the treatment, and may present changes in color, texture and number of hairs. In some cases, permanent alopecia can occur, which can be total, partial or simply present a delay in hair growth. This condition can arise when the chemotherapy agent attacks the stem cells in the hair leaflet that are responsible for the growth of a new hair (Rossi *et al*., 2017).

In a study conducted by Martin *et al.,* (2018), patients who presented grade 2 alopecia during chemotherapy treatment did not show hair improvement or recovery within 48 months after the end of treatment, and some were followed for a period of 10 years and did not manifest hair recovery, even with the help of other treatment methods.

Another study conducted to evaluate chemotherapy-induced permanent alopecia (PCIA) found that 39.5% of patients who suffered alopecia during treatment did not fully recover their hair 6

months after completion, while 42.3% reported PCIA for 3 years after the end of chemotherapy treatment (Kang, 2018).

In article number 8, a study was carried out with 1411 patients who underwent scalp cooling. According to the study, the best results were seen in patients who received taxane-based chemotherapy. 94% of patients using docetaxel and 81% of those using paclitaxel did not need to wear a head covering.

In a study conducted with breast cancer patients treated with taxanes and anthracycline, the patients who participated in the study obtained 57% of hair preservation after the use of capillary cooling, while the group that did not use it obtained 0% preservation. Regarding the sequence of chemotherapy, the patients who received taxane chemotherapy followed by anthracycline with 77% showed the highest efficacy, while those who received the opposite obtained a result of 33% efficacy (Bajpai *et al.*, 2020).

METHOD OF USE OF HAIR CRYOTHERAPY

This category includes studies related to the device, length of stay in the patient, and pre- and post-use care.

According to the articles participating in this study, the efficacy of hair cryotherapy interferes with several factors.

As for the cooling devices used in the studies, the paxman cooling machine was the most used, and its effectiveness was proven in articles 2, 5, 6, 7, 8, 10, 11 and 12.

Regarding the length of stay in the patient, there are several approaches. Articles 2, 5, 6, 7, 10, 11 and 12 report the beginning of the procedure 30 minutes before the infusion of the chemotherapy drug, during the infusion and 90 minutes after. Study number 3 depicts about 30 minutes before, during the infusion and 90 minutes after, with efficacy 45 minutes after the end of the allopeciating medication. Study 4, on the other hand, shows 30 minutes before, during the infusion and 90 to 120 minutes after the end. And study number 14 on the penguin system reports the use of 50 minutes before, during the infusion of the medication that causes alopecia and 4 hours after its end.

Capillary cryotherapy is a method of cooling the scalp through the application of refrigerated caps, such caps when applied trigger a process of vasoconstriction of the blood vessels of the scalp preventing blood flow and consequently preventing chemotherapy from reaching and causing hair loss (Turke *et al.,* 2019).

In the 1970s, the scalp cooling method was performed by placing crushed ice packs on the head and fixed by bandages, with the aim of minimizing hair loss, and it was necessary to replace these bags regularly due to the fact that the heat from the head caused the ice to melt (Dunnill *et al.,* 2018).

Over the years, new technologies have been implemented, ice bags have been replaced by cold air bags, gel caps, and later by an electronic cooling method (Shah *et al.,* 2017).

There are two ways of cooling the scalp nowadays, one is through hypothermic caps that are placed over the patient's head and need to be changed every time as soon as they lose the ice and another way is through cooling systems that are connected to a machine that constantly circulates cold air (Kruse; Abraham, 2018).

Among the most used brands for the scalp cooling technique are elastogel, dignicap and paxman, which we will discuss below.

Elastogel caps are developed with malleable fabric and their interior is composed of glycerin-based hydrogel and remains flexible even at negative temperatures. The cap should be stored at a temperature of -25ºC to -30ºC. Being applied to the patient 15 minutes before the beginning of the infusion of the allopeciating chemotherapy drug, maintained throughout the administration with a change for a new one every 45 minutes, and maintained around 30 minutes after the end of the infusion (Martin *et al.,* 2018).

This type of cap is no longer manufactured today, its acquisition can be made through buying and selling sites on the internet, and on the elastogel company's website it is no longer available. Places that want to make this method available to their patients should have a freezer to store the caps as they must be kept at negative temperatures.

Among the cooling method with the use of machines, we can highlight PAXMAN and DIGNIPAC.

The English Paxman cap appeared in 1997 when Glen Paxman's wife used the scalp cooling method available at the time to prevent alopecia during a treatment for breast cancer and was unsuccessful. In this way, the Paxman family has developed a system that contains a constant cooling method through a machine that circulates a liquid at -4ºC, but maintains the scalp temperature of 18ºC. As it is connected to a machine that does not require a cap change, it is applied to the patient 30-45 minutes before the beginning of the infusion of the allopeciatic chemotherapy and maintained until 90 minutes after its end. depending on the chemotherapy protocol used. Its manufacturer guarantees a 50% to 92% effectiveness of hair preservation (Paxman, 2022).

Its system consists of a silicone cap connected to the machine, a fabric band to protect the frontal region, a secondary cap to fix and keep circulating cold. The manufacturer recommends moistening the hair and applying conditioner before applying the silicone cap to improve conductivity. This device can be used by two people at the same time, as it contains two interconnected systems on the same machine and has caps in three sizes S, M and L.

The Paxman system is FDA (Food and Drug Administration) certified and is now included in the National Comprehensive Cancer Network's (NCCN) Clinical Practice Guidelines in Oncology.

The DigniCap system was developed in Sweden in 1990 by nurse Yvonne Olofsson. Yvonne was an oncology nurse at the time and every day she was faced with the anguish, suffering and impact that alopecia had on the quality of life of her patients. The system was developed by Yvone together with engineer John Kern, who named the device Dignicap, which in Latin means dignity (DigniCap, 2022).

The DigniCap cooling device consists of a cooling machine that controls the time and temperature to be sent, a cooling wrap that is attached and adjusted to the patient's head which receives the low temperature fluids and a thermal cap used above the wrap with the function of isolating the cold. The refrigerant fluid is sent to the wrap by a hose and this fluid is monitored by two sensors, one that controls the temperature sent and one that monitors the temperature that returns to the machine. There is also the possibility of disconnecting the hose to facilitate exits to go to the bathroom, for example (Dignipac, 2022).

Recently, the NCCN began to recommend the use of hair cryotherapy for the prevention of IQA in patients with breast cancer (Silva *et al.,* 2020). Its use is indicated for any patient with solid cancer, on the other hand it is contraindicated for patients with hematological tumors due to the risk of scalp metastasis (Monteiro, 2021).

However, Kruze and Abraham (2018) report that this technique is contraindicated for patients with hematological malignancies, due to the risk of interfering with the efficacy of the treatment, since this method decreases the total circulation of the chemotherapy drug throughout the body. On the other hand, it is also contraindicated for patients who report migraine, agglutinin diseases, and cryoglobulinemia, as such conditions can be aggravated by exposure to cold.

Nowadays there are two forms of scalp cooling on the market that promise to minimize the QIA, one which consists of changing the cap every 25-30 min and another that is connected to a cooling machine that keeps the temperature constant. During the process, areas such as the ears and frontal region should be protected with gauze or tissue to avoid burns at the site caused by the cold (Silva *et al.*, 2020).

Recent studies report that most users of hair cryotherapy tolerate the adverse effects that include headache, scalp pain, and chills. Studies have also reported the incidence of scalp metastasis, but no effective evidence to date (Kruse; Abraham, 2018).

Based on the time the cap remains 45 minutes after the end of the infusion, according to Dunnill *et al.,* (2020), in a study conducted with patients who used docetaxel, the best result of capillary cryotherapy was with patients who remained for 45 minutes after the end of the infusion of the medication. According to the author, this result is based on the fact that from the moment the concentration of the medication decreases, it is no longer toxic to the body, when the scalp is heated again, it allows the drug accumulated in the scalp to be more easily eliminated.

According to Paxman (2022), the permanence time of the cap after infusion depends on the protocol being used. Protocols with combinations of allopeciating chemotherapeutic agents should be kept at 1h30min after, while weekly paclitaxel and docetaxel time changes to 1h.

There is not yet a confirmed standard of post-infusion cooling time (PICT). According to Lugtemberg *et al*., (2022), to evaluate the PICT, the pharmacokinetics and half-life of the chemotherapy drug should be taken into account.

In addition to the length of time the cap remains in the patient, other factors are important to obtain good results and prevent IQR.

According to Bajpai *et al.*, (2020), the effectiveness of scalp cooling depends on three main factors: proper fit of the cap, chemotherapy used, and adequate cold temperature.

Based on the pre- and post-use care of cryotherapy, some authors mention some important precautions for the effectiveness of the process.

Article number 1 and 14 bring that hair should be washed 2-3 days after chemotherapy and not rubbing the scalp, avoid hot baths and use of hot air devices and be careful when brushing hair. At the time of cryotherapy, the hair should be wet and conditioner used to improve conductivity. Areas such as the frontal region and ears should be protected before applying the cap. In article 14, a study was carried out with polyurethane caps that require change every 30 minutes, the author mentions that the hair needs to be cared for 2 weeks before the procedure and remain for months after the end of the treatment.

Articles 3 and 9 state that the hair must be moistened before applying the cap and it must be fitted correctly to the patient, ensuring that all parts are affected. Article 8, on the other hand, states that moistening the hair does not interfere with the result of cooling, as well as long or chemically treated hair.

Hair care is practically the same regardless of the device chosen for use and is very important in the effectiveness of cryotherapy. The manufacturer of the PAXMAN cooling system has put together a manual for home hair care after using cryotherapy. The manual was prepared according to each type of hair and care includes: washing your hair no more than twice a week and not using hot water, not using devices that emit heat, using neutral shampoo and conditioner, not rubbing the scalp and among others (Paxman, 2022).

In addition to those mentioned above, the manufacturer of the dignicap system reports on the importance of combing your hair 2 times a day, using a comb with large teeth, letting it dry naturally, and not using chemical products on your hair, it also reports that it is not necessary to cut your hair (DigniCap, 2022).

In addition to care during the use of cryotherapy, the effectiveness of scalp cooling also depends on home management. Garza *et al*., (2020) highlight that the use of heat, shampoos, and

other hair products that make up parabens and dyes in their formula can negatively interfere with the outcome of IQR prevention.

According to Katz (2017), hair care can interfere with the effectiveness of IQA prevention. Although it is not scientifically proven, it is believed that wetting your hair and applying conditioner can improve the conductivity of cold. In addition, some post-use care should be followed, such as avoiding swimming pools and saunas, avoiding washing hair with warm or hot water, not washing hair for three days after cryotherapy, not using equipment that heats the hair and using neutral shampoos.

In addition to all the pre and post chemotherapy care for the prevention of alopecia, the manufacturer of the Paxman method also indicates the use of scalp cooling for hair recovery. According to Kinoshita *et al.,* (2019), 25% of patients in the group who underwent hair cryotherapy who suffered grade 2 alopecia recovered their hair within 12 weeks after the end of chemotherapy using paxman capillary cooling. In contrast to the control group, 8.3% recovered in the same period of time

ADVERSE EFFECTS OF HAIR CRYOTHERAPY

In this category, we will discuss the adverse effects pointed out in studies on the use of hair cryotherapy. Studies 1, 4, 5, 6, 7, 10, 11, 12, 13, 14 and 15 addressed adverse effects of cryotherapy. Among the most described side effects are headache, nausea, vertigo and sensitivity to cold, the latter being the cause of most dropouts from treatment with cryotherapy. In addition to these, articles 10, 13 and 15 highlight the presence of frostbite in scalp regions.

Frostbite in patients using hair cryotherapy is a rare adverse effect that is rarely mentioned in articles. Belun *et al*., (2016), reported four case studies of patients who experienced scalp burns from the use of hair cryotherapy. The patients were women with breast cancer undergoing chemotherapy treatment. Three of the patients used the penguin device and one used the elasto-gel cold cap. Both patients had burns on the scalp, with the presence of hyperemia, blisters and consequently alopecia. All patients had persistent alopecia or growth retardation and scalp sensitivity.

The first case was a woman diagnosed with invasive breast cancer, who underwent hair cryotherapy with a penguin device, and the patient presented erythema and blistering on the top of the head and frontal region. The second case was a woman diagnosed with triple-negative breast cancer, who underwent first-line treatment on doxorubicin and cyclophosphamide, which presented significant hair loss. As a sequence of treatment, he started with applications of paclitaxel and in his third application, he started hair cryotherapy with elasto-gel cold caps, after a few applications, the patient presented blisters in the left parietal region and great hyperemia in the scalp. Case three is a woman with metastatic breast cancer, who used a penguin device that was not respected for the

infusion time after chemotherapy and was removed soon after the end of the infusion. After two weeks, the patient presented pruritus and alopecia, but continued to wear a cap with cloth protection. Days later, she presented blisters in the frontal region, followed by alopecia. The fourth case is a patient diagnosed with invasive ductal breast cancer, who used the penguin device, and after the third cycle she presented pruritus, crusting and scaling, but persisted with use, resulting in alopecia. Both patients had persistent alopecia and scalp tenderness.

Based on previous reports, the importance of training professionals to perform and monitor patients using the scalp cooling technique is highlighted. It is necessary to understand the process and be prepared to guide and manage the adverse effects. It is important to understand alopecia and know how to assess the severity to avoid possible complications in the patient's health.

It is up to nursing to guide patients regarding the technique, adverse effects, target audience, effectiveness, and care before and after cap use (Monteiro *et al*., 2021). As these are the professionals who are in direct contact with the patient, they must be prepared to answer and clarify any doubts.

In addition to providing care during treatment, the nursing professional becomes close to this patient, providing support to cope with the disease, giving support to him and the family. It is the nursing professional who monitors the entire treatment process and manages the adverse effects, infusions and delays, giving more quality of life to the patient.

Of the 15 articles participating in this study, 11 of them portray the concern about the appearance of skin metastases on the scalp as a side effect of cooling, but so far there is no scientific evidence to prove this theory.

In articles 1 and 10, the author mentions that capillary cryotherapy is not recommended for patients with hematological neoplasms due to the risk of skin metastases. In article 3, a study conducted with breast cancer patients found 0.03% of metastases in patients who did not undergo scalp cooling, compared with 0.04% in patients who did. In article 6 a study was carried out with 100 women and of these only one developed metastases on the scalp after an application of hair cryotherapy, but it was not really proven if this was the cause of the metastasis.

According to Bajpai *et al.*, (2020) Cancer cells can lodge in the scalp as a way to protect themselves from chemotherapy due to the cooling of the scalp, and can later move and metastasize to other sites.

The appearance of scalp metastases is worrisome, the hypothesis is taken into account by the fact that during the use of capillary cooling chemotherapy does not reach the scalp (Saad *et al.,* 2018). On the other hand, a study conducted with women with breast cancer did not identify evidence of scalp metastases. Metastases were most frequently identified in the chest and skin region (Rugo *et al*., 2017).

As much as many studies prove its effectiveness, the scalp cooling device is an equipment of great financial value, in Mexico it varies from $1500 to $3,500 USD, this is equivalent to R$18,168.50 reais per application, an amount that is not paid by the health plan, but the patient must pay if there is interest in using it (Garza *et al*., 2020).

Consequently, due to the amount imposed, it is notable that the device does not reach the less needy population, but only those who can afford it or who have health insurance, in this way, patients who use public health services do not have this technology that would improve their quality of life and consequently change the way they face cancer.

CONCLUSION

At the end of this study, it was noticed that the use of capillary cryotherapy has greatly added to the quality of life of patients undergoing cancer treatment. As it is a system that can only be used in patients diagnosed with solid tumors, this system requires a series of precautions and recommendations to achieve the desired results.

Since 1970, when the process of cooling the scalp to prevent alopecia in cancer patients began, many changes had to be made to achieve the result we have today, which in addition to being more effective is more comfortable and safer for the patient.

It was concluded that capillary cryotherapy is effective to prevent IQA, since in male patients it presents better results. No evidence was found as to why this efficacy is due to the fact that most men have shorter hair or tolerate the process better.

The effectiveness of the technique also depends on the care before, during, and after chemotherapy, such as precautions when washing the hair, exposure to chemicals or utensils that promote hair warming, time of use of the cap, preparation of the hair, and proper size of the cap. Another factor that interferes with the outcome is the type of antineoplastic protocol used by the patient. It is observed that taxane-based chemotherapeutics, such as paclitaxel and docetaxel, have better efficacy compared to anthracyclines.

However, the time of permanence of the cap in the patient after chemotherapy infusion is much discussed by the authors, the discussions are based on 45 min, 60 min and 90 min., but based on studies that prove the Paxman system, the time after infusion depends a lot on the class of chemotherapy used.

The main concerns of using the cooling technique are the appearance of scalp metastases and the risk of frostbite. As for metastases, there are no records that prove this theory, they are still hypotheses that are in the study phase, as for scalp burns, there are case reports about its occurrence and that resulted in persistent hair alopecia.

One of the systems used to cool the scalp, such as elastogel caps, is no longer being produced, but nothing is known about the reason for the cessation of the productions and its acquisition is available on some sales sites on the internet.

Although the system has been in use since 1970, there are still few studies on hair cryotherapy and most of them are in the English language modality.

At the time of the research, it was noticed that the search did not present positive results regarding the terms "hair cryotherapy", but rather "scalp cooling". The vast majority of articles whose research was carried out with the term hair cryotherapy were excluded because they were studies that addressed its use for other purposes.

As it is a high-cost system, its acquisition is still unavailable in the Unified Health System (SUS), while in private systems it is gaining more and more space.

However, nursing plays a very important role during the use of capillary cryotherapy, as it is the professional who receives training to prepare, apply and guide this patient on the use and efficacy of the cap. Thus, this professional must be prepared to accompany the patient, as well as clarify doubts about cryotherapy. Knowing how to assess the degree of alopecia is also the role of nursing and this process is important to prevent the occurrence of scalp burns.

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