CRYOTHERAPY EFFECT IN PREVENTION OF ORAL MUCOSITIS IN ADULT PATIENTS WHO RECEIVED CHEMOTHERAPY: AN EVIDENCE-BASED REVIEW

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Abstract

Prevention and management of oral mucositis (OM) in adult patients who received chemotherapy are challenging issues for health care professionals. Numerous methods have been tested to cope with this problem.

Aims: the goal of this evidence-based review is to identify effectiveness of cryotherapy in prevention of oral mucositis in adult patients who received chemotherapy.

The method: a literature search was performed using an appropriate keywords search in Cochrane, Science Direct and Pubmed databases from 2009 to 2013. However, two exclusive studies that were conducted in 2007 have been included. Nine full papers are included in this review.

The inclusion criteria were : adult cancer patients who had OM, Oral mucositis induced by chemotherapy, using cryotherapy to prevent OM and articles written in English language.

The findings: cryotherapy has an effective method in prevention of OM with chemotherapy regimens that include 5FU regimens and high dose melphalan.

Conclusions: cryotherapy is an effective method for prevention of oral mucositis in patients who received two specific chemotherapy regimens that include 5FU regimens and high dose melphalan. In addition, the efficacy of oral cryotherapy is affected by the types of chemotherapy regimens including the half life for each one and it depends on the causative mechanisms of oral mucositis including direct and indirect mucositis.

Recommendations: researchers recommended doing additional studies (clinical trials) to broaden the potential applications of cryotherapy in clinical settings, with increased sample size in order to generalize findings, and to increase nursing awareness with this method.

Key words: oral mucositis, cryotherapy, chemotherapy

1. Introduction

Oral mucositis (OM) is a common symptom effect of radiation and chemotherapy. It is defined as an inflammation of oral mucosa resulting from cancer therapy typically manifesting as atrophy, swelling, erythema and ulceration (Sonis, 2004).

It has a serious impact on those who are undergoing cancer treatment. It will affect treatment schedule by delay or discontinued treatment, quality of life and aspects of daily living (Brown, 2010). It also increases the possibility of the use of a nasogastric tube or total parenteral nutrition, the need for vascular access, and the use of Opioids (Svanberg, 2007) and increases the length of hospital stay and consequently increases costs (Rubenstein et al., 2004). Thus, OM represents a significant source of morbidity after chemotherapy and radiation therapy.

However, prevention and management of OM are challenging issues for health care professionals. Unfortunately, we are still unable to offer curative solutions to those patients who suffer from OM.

Numerous methods have been tested to cope with this problem. In this evidence-based review, the focus will be to investigate if cryotherapy is a good prevention method for OM or not. The purpose of this review is to identify effectiveness of cryotherapy in prevention of oral mucositis in adult patients who received chemotherapy.

1.1. The PICO Summary and Questions:

P: The population of this review are Adult cancer patients who had OM and who received chemotherapy.

I: The intervention is cryotherapy.

C: The Comparison is between patients who received cryotherapy intervention and patients who did not receive cryotherapy or who are in usual oral care.

O: The desired outcome is to prevent OM and decrease its severity.

1.2. PICO Questions:

1. Does cryotherapy prevent OM ?
2. What is the difference between patients who received cryotherapy intervention and patients who did not during different chemotherapy regimens?
3. Is the efficacy of cryotherapy influenced by different chemotherapy regimens?

2. Methods

Multiple words were used to search for literature on cryotherapy effect on OM. The following words were placed in the online indexes individually and in combination with one another: oral mucositis, cryotherapy, management of oral mucositis, treatment of oral mucositis, cryotherapy and oral mucositis.

The inclusion criteria were:

1. Adult cancer patients who had OM.
2. Oral mucositis induced by chemotherapy only.
3. Using cryotherapy to prevent OM.
4. Articles written in English language.
5. Original research articles
6. Randomized controlled trials

A search in Cochrane, Science Direct and Pubmed databases from 2009 to 2013 was completed. Searching in Science Direct database for the keywords: oral mucositis and cryotherapy between 2009 and 2013 resulted in 84 articles; after analyzing these articles based on the study purpose, objectives, design, major results and conclusion, the selected articles were 3 articles which matched the previous inclusion criteria. Using Pubmed database in searching keywords of oral mucositis and cryotherapy in the period between 2009 to 2013 66 articles were obtained and the net number of articles after analysis were 9 articles; 4 were excluded to prevent redundancy and 2 were abstracts which were also excluded. In Cochrane database the last systematic review paper published in 2013 will include this review, in order to prevent duplication of the previous publications of the same paper in 2008, 2010, 2011 and were not included. However, two exclusive studies that were conducted in 2007 will be included in this review. In sum, nine full papers were appropriate for review.

3. Findings

Cryotherapy has shown a significant effect in prevention of OM in adult cancer patients who received specific chemotherapy treatment. According to the evidence of clinical trials that tested this method, the principle of action of cryotherapy is based on its ability to prevent chemotherapy to reach oral mucosa. Thus, the mechanism of action of cryotherapy is to induce a local cooling of tissues which causes local vasoconstriction and decreased blood flow to oral mucosa which leads to reduction in the distribution of drug through the cells and as a result the risk of oral mucositis formation also decreases (Katranc et al., 2012). Six studies will be reviewed here based on cryotherapy intervention to prevent oral mucositis.

Prevention of OM in High Dose Melphalan:

It has been shown that cryotherapy reduced the incidence and severity of OM caused by high dose melphalan. These hypotheses are supported by a study conducted by Vokurk and his colleagues (2011), which verified the extreme effectiveness of oral cryotherapy in prevention of OM in both single high dose melphalan 200 mg/m² conditioning regimen and multidrug BEAM regimen(melphalan 140 mg/m²) followed by autologous HSCT.

Prevention of OM in 5-flurouracil (5FU) Combined with other regimens:

A randomized controlled study conducted by Heydari, Sharifi and Salek (2012), was aimed to assess the effect of oral cryotherapy on the incidence and severity of chemotherapy-induced oral mucositis in combined chemotherapy regimens. These regimens include : 5- fluorouracil with leucovorin; cyclophosphamide, adriamycin and 5-fluorouracil; cyclophosphamide, methotrexate and 5-fluorouracil. In the assessment of OM degree and severity; World Health Organization (WHO) mucositis grades and patient-based oral mucositis scales were used. The comparison was done between two groups: Experimental group who used cryotherapy and control groups who did not receive cryotherapy, for both groups (EXP and CTR) the differences in percentage of patients treated with three various regimens were not statistically significant. The final result indicated that OM was decreased 50% more in the experimental group than control group. The cryotherapy was applied for 30 to 60 minutes during the chemotherapy treatment.

Katranc and his research colleagues (2012) showed the significant contribution of cryotherapy in prevention of OM.

Prevention of OM in methotrexate (MTX) regimens:

The study conducted by Gori and his research colleagues (2007) tested the effectiveness of cryotherapy in the prevention of oral mucositis in patients treated with low-dose MTX as graft - versus-host disease (GVHD) prophylaxis following myeloablative allogeneic hematopoietic stem cell transplantation (AHSCT). The result of this study showed that cryotherapy during MTX administration does not reduce severe oral mucositis in patients undergoing myeloablative allogeneic HSCT. They relate the reason of this result to multiple factors, including the mode of administration, the

design of the study, the biological effect of post-transplant low-dose MTX in the pathogenesis of oral mucositis and the cellular clearance of MTX by-products, including MTX- polyglutamates, which may be required up to 2 weeks and contribute to delayed toxicity.

Cryotherapy in reducing mucositis and improving patient's nutritional status:

Oral cryotherapy extended its effect further than prevention of oral mucositis to prevent malnutrition or what we can call Cachexia related to OM. So if we could prevent OM we prevent a debilitating effect of OM in a patient's general nutritional status.

Svanberg, Ohrn and Birgegard (2010) aims in their study was to investigate if oral cryotherapy during myeloablative therapy may influence frequency and severity of mucositis, nutritional status and infection rate after BMT. The result confirmed the role of cryotherapy in reducing and prevention of OM and showed the reduction needed in total parenteral nutrition which resulted in improving patient's nutritional status.

Cryotherapy in reducing OM and opioid use:

Oral pain resulted from severe OM induced the need of opioids which have multi side effects that result in a negative impact on the patient's status. So, we need to prevent OM in order to decrease the use of opioids to relieve oral pain induced by OM.

The study conducted by Svanberg and his research team (2007) showed the evidence that patients who received oral cryotherapy had less pronounced mucositis and significantly fewer days with i.v. opioids than control group among patients treated with myeloablative therapy before BMT.

4. Discussion

Cryotherapy is a simple, easy, well tolerated, non expensive and safe method with limited side effects. Also, it does not interfere or endanger the efficacy of antineoplastic agents (Papadeas, Riga & Kalofonos, 2007). In general, using cryotherapy as a primary prevention of OM was supported by statistically significant trials. Thus, focusing on prevention using cryotherapy is better than focusing on symptom management and as it is said prevention is better than cure. So, this will improve nursing performance by shifting their practice from symptom relief to symptom prevention of OM (Fliender et al., 2007). In addition, oral cryotherapy has a positive impact on patients' health, health care providers and on health care organizations overall.

On the other hand, there are some limitations on using this method, and they include: the patient's oral status includes oral hygiene, smoking habit, dental problem, oral lesions, etc. often not tested before beginning of trials, and there is no optimum length of using oral cryotherapy regimen; small sample size in most of the studies decreased the generalization of the result; oral cryotherapy is limited to specific chemotherapy regimens (mainly for short acting drugs rather than long acting drugs) and for specific types of cancer or transplantation (they mainly have a great effect on hematologic cancer and on autologous HSCT rather than allergenic HSCT).

Conclusions

Cryotherapy is an effective method for prevention of oral mucositis in patients who received two specific chemotherapy regimens that include 5FU regimens and high dose melphalan. In addition, the efficacy of oral cryotherapy is affected by the types of chemotherapy regimens including the half life for each one and it depends on the causative mechanisms of oral mucositis including direct and indirect mucositis.

Recommendations/ Implications

It is recommended that researchers do additional studies (clinical trials) to broaden the potential applications of cryotherapy in clinical settings and to investigate this intervention in other chemotherapy regimens and they need to increase the sample size in order to generalize findings. Also, health care organizations are advised to convene conferences for their employees (mainly nurses) focused on the best evidence on prevention and treatment of OM and increase nursing awareness to decrease dilemmas in the best method of prevention and treatment of OM.

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