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## FROM THE EDITOR



**Abdulrazak Abyad**  
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This is a special issue on cancer issues in the nursing field. Most of the papers are from Hashemite University School of Nursing candidates for master studies in oncology.

In the first paper the author reviewed the efficacy of Complementary and Alternative Medicine (CAM) Therapies on Managing Cancer Pain. The author concluded after the review that CAM therapies might serve as useful adjuvants to traditional analgesic therapy and may be ideal in patients who cannot tolerate or may be reluctant to take pain medications. But it is highly suggested that they should be used in conjunction with conventional therapies in an integrative fashion (integrative medicine) and integrated with oncology clinics.

The second review looked at Effectiveness of Therapeutic Touch on Pain Management among Patients with Cancer. The author reviewed 46 articles. The findings of the review showed that TT is one of the CAM (Complementary and Alternative Medicine) that is very effective in pain management among patients with cancer; it has the effect of decreasing fatigue, pain, and enhancing and improving quality of life and maximizing the comfort among patients with cancer.

The third review looked at Nutrients and Colorectal Cancer Risk. The author stated that various nutrients were thought to have various impacts on colorectal cancer. After conducting the selected studies, this review showed that there was a strong association between colorectal cancer and nutrient consumption and that high consumption of fiber, fish meat, calcium, vitamin D, and folic acid had significant impact on decreasing colorectal cancer risk while high consumption of processed red meat and deficiency of calcium, vitamin D, and folic acid was attributed to increase the risk of developing colorectal cancer.

In the fourth paper the author reviewed the management of oral mucositis Secondary to Cancer Therapy. The author reviewed nineteen articles that met the inclusion criteria. The studies revealed that few agents have shown efficacy, which is applicable to a limited type of cancer and cancer therapy. Nurses take a significant role in preventing occurrence of oral mucositis and provide proper interventions by applying updated protocols. Future studies should evaluate if agents that work by different mechanisms can be used in combination to reach maximum therapeutic effect. Further research with a large sample is needed to detect the current agents and other safe and effective agents to alleviate this depleting condition.

The fifth review looked at oral mucositis and pediatric oncology: Prevention as a key Management Measure for Oral Mucositis among Children with Cancer . Oral mucositis is a common complication of cancer treatment and a painful experience. The electronic database was searched using oral Mucositis, cancer, intervention, children ,and management, as keywords. Ten different agents were found with conflicting efficacy for oral mucositis management including; vitamin (E), plants extract (Traumeel S, Glycerine Payayor), Transforming growth factor TGF-beta(2), Benzydamine, Chlorhexidine, Cryotherapy, Glutamine, laser, Debridement, chewing gum, fluoride mouth-washes, and topical application of Miconazole. Limited evidence was found with a variety of levels of strength. Basic Oral Care is the recommended prevention measure that could be considered as the first step of management.

The last paper looked at the role of the nurse in the management of fatigue due to cancer. The result emphasizes that fatigue is a significant crisis in patients with cancer that needs early detection and management . Nurses have to be responsive to the risk factors of fatigue in patients with cancer and carry out a full fatigue assessment and management for the risky cases. Even this review recognized inadequate research; the results give guidelines to the improvement of nursing interventions for fatigue management for patients with cancer.

# EFFICACY OF COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) THERAPIES ON MANAGING CANCER PAIN: A REVIEW

## Abstract

**Background:** Despite widespread use of complementary and alternative medicine (CAM) therapies, very little is known about the efficacy and safety of many of the CAM therapies that cancer patients use.

**Aims:** The aim of this integrative literature review is to assess the efficacy of (CAM) therapies on managing cancer pain.

**Method:** To assess the efficacy of (CAM) therapies on cancer pain, a literature review was conducted using the search engine Google and the electronic database of Pubmed. A list of 36 articles were obtained. A total of 12 articles published from 1978 to 2009, formed the basis of this review. They were included based on the inclusion criteria that: the articles should study the effectiveness of complementary and alternative therapies on cancer pain, were research-based studies, specific for cancer, and included a population of adults, and were written in the English language. 24 articles were in other languages such as Turkish or Chinese, and were not research based, not cancer related, and were discussing pharmacological management not CAMs so were thus excluded.

**Conclusion:** CAM therapies might serve as useful adjuvants to traditional analgesic therapy and may be ideal in patients who cannot tolerate, or may be reluctant to take, pain medications. But it is highly suggested that they should be used in conjunction with conventional therapies in an integrative fashion (integrative medicine) and integrated with oncology clinics.

**Key words:** cancer pain, complementary medicine, alternative medicine, literature review.

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## Introduction

Pain affects most cancer patients, in the advanced and metastatic phase of the disease (Cherny, 2000). Pain prevalence is high: 64% in patients with metastatic, advanced or terminal disease, 59% in patients on anticancer treatment and 33% in patients who had been cured of cancer (Everdingen, Rijke, Kessels, Schouten, van Kleef, & Patijn, 2007). Management of pain is crucial to improve the quality of life of patients. There are two methods of pain relief in cancer patients, pharmacological and non-pharmacological (Aghabati, Mohammadi, & Pour Esmail, 2008), where (CAM) therapies are considered as the non-pharmacological methods that are used widely, especially among cancer patients (Wells, 2000) and which have been defined by the National Center for Complementary and Alternative Medicine (NCCAM) as a group of diverse health care systems, practices, and products that are not presently considered part of conventional medicine.

In spite of the mass use of CAM therapies, very little is known of the efficacy and safety of many of the CAM therapies that cancer patients use (Ernst, 2000), and limited research efforts have been directed toward evaluating the efficacy of (CAM) therapies. There is a need to discuss such therapies; because there are many obstacles affecting the delivery of them including lack of qualified personnel (44.4%), and insufficient staff knowledge of how to structure complementary therapy services (22.2%). Other obstacles

included lack of funding, difficulty defining complementary therapy services, and lack of time (Running, Shreffler-Grant, & Andrews, 2009). It is also known that patients frequently do not discuss CAM therapies with their physicians (Eisenberg, Davis, & Ettner, 2000).

The aim of this article is to provide an integrative review to evaluate the efficacy of CAM therapies for cancer pain; in order to improve staff knowledge about these type of therapies, which can be integrated with other pharmacological methods; to increase comfort, relieve pain, and improve quality of life for patients with cancer.

## Method

To assess the efficacy of complementary and alternative medicine (CAM) therapies on cancer pain, a literature review was conducted using the search engine Google and the electronic database of Pubmed, using the following key words: cancer pain, complementary medicine, alternative medicine, literature review. The key words were used in different combinations. A list of 36 articles were obtained and reviewed for possible inclusion in this review based on the inclusion criteria that the articles should study the effectiveness of complementary and alternative therapies on cancer pain, was a research-based study, specific for cancer, and included a population of adults, and was written in the English language. A total of 12 articles, published from 1978 to 2009 were included and formed the basis of this review. The excluded

articles were in other languages such as Turkish or Chinese, were not research based, not cancer related, and discussed pharmacological management, not CAM.

The included articles within this integrative research review were a combination of cross-sectional descriptive surveys, integrative reviews, and systematic reviews of randomized clinical studies. The focus of the included studies was in evaluating CAM therapies for cancer-related pain, assessing cancer patients' utilization of complementary and alternative medical providers and the associated expenditure by specific treatment phases, and identifying availability of complementary therapy services.

### Discussion

Despite the major advances in pain management strategies and methods, cancer pain is undertreated in 80% of patients with cancer (Miaskowski, Zimmer, Barrett, Dibble, & Wallhagen, 1997). Early studies aimed to identify factors relating to ineffective pain management, which fall into three categories: the health care system, health care providers, and patients (Fazeny, Muhm, & Hauser, 2000).

Although complementary and alternative medicine (CAM) therapies are widely used by patients with cancer, they have been a subject of debate (Koretz & Rotblatt, 2004). Bardia, Barton, Prokop, Bauer, Timothy, and Moynihan (2006) identified the effectiveness of complementary and alternative medicine (CAM) therapies on reducing cancer pain by reviewing eighteen randomized controlled trials (RCTs). The results revealed that seven trials reported significant benefit for the following CAM therapies: acupuncture, support groups, hypnosis, relaxation/imagery, and herbal supplement/HESA-A. Seven studies reported immediate post intervention or short-term benefit of the following CAM interventions: acupuncture, music, herbal supplement, Ai-Tong-Ping, massage, and healing touch. Four studies reported no benefit

of CAM interventions: music, and massage in reducing cancer pain compared with a control arm, and concluded that CAM modalities such as hypnosis, imagery, support groups, acupuncture, and healing touch seem promising, particularly in the short term, but none can be fully recommended because of the paucity of rigorous trials.

Another work by Pan, Sean Morrison, Ness, Fugh-Berman, and Leipzig (2000) aimed at evaluating the efficacy of complementary and alternative medicine (CAM) modalities in treating pain, dyspnea, and nausea and vomiting in patients near the end of life, by reviewing 21 studies of symptomatic adult patients with incurable conditions who were in the later stages of illness. Although this study evaluated the efficacy of CAM therapies in treating other signs and symptoms rather than pain alone, the majority of articles evaluated CAM in cancer patients, most often to treat pain. The results indicated that many CAM therapies have a favorable benefit/ risk ratio and may be useful adjunctive therapies to conventional (allopathic) medicine.

Adams and Jewell (2007) reviewed the role of CAM therapies in the management of cancer, from the view of both patients and health professionals and highlighted issues relating to the efficacy of CAM used by cancer patients. They found that there is an increase in the use of complementary and alternative medicine among cancer patients. Most of the patients use CAM to 'complement' the conventional therapies of radiotherapy, chemotherapy, hormone therapy and surgery. On the other hand insufficient or lack of knowledge on the part of health professionals could be a factor for the lack of approval for CAM use and the subsequent negative attitudes and beliefs. In general, however, health professionals have expressed positive views when CAM is used 'complementarily' and not as an 'Alternative'. The final results show that CAM can contribute to improving

the quality of life of cancer patients and their general well-being.

Molassiotis et al. (2005) conducted a descriptive cross-sectional survey on 127 colorectal cancer patients across seven European countries. The aim of this study was to explore the use of complementary and alternative medicine (CAM) in cancer patients across a number of European countries. Data were collected through a 27 items questionnaire which included demographic data (age, gender, occupation, education, household income, marital status, number of people living in the household and ethnicity), clinical data (site of primary cancer, standard treatments received previous and current standard treatment) and questions about CAM use. Over 47% of the patients reported using CAM with the view of increasing the body's ability to fight off the disease while just fewer than 45% of patients believed that CAM could help improve their physical well-being. The final conclusion of this study, is that it is imperative that health professionals explore the use of CAM with their cancer patients, and educate them about potentially beneficial therapies in light of the limited available evidence of effectiveness, and work towards an integrated model of health-care provision.

Another descriptive survey of hospices' use of complementary therapy by Running, Shreffler-Grant, and Andrews (2009) was conducted to identify complementary therapy services available to, and provided for, clients receiving hospice care, and concluded that some complementary therapy techniques, however, with the appropriate knowledge and training, could be integrated into routine care provided by existing nursing staff to relieve pain, and improve quality of life. Educational interventions for existing hospice staff could be designed, implemented, and evaluated to address the barriers concerning lack of qualified personnel and insufficient knowledge about complementary therapy.

Deng and Cassileth (2005) studied the effectiveness of complementary therapies for pain, anxiety, and mood disturbances, and discussed the rationale, expectation, and necessary precautions involved with combining complementary therapies and mainstream care. The authors suggested that complementary therapies such as acupuncture, mind-body techniques, massage, and other methods can help relieve symptoms and improve physical and mental well-being and they are safe assuming they are provided by licensed, competent practitioners. Self-hypnosis and relaxation techniques help reduce procedural pain. Acupuncture is well documented to relieve chronic cancer pain, although Complementary therapies are helpful for some but not all patients. Parameters that identify "good responders" are lacking.

Corbin (2005) reviewed and summarized the literature on massage and cancer, to help provide the clinician with information to help facilitate discussions with patients. The results revealed that therapeutic massage is widely considered to be safe, although adverse events have been reported. Also there is strong evidence for benefits of massage for stress and anxiety reduction, although research for pain control and management of other symptoms common to patients with cancer, including pain, is promising. The author suggests that oncologists should feel comfortable discussing massage therapy with patients and be able to refer patients to a qualified massage therapist as appropriate.

Finlay and Jones (1996) studied the effectiveness of hypnotherapy on acute cancer pain episodes, and coping enhancements, by examining 256 patients who had hypnotherapy during a period of almost three years. The conclusion of this study described that, despite the limitations of a retrospective questionnaire, findings suggest that hypnotherapy, used within strict guidelines in patients with advanced cancer, is a safe complementary

therapy to enhance coping, and manage pain.

Munro and Mount (1978) outlined the rationale of using music therapy in palliative care and offered preliminary observations on the impact of this underused therapeutic tool, by assessing six case studies who received music therapy for managing cancer pain and other cancer related problems. Authors concluded that, music therapy had made a significant contribution to a wide variety of palliative care problems. The presence of music in the hospital had been well received by patients and their families.

Lu, Dean-Clower, Doherty-Gilman, and Rosenthal (2008) studied the efficacy and safety in treating and preventing cancer-related symptoms including pain, chemotherapy-related neutropenia, cancer fatigue, and radiation-induced xerostomia with the integration of acupuncture into cancer care. By reviewing randomized clinical trials the authors found that the evidence currently available has suggested that acupuncture is a safe and effective therapy to manage cancer and treatment related symptoms, while giving patients the ability to actively participate in their own care plan.

Thomas and Weiss (2000) conducted a literature review to examine the effectiveness of three non-pharmacological strategies that are effective in reducing pain caused by cancer - patient psycho-education, supportive psychotherapy, and cognitive-behavioral interventions, are reviewed. Research indicates that these psychotherapeutic interventions can offer significant benefits such as increased relief from pain and associated emotional distress, if an adjunct to pharmacotherapy.

Aghabati, Mohammadi, and Pour Esmail (2008) studied the effect of Therapeutic Touch (TT) on pain and fatigue in cancer patients undergoing chemotherapy. The authors recruited a sample of ninety patients

with cancer, who were randomly assigned into one of the three groups (experimental, placebo and control) using a randomized clinical trial (RCT). The experimental group received TT; the placebo group received a mimic treatment that resembled TT to the naive observer, and the control group received routine care. The study results showed that the TT (significant) was more effective in decreasing pain and fatigue of the cancer patients undergoing chemotherapy than the usual care group, while the placebo group indicated a decreasing trend in pain and fatigue scores compared with the usual care group.

### Conclusion

Under-treated pain is considered a major issue for patients with cancer, so focus should be directed toward improving management of cancer pain via pharmacological or non-pharmacological methods. Hence there is an increased usage of complementary and alternative medicine (CAM) therapies among cancer patients.

CAM therapies might serve as useful adjuvants to traditional analgesic therapy and may be ideal in patients who cannot tolerate or may be reluctant to take pain medications. But it is highly suggested that they should be used in conjunction with conventional therapies in an integrative fashion (integrative medicine) and integrated with services provided by oncology clinics, not as an alternative therapy. Future research efforts should be directed toward dissemination of evidence-based applications of such therapies.

It is also highly recommended that clinical directions should be toward improving health care providers' knowledge about the availability and the effectiveness of different types of complementary and alternative medicine (CAM) therapies and the patient should be involved in the process of decision making regarding treatment options and available modalities.

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# NUTRIENTS AND COLORECTAL CANCER RISK

## Abstract

Various nutrients are thought to have varying impact on colorectal cancer. The aim of this review was to clarify the effect of a variety of types of nutrients on colorectal cancer. Pubmed and Ovid databases were searched for articles that investigate the association between nutrients and colorectal cancer using the key words colorectal cancer, adenoma recurrence, dietary fiber, meat, calcium, vitamin D, and folic acid. After searching, research based articles, prospective cohort studies, and case-control studies were used to conduct this review.

The inclusion criteria of the study was:

Researched based article, applied among human sample, published between 2000 and later, and written in the English language. While exclusion criteria of the studies was: Studies on animals, and those observed among pediatric participants. After conducting the selected studies, this review showed that there is a strong association between colorectal cancer and nutrient consumption and that high consumption of fiber, fish, meat, calcium, vitamin D, and folic acid had significant impact on decreasing colorectal cancer risk while high consumption of processed red meat and deficiency of calcium, vitamin D, and folic acid was attributed to an increase in the risk of developing colorectal cancer

**Keywords:** Colorectal cancer, nutrients, chemo-preventive, dietary fiber, meat, calcium, vitamin D, and folic acid

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## Introduction

Colorectal cancer in 2009 was the third most common cancer regarding incidence and death in USA. It represented about 10% of all cancer cases in the same year (American Cancer Society, 2009). According to the World Health Organization (WHO), 639,000 deaths occurred in 2004 worldwide as a cause of colorectal cancer (WHO, 2004).

Many risk factors were attributed to colorectal cancer. These risk factors were classified as modifiable risk factors, like alcohol consumption and smoking, and non-modifiable risk factors like age and heredity ( Su & Arab, 2004; Liang, Chen & Giovannucci, 2009). According to the WHO it was thought that 30% of all cancer cases can be prevented by adjusting the modifiable risk factors (WHO, 2004). Determining the modifiable factors help people with high non modifiable factors to minimize the chance of developing the disease by adjusting the modifiable factors.

Diet is considered one of the most important modifiable factors. It is thought to have a strong association with colorectal cancer. Various types of nutrients had varying effects on colorectal cancer. Some forms of nutrients have a healthy effect on epithelium colon cells and are considered as chemo-preventive, e.g. fiber, vitamins and calcium, while other forms have a carcinogenic effect and increase the risk of developing the disease, such as meat and fat, and some nutrients had neither chemo-preventive nor

carcinogenic effects regarding the disease.

This review was conducted on update evidence about the relationship between colorectal cancer and major nutrients like fiber, meat, calcium, and some vitamins.

### Dietary Fiber

Dietary fiber is a component of plant food, that is indigestible by human body enzymes (Anderson et al., 2009).

It is classified into two groups according to its solubility in water: Soluble and insoluble fiber. Soluble fiber is found in legumes, root vegetables, fruits, beans and carrots, while insoluble fiber is found in whole grain foods, wheat, green beans, seeds, and flax seed. Fiber makes the stool more soft and quickens the transit time through the guts, which has a positive effect on decreasing colorectal cancer risk.

A large prospective cohort study that investigated the relationship between dietary fiber and whole grain intakes and invasive colorectal cancer, found that there was no significant association between fiber intake and risk of developing colorectal cancer, while whole grain intake had a positive effect on decreasing colorectal cancer risk (Schatzkin et al., 2007).

Another large prospective cohort study in Japan that examined the relationship between dietary fiber intake and risk of developing

colorectal cancer among the population whose fiber intake were lower than desired, mentioned that increasing the consumption of whole dietary fiber was associated with decreasing the risk of developing colorectal cancer (Wakai et al., 2007).

Many studies suggested that fruit and vegetables had a positive effect on decreasing colorectal cancer risk regarding their components of soluble fiber. Terry et al. (2001) showed that consumption of fruit and vegetables in less than desired servings daily, attributed to developing colorectal cancer about 1.65 times more than those whose consumption of fruit and vegetables met the desired amounts. Levi, Pasche, Lucchini, and Vecchia (2001) examined in a case control study the association between the consumption of various types of fiber and the risk of colorectal cancer, and showed that high intake of total fiber had significantly attributed to a decrease in colorectal cancer risk, and that high fruit and vegetable diets decreased colorectal cancer risk by 22% and 40% respectively. Nomura and colleagues in their study mentioned that the consumption of vegetables and fruit leads to a decreased colorectal cancer risk and that was more among males than females; also the reduction in risk was more in colon cancer rather than rectal cancer (Nomura et al., 2008).

Whether fiber intake has a positive effect or not on decreasing the recurrence of colorectal cancer was not clear. Lanza et al. (2006) suggested that high dry bean intake significantly attributed to a decrease in the likelihood of recurrence of adenoma polyps. Alberts and colleagues conducted a randomized study that examined the relationship between wheat bran fiber supplement and its impact on the recurrence of colorectal adenomas, after daily supplementation with either 13.5 g or 2 g of wheat bran fiber for participants who underwent removal of colorectal adenomas within the three months

that preceded the wheat bran fiber supplementation. It found that there was no significant association between wheat bran fiber supplementation and decreasing the recurrence of colorectal adenoma polyps (Alberts et al., 2000).

Michels et al. (2005) in two large cohort studies investigated the relationship between fiber intake and colorectal cancer, and showed that there was no significant relationship between fiber intake and decreasing colorectal cancer risk, and the minor impact of fiber intake in decreasing colorectal cancer was related to lifestyle and other dietary factors rather than to the fiber supplementation.

### **Red Meat**

Studies suggested that consumption of red meat may have a positive effect on developing colorectal cancer. These effects were related to the nature of meat and its components, and also related to the method in which meat was prepared and the change that occurred to its components after cooking.

Sandhu, White, and McPherson (2001) in their meta-analysis indicated that the risk of colorectal cancer will increase about 12-17% if the daily supplement of red meat increases by 100g. Joshi et al. (2009) indicated that weekly consumption of three serves or more of red meat lead to an increase in the risk of developing colorectal cancer.

The likelihood of meat increasing the risk of colorectal cancer was highlighted in many studies on the changing in red meat's component after cooking, rather than the carcinogenic effect arising from natural components. The effect of benzopyrene and heterocyclic amines which are both created during the cooking process of red meat, and their carcinogenic characteristic are described as the main cause that increases the likelihood of consumption

of processed red meat and the development of colorectal cancer. Sandhu et al. (2001) showed that a significant risk of colorectal cancer was attributed to processed meat consumption; that increasing daily intake by 25 g will increase the risk of developing colorectal cancer by 49%. Gunter et al. (2005) found that consumption of 10 nanogram /day of benzopyrene and 10 g of barbecued meat will increase the risk of developing large adenoma by 6% and 29% respectively. Martinez and colleagues indicated that exposure to heterocyclic amines is significantly related to the recurrence of adenoma polyps (Martinez et al., 2007).

Unlike red meat, fish consumption was attributed to a decrease in the risk of colorectal cancer. This result was supported by evidence from Japan that "data showed frequent raw/cooked fish intake to be associated with decreased odds ratio (OR) 0.68 with 95% confidence interval (CI) 0.47-0.99 for male colon cancer. A marginal decrease in the OR (OR 0.58, 95% CI 0.31-1.07) was also detected for female rectal cancer." (Yang et al., 2003). Another study supported this result and suggested that high intake of fish had an inverse relationship with the risk of adenoma polyps recurrence (Mathew et al., 2004).

### **Vitamin D and Calcium**

Vitamin D and serum calcium were thought to have protective effects against cancer, and that low serum levels promote normal cell characteristics. Vitamin D which is one of the fat soluble vitamins, has an important role in calcium absorption in the intestine and many cellular functions, like regulation of cell division, differentiation of cell, and cell apoptosis; disrupt of these functions can attribute to carcinogenic change (Ingraham, Bragdon & Nohe, 2008).

In a large case-control study in 10 European countries, participants with high serum concentrations of vitamin D had a lower risk of developing colorectal cancer compared to

those with lower serum concentrations, by 40%, and a strong relationship was found for colon cancer, rather than rectal cancer (Jenab et al., 2010). Mizoue et al. (2008) found that the risk of developing colorectal cancer was lower by a third among those whose serum level of calcium was high compared to participants with low levels of calcium. It was also found that vitamin D supplementation had a significant effect on decreasing colorectal cancer risk, especially among people suffering from vitamin D deficiency.

Another study attributed the positive association of vitamin D and calcium with colorectal cancer to the effect of vitamin D and calcium in promoting apoptosis rather than to the disruption that occurred in DNA as a result of decreasing serum levels. Miller et al. (2005) who investigated the association between vitamin D and calcium intake and its effect on elevating apoptosis in epithelial tissue of the rectum, suggested that both vitamin D and calcium had a positive effect on promoting apoptosis. Also apoptosis increased about 3 times in people with high calcium intake compared to those in the lower level.

On the other hand, Wactawski-Wende and colleagues said that there was no association between vitamin D and calcium supplementation on risk of developing colorectal cancer, and that postmenopausal women who received 1000 mg of calcium and 400 IU of vitamin D3 daily for seven years hadn't shown any difference in the development of colorectal cancer compared to those who received a placebo (Wende et al., 2006).

The association between vitamin D and calcium level and its effect on recurrence of colorectal adenoma polyp was also examined. In comparing highest versus lowest level of serum among patients diagnosed with colorectal adenomas previously, found that there was a weak inverse effect of vitamin D and calcium intake, and the

recurrence of adenoma (Hartman et al., 2005). Grau and colleagues suggested that calcium and vitamin D supplementation had a significant attribution in decreasing colorectal adenoma recurrence when they work in conjunction with each another, and there was no significant effect when they work discretely (Grau et al., 2003).

### **Folic Acid**

Folic acid is a water soluble vitamin known as vitamin B9. Level of folic acid was thought to have an inverse relationship with development of colorectal cancer. The association between folic acid level and risk of cancer in general arises from the fact that folic acid has an important role in repairing and synthesizing DNA in the nucleus, and decreasing the level of it leads to many disruptions (Weinstein et al., 2003).

Some studies suggested that the amount of folic acid which was obtained from a meal will affect the risk of developing colorectal cancer. A large case cohort study was conducted to examine if there was a relationship between folic acid consumption and the risk of developing colorectal cancer. They found that the risk of developing colorectal cancer will decrease by 40% among women whose dietary intake of folic acid is high, compared to those with low intake (Terry, Jain, Miller, Howe & Rohan, 2002).

Alcohol consumption was thought to have an effect on increasing colorectal cancer occurrence especially if its consumption was combined with low serum folic acid. Fuchs et al. (2002) indicated that there was a significant inverse relationship between folic acid consumption and colorectal cancer occurrence among women, and that the relationship was stronger among women with a family history. It is also stronger among those who consume alcohol. Engeland and colleagues mentioned that low folic acid intake and alcohol consumption attributed to development of colorectal cancer (Engeland., 2003).

The direct effect of folic acid supplementation on decreasing the recurrence of colorectal adenoma has been proposed also. To examine the relationship between folic acid supplementation and the recurrence of colorectal adenoma, prospective cohort studies were conducted where participants received either 1 mg per day or placebo for more than three years. They found that supplementation of folic acid had an inverse relationship with the recurrence of colonic adenomas in participants whose plasma folic acid level was below average, but no change occurred in participants whose plasma folic acid level was of average level or above (Wu et al., 2009). Jaszewski and colleagues indicated that supplementation of folic acid in high amounts had a more significant impact on decreasing adenoma recurrence, than daily supplementation of 5 mg of folic acid for three years, in decreasing the recurrence of colonic adenomas to about two thirds of all cases, compared to the placebo group (Jaszewski et al., 2008).

### **Conclusion**

Many risk factors were attributed to the development of cancer such as fat and low fiber diets. This being easy to adjust, and knowing the effect of nutrients on colorectal cancer should lead to a decrease in the risk of developing the disease.

After conducting this review, there was moderate evidence that dietary fiber of both types had a healthy effect on decreasing the risk of colorectal cancer, and more evidence was found regarding whole grain and vegetable fiber. On the other hand, it is not clear if there was a relationship between fiber intake and decreasing the recurrence of colorectal polyps. The result was contradictory. We therefore need more research to clarify the association.

Unlike dietary fiber, high red meat intake had a significant association with increasing the risk of colorectal cancer/It also had an association with increasing the recurrence of

polyps. The direct impact of red meat on increasing the risk of colorectal cancer was more attributed to the process of meat consumption and that was because of benzopyrene and heterocyclic amines which are both created during the cooking of red meat. On the contrary, fish consumption had a healthy effect on decreasing the risk of colorectal cancer. It also decreases the recurrence of polyps.

Vitamin D and calcium also had a healthy effect on risk of colorectal cancer. High levels of both lower the risk for developing colorectal cancer compared to low levels. They also promote apoptosis. While some researchers suggested that no significant relation was found between vitamin D and calcium, and colorectal cancer, other research mentioned that the effect of vitamin D and calcium can decrease the incidence of colorectal cancer when both act with one another, but had no significant effect when they work discretely. No significant evidence was found between high intake of vitamin D and calcium and decreasing the recurrence of colon polyps.

The review indicated that level of folic acid had an inverse effect with risk of colorectal cancer; and low levels of serum folic acid had a strong association with increasing colorectal cancer risk, especially if that is combined with alcohol consumption. Strong evidence was found that folic acid supplementation decreased the recurrence of colon polyps.

Colorectal cancer can be prevented by adjusting diet. People at high risk should be recommended to eat more fruit, vegetables, beans, eggs, milk, and fish; nutrients that decrease the risk of developing colorectal cancer, and preventing the recurrence of new polyps.

Because of the strong association between colorectal cancer and low plasma levels of calcium, vitamin D, and folic acid; plasma

levels of previous nutrients should be assessed in high risk people, especially those who are alcoholic.

As western diet consumption increases continuously, health education and social enlightenment about the risk of that diet will have important implications regarding the results of this review.

The risk arises from the high fat and low fiber components of fast food, and that risk increases if the fast food is part of a daily routine. Health education may encourage people to more healthy practices especially those with a high risk of developing the disease.

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# MANAGEMENT OF ORAL MUCOSITIS SECONDARY TO CANCER THERAPY: A REVIEW

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## Introduction

This literature review discusses the management of oral mucositis (OM), which is guided by Roy Adaptation Conceptual Model. Oral Mucositis (OM) is a significant problem among cancer patients secondary to cancer therapy, and a major source of additional illness and suffering, despite the use of a variety of agents to treat it (Lalla, Sonis, & Peterson, 2008).

The incidence of oral mucositis for patients with tongue cancer who are receiving chemoradiation is close to 100% (Sonis, 2009) and close to 100% in some bone marrow transplantation (BMT) myeloablative regimens as well as radiotherapy for head and neck cancers to less than 10% in solid tumors. (Barasch & Peterson, 2003; Barasch, Epstein & Tilashalski, 2009). Mucositis refers to the inflammatory process of the mucous membranes of the oral cavity and the gastrointestinal tract. Clinically, oral mucositis is characterized by generalized erythema, pseudomembranous degeneration, frank ulceration, and hemorrhage (Cheng, 2007). Chemotherapy-induced mucositis usually develops within 4-7 days after initiation of treatment and peaks within 2 weeks. Radiation-induced mucositis typically reaches full severity at 30 Gy, and lasts for weeks or even months. (Raber-Durlacher, Elad & Barasch, 2010).

Nursing needs to recognize the management of oral mucositis by using supportive care measures which are focused in palliation rather than pure treatment. It is multifaceted problem which affects all aspects of a patient's quality of life.

This review will contribute to exploring the relationship between oral mucositis and types of cancer using multi clinical practice guidelines for managing oral mucositis.

## Abstract

**Background:** Mucositis is a multifaceted problem characterized by generalized erythema, ulceration, and hemorrhage. This review concerned the management of oral mucositis (OM) secondary to cancer therapy to promote adaptation of patients with oral mucositis. This review is guided by the Roy Adaptation conceptual Model which considers OM as a focal stimulus which affects patient well-being.

**Aims:** To describe which agent can be most effective to manage oral mucositis according to the type of cancer and cancer therapy; to enhance nursing role in applying updated guidelines, to manage mucositis, which are in the literature review.

**Methods:** Nineteen articles met the inclusion criteria (update research from 2007 to 2010): in English language, adult patients received chemotherapy or radiotherapy or both) with Key concepts: "oral mucositis", "management" and "cancer therapy", which we found in Cinahl, Medline and Cochrane databases.

**Results:** Current clinical management of oral mucositis is largely focused on the palliative measures which are approved to manage OM, such as using morphine to manage pain associated with OM, applying good oral hygiene to prevent and treat

OM, using benzydamine with the patient receiving radiotherapy especially with head and cancer, cryotherapy with the patient receiving chemotherapy, growth factor, especially with head and neck cancer patients and with patients with lymphoma receiving radiotherapy, and using laser therapy with patients receiving chemoradiation before HSCT.

**Conclusion:** Few agents have shown efficacy, which is applicable to limited types of cancer and cancer therapy. Nurses have a significant role in preventing occurrence of oral mucositis and providing proper interventions by applying and updating protocols. Future studies should evaluate if agents that work by different mechanisms can be used in combination, to reach maximum therapeutic effect. Further research with large samples is needed to detect the current agents and other safe and effective agents to alleviate this debilitating condition.

**Recommendations:** Oncology nurses are crucial in developing the evidence regarding those agents and employing the appropriate interventions for specific patient needs. Additional randomized, controlled trials are required to determine other agents with sufficient evidence to manage OM. Until that time, it is necessary to follow evidence based practice guidelines to improve patients' outcomes.

To describe the most effective measures to manage oral mucositis according to the type of cancer.

To address the nursing role in applying updated guidelines and protocols to manage oral mucositis effectively.

### Literature review

The purpose of this literature review is to describe which agent can be most effective in managing oral mucositis according to the types of cancer therapy, to enhance the nursing role in applying updated guidelines for managing oral mucositis, which are present in evidence-based practice and exist in literature.

Relevant literature review was obtained from Cinahl, Medline and Cochrane databases. The inclusive key concepts used for the search included "oral mucositis", "management " and "cancer therapy". From the inclusion criteria we obtained up to date research from 2007 to 2010 in English language, where adult patients received chemotherapy or radiotherapy or both. Nineteen relevant articles were taken, which exactly matched the key words that were reviewed.

A review article conducted by Bowen and Keefe in 2008, describes the latest advances in defining mechanisms of mucositis pathobiology, which results from the effects of cytotoxic agents on the epithelial cells of the oral mucosa. physiologically, mucositis was described as having 5 phases, which are overlapping and interactive. The five phases are:

Initiation, the cytotoxic agents initiate damage through the generation of reactive oxygen species which activates secondary signaling.

Primary damage /up-regulation; the activation of the necrotic factor (NF), which leads to induction of apoptosis and unregulated inflammatory cytokines in cells.

Message generation, a feedback loop occurs whereby pro-inflammatory cytokines, TNF act to reinforce NF activation.

Ulcerative phase is associated with loss of mucosal integrity and bacterial colonization with further pro-inflammatory cytokine production.

Healing occurs with renewal of epithelial proliferation and differentiation of epithelial cells to restore the integrity of the mucosa.

Clinical manifestations of mucositis can include intolerable pain which requires narcotic analgesics, altered oral function that requires parenteral nutrition, and increased risk of developing systemic infections, which cause prolonged hospitalization and increased economic burden. (Bhatt, Vendrell, Nau, Crumb & Roy, 2010).

The measurement of oral mucositis was discussed in 2008 by Lalla, Sonis and Peterson, using various scales such as WHO scale (World Health Organization) which focused on objective data. Another scale was NCI (National Cancer Institute) CTCAE (Common Terminology Criteria for Adverse Events, version 3) which focused on subjective and objective data and OMAS (Oral Mucositis Assessment Scale) emphasized assessing nine sites in the oral cavity.

Bowen and Keefe (2010) discussed the currently known mucositis management and the development of novel treatments found in the recent Cochrane Library review that contains 33 interventions which were studied.. Of those two pharmaceutical agents; Amifostine and Benzydamine have been included in the updated clinical practice guidelines for the prevention and treatment of mucositis. Amifostine is a free radical which exerts its effects by reducing direct DNA damage and reducing up-regulation of inflammatory pathways. Benzydamine is recommended for the prevention of mucositis in radiation patients

It has anti-inflammatory action by inhibition of pro-inflammatory cytokines, analgesic, anesthetic and antimicrobial effects.

Additional study conducted by Kazemian, Kamian, Aghilim, Hashemi and Haddad in 2009 resulted in the finding that benzydamine oral rinse is effective, safe, and well tolerated for prophylactic treatment of radiation-induced oral mucositis in head and neck tumors.

Still, Palifermin remains the only agent approved currently by the FDA for the prevention and treatment of mucositis, by inhibition of epithelial cell apoptosis and DNA damage, up-regulation of detoxifying enzymes, and down-regulation of pro-inflammatory cytokines. Palifermin (recombinant human Keratinocyte growth factor) has been studied extensively and reviewed by Barasch, Epstein and Tilashalski in 2009. The results of these studies clearly indicated the efficacy of the drug in reducing therapy-induced mucositis (severity) and improving short-term outcomes in chemoradiotherapy-treated hematologic cancer patients. Additional studies are necessary to determine the efficacy of palifermin for chemoradiation-induced mucositis among head and neck cancer patients.

According to data on mouthwash for mucositis pain; ketamine mouthwash may be a viable treatment option in mucositis pain in a study conducted by Ryan, Lin and Atayee in 2009. It can lead to decreased nociception and inhibition of the inflammatory process which would be beneficial in the treatment and palliation of mucositis. Another mouthwash mentioned was morphine. Bossert et al. (2010) conducted a randomized double-blinded, placebo controlled, crossover pilot study assessing the analgesic effects of morphine which is applied topically to painful oral mucositis. The result suggested a possible analgesic effect of topical morphine in line with previous studies which indicated that

mucositis pain was alleviated significantly after use. Moreover, regarding other routes of administering morphine, Clarkson, Worthington and Eden (2008) conducted a review for twenty-six randomized controlled trials involving 1353 patients comparing agents prescribed to treat oral mucositis in people receiving chemotherapy or radiotherapy or both. The results revealed that there was no evidence of a difference, between patients receiving morphine by patient control anesthesia (PCA) and morphine infusion.

In addition, nineteen patients with head and neck cancers receiving radiotherapy treated with buprenorphine transdermal formulation (BPS-TDS) for oral mucositis pain, lead to pain control, with limited dosages and without significant side effects. (Huscher et al; 2010).

Another agent is oral cryotherapy which significantly reduced mucositis, pain and suffering, number of hospital days, and need for total parenteral nutrition, in an experimental group (of 39 patients) in a randomized controlled trial which included 78 patients with BMT conducted by Svanberg, Ohran and Birgegard (2010). In this study, the number of patients with BMT was small, so there is a need for further experimental studies with larger samples to investigate the influence of cryotherapy on BMT patients.

Moreover, intervention review conducted by Clarkson and his colleagues in 2010, was found in the Cochrane library, which contains data from thirty-two trials involving 1505 patients. The results indicated that there was no evidence of a difference in mean pain score between PCA and continuous infusion; however, less opiate was used per hour for PCA, and the low level laser showed a reduction in severe mucositis when compared with the sham procedure.

Multiple studies have indicated that low-level laser therapy (Schubert

et al; 2007) can reduce the severity of chemotherapy and radiation-induced oral mucositis by reducing the level of reactive oxygen species and/or pro-inflammatory cytokines that contribute to the pathogenesis of mucositis. A supportive study conducted by Simoes et al. (2009) analyzes the effect of different protocols of laser phototherapy (LPT) on the grade of mucositis and degree of pain in patients under radiotherapy. Lower laser phototherapy (LPT) three times a week also maintained the same pain levels.

Hong et al. (2009) conducted a study to evaluate the human recombinant epidermal growth factor (rhEGF) which is a single-chain polypeptide that plays a role in epithelial cell proliferation, growth and migration. Thus, EGF has radical effects on wound healing and tissue generation. It is administered at 25 microgram per day for seven days in head and neck cancer and lymphoma patients with irradiation (with or without combined chemotherapy) who had developed severe oral mucositis (>grade 3). OM grade was significantly decreased ( $P = 0.0000$ ). This finding suggests that rhEGF is effective and safe for the treatment of radiation-induced mucositis. Further studies are needed to determine the optimal dosage and fractionation schedule. There is weak evidence that allopurinol mouthwash, granulocyte macrophage-colony stimulating factor, immunoglobulin or human placental extract eradicates mucositis, from twenty-six trials involving 1353 patients found in the Cochrane library which was searched by Clarkson, Worthington and Eden in 2008. Their recommendations: further randomized clinical trials should be conducted to assess the effectiveness of allopurinol mouthwash, granulocyte macrophage-colony stimulating factor, immunoglobulin, and placental extract on OM.

A review conducted by Durlacher, Elad and Barasch (2010) and clinical recommendation which was written

by Peterson, Bensadoun and Roila (2009) on behalf of the ESMO guidelines working group, included the recommendation and clinical practice guidelines for managing oral mucositis which was classified into four categories; firstly; basic oral care, - the panel suggested using a soft toothbrush, and applying validated tools to regularly assess oral pain and oral cavity health. The second was radiotherapy prevention; using the midline radiation blocks and three-dimensional radiation treatment to reduce mucosal injury, and use benzydamine for prevention of radiation-induced mucositis in patients with head and neck cancer receiving moderate-dose radiation, sucralfate, antimicrobial lozenges and chlorhexidine should not be used for the prevention of radiation induced oral mucositis. The third chemotherapy prevention routine, using oral cryotherapy for 30 minutes with patients receiving bolus 5-fluorouracil (5-FU) and 20-30 min of oral cryotherapy with patients receiving bolus doses of edatrexate, acyclovir and its analogues should not be used routinely to prevent mucositis. The fourth category was chemotherapy treatment; the panel suggested that chlorhexidine not be used to treat oral mucositis. In high dose chemotherapy, use keratinocyte growth factor-1 (palifermin) in a dose of 60 mg/kg/day for 3 days prior to conditioning treatment and for 3 days post transplant for prevention of oral mucositis. The panel suggested that Granulocyte-macrophage colony-stimulating factor( GM-CSF) mouthwashes not be used for the prevention of oral mucositis in patients undergoing hematopoietic stem cell transplantation (HSCT), and the panel suggested using low-level laser therapy (LLLT) to reduce the incidence of oral mucositis associated with pain in patients receiving high-dose chemotherapy or chemoradiotherapy before HSCT.

A new oral protocol was implemented with 12 patients undergoing hematopoietic cell transplantation compared with a retrospective control group under the previous standard of care in 2010,

2010, including daily nursing mucositis evaluation, brushing twice daily with soft toothbrush, using cryotherapy, chlorhexidine mouthwash which is discontinued at first sign of mucositis and using normal saline mouthwash, caphosol mouthwash, magic mouthwash and Cepastat Lozenges (Sugar Free) as needed, Palifermin, 60 mcg/kg/day IV bolus before 24-48 hours myelotoxic therapy, then IV bolus three consecutive days after myelotoxic therapy. The new protocol resulted in a decreased incidence (100% vs. 75%) and duration of mucositis. Days of maximum grade one and grade three mucositis were decreased by 56%, and 70%, respectively. The days of narcotic use were reduced by 19%. The incidence of infection measured by days of febrile neutropenia and antimicrobial therapy were reduced. Finally, the overall length of hospital stay was reduced by 7 days. So we need more experimental studies with large samples to generalize the results.

## Conclusion

Mucositis is a multifaceted problem with complex mechanisms of pathobiology, which affects all aspects of quality of life. Clinical management of oral mucositis is largely focused on palliative measures such as pain management, maintenance of good oral hygiene and therapeutic management which is applicable to limited types of cancer and cancer therapy. Most studies explore the action of agents on the process of mucotoxicity to manage mucositis and to reach maximize quality of life (QOL).

## Nursing Implications

Based on this review, nursing plays a key role in managing oral mucositis by applying recently updated evidence-based clinical management guidelines. Further research is needed to detect other safe and effective agents to alleviate this depleting condition and to predict the risk of developing mucositis, so patients can be targeted for therapy in a more cost-effective manner.

## Recommendations:

At this time, oral care, cryotherapy, and palifermin are the only management strategies for which sufficient evidence for practice exists. Additional randomized, controlled trials are required to determine other agents with sufficient evidence to manage OM. Until that time, it is necessary to follow evidence based practice guidelines to manage OM, which requires continued nursing efforts to educate patients how to apply those guidelines and develop nursing care plans for each patient to improve patient outcomes. Oncology nurses are crucial in developing the evidence in those areas and employing the appropriate interventions for specific patient needs.

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# NURSING ROLE IN FATIGUE MANAGEMENT AMONG PATIENTS WITH CANCER

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## Introduction

The diagnosis of cancer brings about many changes in the lives of patients and their families. Patients are suddenly placed in the position of coping with a wide array of new situations, such as pain and fatigue symptoms, uncertainty of prognosis and change in social relationships. During this time, it is important to help patients with cancer to find social and emotional support. Their symptoms have to be managed adequately in order to support their mood, role and social functions, adaptation skills, cancer management, and their general quality of life.

Fatigue is an overwhelming incident that restricts physical capability and the power store essential for suitable performance and social involvement. It also worsens morbidity and mortality. Its diverse factors and multi-dimensional manifestations cause a huge challenge regarding its diagnosis and management. Indeed, there was insufficient research on fatigue management for patients with cancer.

This literature may imply that this problem is poorly recognized and under treated in patients with cancer.

Despite cancer related fatigue occurrence and its impact on the quality of life, there has been an under -estimation of the relationship between nursing intervention and fatigue management.

Individualized instruction counseling is not adequate to help cancer patients to control fatigue, although fatigue is a universal occurrence and a regular symptom among patients with cancer. The management has not received sufficient consideration in nursing practice. Health care interventions for improving this condition have been narrowly researched. Some studies have even indicated that nurses were not capable of being familiar with this

## Abstract

Fatigue is a compound experience related to numerous backgrounds and has harmful consequences. Fatigue is common in patients with cancer. It is not adequately recognized and managed by nurses and has been under-treated.

**Objective:** The purpose of this review is to provide more focus and knowledge on possible mechanisms for Cancer related fatigue management, to prevent and manage the fatigue related to cancer or cancer treatments.

**Methods:** A systematic search of the literature was undertaken to identify research evidence on nursing fatigue management among patients with cancer. Three databases (i.e. Medline, CINAHL and Pubmed) were searched, resulting in 24 eligible studies.

**Findings:** The major results propose that multiple nursing interventions are adjuvant treatment beside the traditional treatment, and social, spiritual, psychological support and mind body interventions.

**Conclusions:** The result of the review emphasizes that fatigue is a significant crisis in patients with cancer and needs early detection and management. Nurses have to be responsive to the risk factors of fatigue in patients with cancer and carry out a full fatigue assessment and management plan for the risky cases. Even this review recognized inadequate research, and the results give guidelines as to the improvement of nursing interventions for fatigue management for patients with cancer.

**Keywords:** Fatigue, management, nursing intervention, patients with cancer.

symptom in cancer patients (Tiesinga et al.2002).

Fatigue is considered as a main, recurring and demanding symptom related to cancer and cancer treatment and is common in approximately more than 75% of patients (Kwekkeboom, Cherwin, Lee, & Wanta, 2010).

Fatigue is the most common symptom associated with cancer treatment and has the potential to have a profound, negative effect on the patient's quality of life (Ream, Browne, Glaus., 2003).

Conventional management of fatigue or other symptoms has focused on the use of drug treatment such as analgesics, psycho stimulants, hematopoietic growth factors, or sedatives. The end result is feelings of fatigue or lack of alertness throughout the day, which may well exaggerate fatigue and cause muscle pain. It appears that the pain-fatigue symptoms cannot be optimally managed with the use of medications alone. Other treatments associated with multiple nursing interventions are the adjuvant treatment beside the traditional treatment. These nursing interventions may include health education, distraction techniques, and social, spiritual and psychological support as well as mind body intervention.

In order to identify concepts of fatigue, fatigue has been recognized as a personally reported extremely unlikable experience usually described as being "odious", 'troublesome', 'comfortlessness' and even 'overwhelming' (Trendell,2000).

The fatigue occurrence has a medical, physical and psychiatric factor, and can also be idiopathic. Fatigue occurrence is multi-dimensional in nature, and fatigued individuals may present with a lower physical capacity, as the sensation of fatigue is personally reported (Ream & Richardson, 1996), (Tiesnga et al., 1996) and (Trendell,2000).

The purpose of this review is to describe the commonly used nursing interventions for fatigue management in patients with cancer. Focus was placed on the fatigue phenomenon associated with cancer especially.

#### **What is already known about the topic?**

- Fatigue is complex phenomenon commonly experienced by patients with cancer.
- Fatigue is known to be a prevalent problem in the patient with cancer associated with disease process or treatment such as chemotherapy.

#### **What this paper adds**

- Reviews international research on nursing role (multiple intervention) in fatigue management among patients with cancer.
- Presents a fuller picture about fatigue phenomenon and its related factors in patients with cancer.
- Highlights the needs to develop more research-based evidence for improving Symptoms of fatigue among patients with cancer.
- Highlights the commonly used nursing intervention for fatigue management in patients with cancer.
- Considers nursing intervention as adjuvant management in parallel with and beside traditional management.

#### **Method**

Relevant research studies were sourced using the databases Medline, CINAHL, and Pubmed and the keywords: 'fatigue', 'management', 'patient with cancer', and 'nursing intervention' were used. Studies were included if they focused on fatigue among patients with cancer. Papers focused on fatigue of other specific disease groups was excluded. As such the fatigue experience would be more affected by the nature of the disease. Other exclusion criteria includes studies which

- (1) were published in non- English language;

- (2) non-nursing intervention papers.
- (3) Other research with topics related to fatigue management.

#### **Findings**

(Joyce, Schwartz, and Huhmann , 2008) considered that fatigue can be managed by Exercise. Intervention is described by the national comprehensive cancer organization as the type of exercise, and its frequency, intensity, and duration depending on the patient's need. They recommend that all patients should be encouraged to participate in regular physical activities like aerobic exercise or strength training if needed, according to the patient's physical status.

Another intervention recommended by Margaret and colleague is energy conservation that aims to attain balance between activities and breaks by prioritizing and planning patient's daily activities like sleep practices that avoid extended naps, using the bed just for sleep and sexual activities only, standard sleep times and avoiding stimulations like caffeine intake.

Many relaxation exercises are found to be useful in cancer related fatigue relieving such as relaxing muscles of the face, mouth, and jaw, or abdominal breathing (using muscles of the abdomen). Interventions that ask the patient to form mind imagery of positive physical or emotional effects are also effective in fatigue management. This is technique is called imagery/hypnosis technique (Kwekkeboom, Cherwin Lee, & Wanta , 2010). Another effective intervention mentioned by Kristine and colleagues is Cognitive-Behavioral Therapy, which has shown positive effects were significantly achieved by using Cognitive-Behavioral Therapy that aimed to change a patient's belief regarding controlling their feelings and behaviors, to control their response to symptoms by education or counseling.

Meditation exercises such as yoga were reported by Carlson and Garland (2005) as one of the

interventions that can be used for fatigued patient management with beneficial effects by focusing on strengths and eliminating weaknesses caused by the fatigue experience.

Mind-body intervention may offer a valuable addition to the treatment schedule. Examples include relaxation, hypnosis, imagery, meditation and cognitive or behavioral techniques. Other interventions to enhance coping, diminish stress and anxiety and improve the pain-fatigue-sleep disturbance symptom cluster. Mind-body interventions may be practical in changing harmful beliefs about cancer, the original root of symptoms, or in explanation how the symptoms are presented. The intervention develops mood and hopeful feelings toward a patients' ability to deal with fatigue. This nursing intervention will improve relaxation and reduce pressure and nervousness associated with the symptoms. Sensitivity to pain sensations may be reduced, allowing more restful sleep, and reducing fatigue by the physical and mental effects of relaxation (Parker et al., 2005).

A comparative study conducted by Ferrier (2007) showed that using music to induce relief of fatigue is more beneficial than in other groups that didn't use music for relaxation and to decrease fatigue in cancer patients receiving chemotherapy and reported significantly less fatigue in the music group.

Education has an important role in fatigue management for patients with cancer especially for patients who start cancer treatment and have related fatigue. This education includes detail about prolonged occurrence of fatigue and its potential to increase in severity over time and avoid false suggestions that levels of fatigue around one week following chemotherapy administration will decrease spontaneously (Miller and colleagues(2007), Caprice and colleagues (2005)). Sleep therapy

and nutrition therapy are most appropriate management strategies and related education should be clear for those caring for patient with cancer.

Overall the interventions which were mentioned previously are the basis of nursing health education that contributes in guiding the patients regarding the appropriate strategies for fatigue management and the most effective education mechanism is informational audiotapes. Audiotapes ensure that all patients have access to the same information and are not dependent on the patient's ability to read. However, it is important that the audiotapes are easy to listen to as they provide standardized, complete information, improve comprehension and reduce learning time. In a study to examine the effectiveness of education in helping patients manage the fatigue from cancer chemotherapy, we used a structured audio-taped educational intervention to assist patients in managing or relieving fatigue. This study reported that education is effective for fatigue management and the most appropriate technique is audio tapes compared to written information. (Williams & Schreier, 2005). Other effective interventions to relieve fatigue mentioned in the study include getting more sleep distraction, such as listening to music, watching television, reading, keeping busy, using pleasant imagery, planning activities, using behavioral interventions and walking and exercising.

Bautman et al. (2008), Liao and Ferrell (2000) reported similarly that fatigue was autonomously indicated by the existence of physical soreness and deprived walking ability. These studies recognized the cancer disease process of chemotherapy, physical inactivity and dietary risk as significant causal factors of fatigue of fatigue in patients with cancer. Martin et al (2006) showed that maintenance of oneself physically dynamically develops better mood and avoiding of sadness, in order to keep a human from complaining of psychological-related fatigue.

Good dietary status helps to avoid the progress of fatigue-related physical complaints such as anemia. Life-style is a significant source for protecting patients with cancer from becoming fatigued. The association of psychological factors and fatigue has been confirmed by Wijertani et al.(2007)

## Discussion

Although there has been a development in cancer treatment, challenges regarding fatigue management have also increased related to treatment development. Health professionals will be increasingly challenged to build up fatigue management interventions so the trend is to support the current strategies of activity like sleep therapy and nutritional interventions (Berger. 2002).

Through a review of the findings from studies which examined fatigue in patients with cancer, this review provides a comprehensive picture of the fatigue phenomenon in patients with cancer. The research evidence clearly illustrates that fatigue is a distressing and overwhelming experience affecting the overall well-being of patients with cancer. Its debilitating effects restrict physical capability and the power store necessary for suitable performance and social participation. Many patients with cancer report disappointment with their undesirable performance. Such thoughts may decrease their sense of being able to manage and ultimately reduces their state of mind. So far, the complications of fatigue pose a challenge regarding suitable diagnosis and treatment. The lack of studies on fatigue management may imply that this problem is weakly documented and undertreated in patients with cancer. Such insufficient care would pose a risk to the functional capability of fatigued patients with cancer and worsen their morbidity and mortality outcomes.

Fatigue has been a more common research topic in chronic disease management.

The findings on the experience of fatigue in patients with cancer are similar to those identified in patients with other chronic illnesses such as congestive heart failure, especially in terms of the physical and psychosocial impact (Fitch, Mings, and Lee, 2008) And (Falk et al., 2007). So fatigue has a universal manifestation irrespective of its essential causes. Key differences are in the fatigue experience related to the disease and the associated treatment of patients with cancer.

Indeed, previous studies also indicated that fatigue in patients with chronic illness are strongly associated with the disease severity (Falk et al., 2007), other disease-specific symptoms (Yennurajaligam et al, 2008), health perception (Yu, Lee and Woo., 2004) and frequency of disease exacerbation (Baghai et al., 2009). Such differences between patients with chronic illness may explain the variation in their ways of coping with the fatigue experience.

Therefore, nurses and other health care professionals need to take a more active role in assessing fatigue in patients with cancer. This requires a good awareness of the high risk group for fatigue, so that further assessment of this symptom can be conducted in educational course planning. Our review suggests that there is a lack of research-based evidence to inform regarding the practice. Based on our findings about the nature of fatigue and its related factors, fatigue may be managed from the biomedical, physical and psychological perspective by multiple nursing Interventions, besides traditional treatment. These nursing interventions may include health education and distraction techniques. Social support, spiritual support, psychological support by listening to music or the holy Qur'an according to cultural background may also provide mind body intervention. (Nied and Franklin., 2002) in order to maintain an individual's physical capacity, exercise therapy may be a valuable strategy to reduce fatigue in patients with cancer.

From the biomedical and physical perspective, it is important for nurses to make efforts to alleviate this psychological component of fatigue in patients with cancer.

Relaxation therapy is well-recognized to have an effect on relieving psychological distress. The evidence indeed suggests the beneficial effect of relaxation therapy in relieving fatigue among patients with chronic illness (Yu et al., 2007).

Further investigation of the cultural influence on fatigue experience would also be significant to focus on developing culturally relevant care for fatigue management.

This review focuses more on the common management for cancer related fatigue like exercise intervention, energy conservation, relaxation exercises, mind imagery, imagery/hypnosis technique, Cognitive-Behavioral Therapy, using music, distractions as a technique and health Education which have an important role in fatigue management in patients with cancer.

### Conclusion

Fatigue is known to be a significant health problem in patients with cancer. This review indicated that it is in fact a distressing condition that compromises the quality of life and other health outcomes of patients with cancer. However, the complexity of this phenomenon and multi-dimensional manifestation imposes real challenges to health professionals in managing this distressing symptom. The findings of this review provide opening indications on how to assist patients with cancer to cope with the fatigue experience. More effort needs to be placed on developing research-based evidence to improve fatigue management. Also this study would provide a basis for future intervention to identify what patients can do to relieve their fatigue through self care behavior, such as physical, psychological, social and spiritual aspects of care, that can have a tremendous impact on the lives of patients and family members.

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# EFFECTIVENESS OF THERAPEUTIC TOUCH ON PAIN MANAGEMENT AMONG PATIENTS WITH CANCER - LITERATURE REVIEW

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## Abstract

**Aims:** This paper aimed to evaluate the effectiveness of therapeutic touch as Complementary and alternative management of pain among patients with cancer.

**Method:** A systematic search was conducted via Pubmed, Ebsco, and Medscape, to identify the aim of this literature. Of these 46 articles ,10 articles met the inclusion criteria and were included in the review, using the keywords therapeutic touch, cancer pain, and pain management. All the keywords were searched using the “including related terms” option. The search only included all records from January 2000 through to April 2010.

**Result:** Among these 46 articles that were found, just 10 articles met the inclusion criteria. These articles related to trials conducted in different countries such as the USA, Canada, UK, Iran and Israel. The result was that TT was effective in all these articles and it not just decreases the pain, but also decreases fatigue and maximizes the health, comfort and quality of life and it is used in different stages and types of cancer.

TT is one of the useful therapies that decreases pain and increases quality of life among patients with cancer pain.

**Conclusion:** TT is one of the CAM (Complementary and Alternative Medicine) techniques that is very effective in pain management among patients with cancer. It has the effect of decreasing fatigue, and pain, enhancing and improving quality of life and maximizing comfort among patients with cancer.

**Significance:** Cancer pain is still managed poorly. There are many side effects from using pharmacological pain management. TT (therapeutic touch) is a part of medicine that is almost forgotten these days. We need to study this therapy to examine its effect on pain management among patients with cancer.

## Introduction

Pain is one of the major health care problems for patients with cancer (Portenoy RK, Lesage P. Management of cancer pain. Lancet 1999). Despite the diffusion of several guidelines for cancer pain management, including well-known recommendations of the World Health Organization (WHO) and other organizations of health care providers (World Health Organization. Cancer Pain Relief, 2nd edition1999). Pain among cancer patients is still one of the most serious complications that face all patients during their disease process.

In the last several years, many hospitals and centers have developed strategies for pain management programs that aimed to minimize pain and increase the feeling of comfort for patients with cancer by using different modalities.

In this literature review we aimed to evaluate the effectiveness of therapeutic touch on pain management among patients with cancer, as we know that there are different treatment modalities in cancer pain. There is pharmacological management such as sedation and pain killers and non-pharmacological strategies such as complementary and alternative management (massage therapy, therapeutic touch, music, group therapy etc), in this study we chose therapeutic touch as one of the treatment modalities of pain in cancer patients. Following are some definitions of the key words (cancer, pain management, therapeutic touch) that I used in this review in order to understand it:

Cancer is a class of diseases in which a group of cells display uncontrolled growth, invasion (intrusion on and destruction of adjacent tissues), and sometimes metastasis (spread to other locations in the body via lymph or blood.)

These three malignant properties of cancers differentiate them from benign tumors, which are self-limited, and do not invade or metastasize. Cancer affects people at all ages with the risk for most types increasing with age. Cancer caused about 13% of all human deaths in 2007 (7.6 million). In Jordan cancer was the second leading cause of death among the population according up to 2007.

One of the most common symptoms of cancer in all stages, is pain. Whether this pain is from the cancer disease progress itself or from side effects of different treatment modalities such as radiation, chemotherapy and surgery. Cancer pain is one of the most important focuses in palliative care of cancer. In order to understand cancer pain, we should identify what pain is, There are many ways to define pain. A useful definition is from pain expert Margo McCaffrey, MSN, RN, FAAN: "Pain is whatever the experiencing person says it is, and exists whenever he says it does." The International Association for the Study of Pain says it is "an unpleasant sensory and emotional experience in association with actual or potential tissue damage, or described in terms of such damage, pain is a sensation that hurts, and it has both physical and emotional aspects to consider.

Pain, which can be caused by the disease itself or by treatments, is common in people with cancer, although not all people with cancer will experience pain. Approximately 30% to 50% of people with cancer experience pain while undergoing treatment, and 70% to 90% of people with advanced cancer, experience pain (Lesage P. and Portenoy RK. *Cancer Control; Journal of the Moffitt Cancer Center* 1999;6(2):136-145).

Therapeutic Touch (TT) is a form of "energy healing" popular in the American nursing community. In the words of its official organization, "Therapeutic Touch is an intentionally directed process

of energy exchange during which the practitioner uses the hands as a focus to facilitate the healing process." (1) TT is used by nurses in a variety of settings, from the office to the Intensive Care Unit (ICU). However, there is as yet no meaningful evidence that it is effective.

Therapeutic Touch was developed in the early 1970s by two people: Dolores Krieger, PhD, RN, and a self-professed healer named Dora Van Gelder Kunz. At first, TT involved setting the hands lightly on the body of the patient, but the method rapidly evolved into a non-contact, "energy healing" method. Today certified practitioners can be found in virtually all parts of the U.S. and in much of the world. TT is available in mainstream health care facilities including hospices, hospital-based alternative health programs, and even ICUs.

Therapeutic Touch is sometimes described as a scientific version of "laying on of hands," a technique practiced by faith healers. However, there is more spirituality than science to this method; it makes use of beliefs and principles common in spiritual healing traditions but alien to current science culture.

According to TT, the body has an "energy field," and, without physical contact, the energy field of one person can substantially affect the energy field of another. The practitioner is said to heal, balance, replenish, and improve the flow of the patient's energy field, thereby leading to enhanced overall wellness. However, there is no meaningful scientific evidence for any of these beliefs.

### Methods

Data bases were searched by online medical search engines like Pubmed, Ebsco, and Medscape using the keywords therapeutic touch, cancer pain, and pain management. All the keywords were searched using the "including related terms" option. The search only included all records from January 2000 through to April 2010.

The inclusion criteria and exclusion criteria were established to make the review significant. the inclusion criteria included the following:

- 1) observational and experimental studies,
- 2) to be written in English only
- 3) published between January 2000 and April 2010,
- 4) using the therapeutic touch as one of the CAM (complementary and alternative management) options ,
- 5) and using it for pain management for the patient - with different types of cancer - either alone or with other modalities. Articles were excluded if therapeutic touch was used in treatment of pain among patients without cancer;
- 6) random assignment, either placebo or control;
- 7) investigations;
- 8) peer-reviewed journal;
- 9) abstracts.

Because published studies of TT are a recent occurrence and are few, no attempt was made to narrow to a specific issue, diagnosis, or patient population. Only 10 articles met the established review criteria.

### Result

Three major electronic databases were searched. Forty-six (46) articles were found during searching. 10 articles were identified with potential for the review and that met the inclusion criteria. Among these potential articles there were four (4) articles talking about therapeutic touch and healing touch, three (3) articles talking about massage therapy and CAM, and one study talked about CRC and therapeutic touch as one of the treatment modalities. The studies were from different locations such as the United Kingdom, USA, Iran, Canada, Israel.

These articles did not focus on particular types of cancer but focused on pain as a complication of cancer in general, and in different stages, although there was an article about CRC and using CAM in maximizing quality of life and increasing the comfort of patients

with this kind of cancer (Maida J Sewitch, Yamina Rajput 2009). Most of the research involved the use of therapeutic touch to decrease the pain after being treated with chemotherapy or radiotherapy while some focused on using this technique with other modalities. The articles concluded that TT is one of the useful therapies that decrease pain and increase quality of life among patients with cancer pain (Nahid Aghabati, Esa Mohammadi and Zahra Pour Esmail 2008). Although this method of therapeutic touch is a forgotten art the medicine it has a significant effect on patients with cancer pain (Soren Ventegodt; Mohammed Morad, and Jav Merrick 2004).

### Discussion

This review concluded that using therapeutic touch in pain management among patients with cancer is effective. TT was more effective in decreasing pain and fatigue of the cancer patient undergoing chemotherapy than the usual care group (Nahid Aghabati, et al 2008). On the other hand massage touch and TT lowered anxiety and healing touch lowered fatigue and both lowered total mood disturbances (post white et al ). Wez et al found in their research on therapeutic touch that the healing by gentle touch decreased pain in clients with cancer within the six sessions of treatment. According to Maida J Sewitch, Yamina Rajput in a literature review of CAM use by CRC patients in 2009, up to 75% of CRC patients using at least one CAM such as TT improved general health and well-being. They stated that the use of CAM in future, can affect quality of life over time and in relation to changing health states, cancer stage and treatment. Another research article viewed showed that massage and TT have immediately beneficial effects on pain and mood among patients with cancer, especially in advanced stages. (Jean S. Kutner; Marlaine C Smith et al. Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer 2008).

When touch is combined with therapeutic work on mind and feelings, holistic healing seems to be facilitated and many problems can be solved in a direct and easy way in the clinic without drugs, (Soren Ventegodt; Mohammed Morad and Jav Merrick 2004). There are many ways of touching, like therapeutic massage (TM), healing touch (HT), Reiki or therapeutic touch (TT), which can be classified as energy or metaphysical therapies, one of the five domains created by the National Institutes of Health (NIH) Office of Complementary and Alternative Medicine CAM (Rousch, R 2003) . A Medline (PubMed) search on January 29th, 2004 found 470 records under the heading of TT. Many studies are published in nursing journals with evidence that TT has the ability to cause relaxation, as well as laboratory evidence for physiological change towards relaxation and improved immune function, but the last entry was a study on improvement of symptoms in cancer (Post-White, J., Kinney, M.E., Savik, K., Gau, J.B., Wilcox, C., and Lerner, I. (2003). At the end of this literature search there was evidence about the effectiveness of therapeutic touch and other CAM on pain management among patients with cancer. As we see in this review there is motivation to use CAM as a mode of treatment of pain among patients with cancer.

### Implication

The positive findings of this review support the premise that non pharmacological intervention such as TT as a CAM is effective in decreasing pain and fatigue of cancer patients. This information can provide valuable knowledge about TT. To be more specific in future we should undertake more investigations and study, to answer question like when TT should be used, and what is the best time and length of duration of TT during interventions. Another question to be studied is should we use TT in any stage of cancer and is it useful in the end stage of cancer when patients go to the palliative unit and have palliative treatment. All these studies should be undertaken to answer the question.

We as nurses should practice TT with patients who have pain from cancer at all times because we are in direct contact with the patient more than doctors or other health care providers, and TT can be applied in different places not just in hospitals e.g. homes, and day care, and it does not require any additional equipment. Finally we recommended to use TT as one of the CAM approaches beside other treatment modalities in order to provide more health comfort and to enhance the quality of life of patients with pain. This therapy is considered non invasive and does not require any specialized equipment. We can minimize the pain and fatigue by using this method, rather than using pharmacological methods which cause side effects and also increase the side effects of cancer in many stages. Here in Jordan we use this technique in many settings especially in KHCC (King Hussein Cancer Center) through a team called the pain team that wears the sign of (NO PAIN) above their chest.

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## PREVENTION AS A KEY MANAGEMENT MEASURE FOR ORAL MUCOSITIS AMONG CHILDREN WITH CANCER: REVIEW OF LITERATURE

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### Introduction

Oral mucositis (OM) is the most common and serious side effect of cancer treatment (Epstein 2003; Sonis 2004). Chemotherapy, stem cell transplantation regimen, and irradiation are the most common reported causes of mucositis. The rate of incidence reached 46%-70% for children undergoing cancer treatment (Figliolia et al., 2008; Gandemer et al., 2007). Oral Mucositis can be defined as the change in mucosal membrane of the oral cavity secondary to cancer therapy. Oral mucositis is characterized by thinning out of the oral tissue, atrophy, erythema, ulcerative lesions and severe pain (Cheng, Molassiotis, Chang, Wai, & Cheung, 2001; Epstein & Schubert, 2003). The lesions could be developed as a result of high mitotic and rapid epithelial turn over and maturation rate of mucosal membrane (Kennedy & Diamond, 1997). Mucositis commonly causes severe pain and discomfort that affects oral intake as well as the child's ability to communicate and sleep (Green, Horn, & Erickson, 2010) This can significantly affect the quality of life, completion of the treatment regimen, and utilization of health care services through recurrent hospitalization. According to Kwong (2004) children with OM require hospitalization due to pain and for nutritional support which influences the effectiveness and cost of the whole treatment of cancer.

In studies that investigate oral mucositis (OM) among adults, several approaches have been used for different purposes, and a paucity of these approaches have been tested in pediatric settings. The limited information of each intervention, however; is conflicting in terms of what nurses can adopt in daily practice in order to reduce the incidence and minimize the complications of Oral mucositis. This review of the literature aims to summarize oral mucositis risk

### Abstract

Oral mucositis is a common complication of cancer treatment. Painful experience, discomfort, and high risk for infection are associated with oral mucositis. Oral-mucositis affects children's physically and psychologically in addition to the cost burden. Moreover child quality of life is negatively affected by frequent hospitalization. This review of the literature aims to summarize oral mucositis risk factors as well as identify the recent intervention for oral-mucositis management in children with cancer. A total of 37 studies were identified and retrieved from a systematic search of computerized databases: Medline (U.S. National Library of Medicine), EBSCO-host, and Science Direct from January 2000 to December 2009. The electronic database was searched by using oral Mucositis, cancer, intervention, and management as keywords. However, literature derived from this combination of keywords was mostly oriented toward adult oncology patients. Therefore an addition of the search term "children" to the keywords proved necessary. Eighteen randomized-clinical-trials, two meta-analyses, two qualitative studies, and one non-experimental study were found and reviewed. Ten different agents were found

with conflicting efficacy for oral mucositis management including; vitamin (E), plants extract (Traumeel S, Glycerine Payayor), Transforming growth factor (TGF)-beta(2), Benzydamine, Chlorhexidine, Cryotherapy, Glutamine, laser, debridement, chewing gum, fluoride mouth-washes, and topical application of Miconazole. Limited evidence was found with variety in level of strength. Basic oral care is the recommended prevention measure that could be considered as the first step of management.

**Key words:** Oral Mucositis (OM), Pediatric Oncology, Management, Intervention, Prevention

factors in addition to describing the evidence-based research conducted in the management of oral mucositis among children with cancer.

## Methods

The Pub-Med, Science Direct, and EBSCO data-bases were searched for studies published from January 2000 to December 2009, using the following key words: Mucositis, cancer, intervention, prevention, management, and children. All articles found with this search were retrieved and included if in inclusion criteria. Included criteria were Randomized clinical studies involving child subjects and systematic review or Meta-analysis studies that include research investigating mucositis in children, written in English, whose aim was the management of mucositis in children undergoing cancer therapy. Data was ranked according to the Hierarchy of Evidence for interventional studies. A total of 18 Randomized clinical trials, two meta-analyses, two qualitative studies and one non-experimental study were found in the review which revealed five studies on glutamine, plants extract (N)= 2, Transforming growth factor 1TGF-beta N=(2) Chlorhexidine (N)= 6 Cryotherapy (N)=1, laser (N)= 3, Debridement approach(N)=1 chewing gum(N)=and one fluoride mouthwash, with topical application of Miconzole.

OM develops from the interaction between various mucosal components and the oral environment that includes epithelium and extracellular matrix (Sonis et al., 2004). OM has five phases: initiation, up-regulation and message generation, amplification and signaling, ulceration, and healing. Initiation of oxidative stress and reactive oxygen species (ROS) by chemotherapy or radiation lead to direct injury to cells, tissue and blood vessels. Regulation with generation of messengers, that lead to apoptosis of sub mucosal and basal epithelial cells, signal amplification, prolonged tissue injury with biological alteration even though it may appear normal ulceration with inflammation, due to invasion of colonized organisms into sub mucosa, and, finally healing

which starts with a signal from the extracellular matrix. This leads to a renewal of epithelia proliferation and differentiation and re-establishment of the local microbial flora (Redding, 2005; sonis et al., 2004). Fungal were the common isolated organisms from oral mucosal lesions followed by bacterial, while ulcers were the common presentation (70%) (Anirudhan, Bakhshi, Xess, Broor, & Arya, 2008). The time course of change of oral mucosal membrane is taken from first day up to twentieth day after starting chemotherapy (Cheng, Molassiotis, Chang, Wai, & Cheung, 2001) while signs and symptoms of mucositis can be identified five to seven days after chemotherapy (Kuhn, Porto, Miraglia, & Brunetto 2009).

## Risk factors and associated conditions

Risk factors for developing mucositis are vague (some factors include: tumor type, anti-neoplastic agent, radiation source, treatment dosage, treatment schedule, combination of treatment, duration of exposure, systemic clearance of drug during treatment and genetic factors. Cancer type is found to be a risk of OM. In analysis of 169 pediatric patients done by Figliolia and her colleagues reported that 46% of patients who were treated for OM were diagnosed with acute lymphoblastic leukemia (Figliolia et al., 2008). Although the type of chemotherapy regimen was thought to be the only factor independently associated with the risk of oral mucositis (Gandemer et al., 2007), genetic factors can explain the differences in an individual's liability for developing OM within the same groups of patients under the same regimen. The genetic hypothesis that people with defects in metabolic enzymes, decreased level of Anti-apoptotic gene and DNA-repair mechanisms impairment may be at high risk for developing of OM (sonis et al., 2004). Another study conducted using a convenience sample of 641 patients (395 boys and 246 girls) diagnosed with different type of malignancies, resulted in an association between

ABO blood group and mucositis patients treated by standard chemotherapy. This study showed that blood group O patients were at higher risk of developing OM (Otmani, Alami, Soulaymani, El Mokhtari, & Khattab, 2008)

According to the anti-neoplastic agent, the risk of developing OM increases with certain drugs, the anti-metabolite agents were the most frequently associated with oral mucositis (El-Housseiny, Saleh, El-Masry, & Allam, 2007a). A study conducted using a convenience sample of 241 children treated by antilogous bone marrow transplant, reported that the alkylating agent Busulfan had the highest prevalence of mucositis with 63.5% (Fadda, Campus, & Luglie, 2006) while Cytrabine had the most toxic effect (Cheng et al., 2001; Mori et al., 2008)

MTX was suggested to be a risk factor for mucositis. The effect of high-dose Methotrexate in the pediatric population with different diagnoses such as leukemia and osteosarcomas were reported. The differences in MTX plasma level, concentrations, and the cycle number of MTX were correlated with oral mucositis severity (Cheng, 2008; Maiguma et al., 2008; Peyriere et al., 2004).

OM in children was associated with neutropenia and nausea/vomiting. Neutropenic children experience a higher incidence of mucositis (Anirudhan, Bakhshi, Xess, Broor, & Arya, 2008). In 38 children, level of nausea/vomiting was positively associated with OM (Cheng, 2008). Oral ulcer was associated with Herpes Simplex Virus HSV (Sepúlveda, Brethauer, Rojas, Fernández, & Le Fort, 2005). One study linked the HSV with the extended mucositis period and results in poor response to initial therapy (Ramphal et al., 2007). For patients who are treated with radiotherapy, OM severity depend on the type of radiation fractionation schedule, Total cumulative dose and irradiated tissue volume (Miralbell, Allal, Mermillod, & Pastoors, 1999). The altered fractionation

radiotherapy (RT-AF) patients experienced severe mucositis compared to patients who received conventional radiotherapy with the main incidence of 80% for all patients (Trotti et al., 2003). The incidence of (OM) in adult patients receiving radiotherapy rated 80% while patients receiving chemotherapy rated 98% (Sonis et al., 2004). In childhood cancer, mucositis is more observed and poorly documented; mucositis can approach 35%-49% in children with acute lymphoblastic leukemia (Maiguma et al., 2008 ; Stokman et al., 2006) and up to 70% after high-dose chemotherapy (Gandemer et al., 2007). OM is frequently described as one of the common distress symptoms reported by pediatric oncology nurses. Nurses' Distress and Interventions for Symptoms Survey (NDISS ) reported that mouth sore presented in 82% as one of the common distressing symptoms that face 401 pediatric nurses. Also evident from this study was the use of mouth care/hygiene as the first nursing intervention (Rheingans, 2008). Consistent with other studies focused on symptom management, oral mucositis (OM) is found to be one of the seven common symptoms experienced by children with cancer (Hockenberry, 2004).

Oral mucositis is source of extra morbidity which increases health care costs and affects patients' quality of life (Sonis et al., 2004). About 27% of patients were re-admitted to hospital for mucositis management (Kwong, 2004) which increases the overall cost for cancer treatment.

In addition to the pain and discomfort, mucositis can result in under-nutrition and sepsis. A study investigating the complication of oral mucositis found that two out of six children were candidates for serious complications for OM; sequentially the patients were re-admitted to hospital (Anirudhan, Bakhshi et al., 2008).

Oral mucositis has a complex biopsychosocial impact on children's

lives and their families (Brown et al., 2009; Cheng, 2009). Children preferred not to eat during OM (Green et al. 2010) because of pain on chewing and swallowing. Therefore the limited oral intake results in serious nutritional impairment. The dilemma of eating and the experience of negative emotion in addition to physical impairment makes OM a challenging situation for both nurses and patients' families. Therefore children needed more activities coordinated by the ward to distract them from their OM, as well as psychological support from the health care professionals (Cheng, 2009).

### Intervention Approaches

Recent and ongoing approaches to manage radiation-induced mucositis are discussed by Trotti and his colleagues. They reported that (Sucralfate, Glutamine, Povidone-Iodine and Prostaglandins) have no evidence or need further investigation with regard to their usefulness in reduction or prevention of mucositis. It is found that Mucosal-Sparing Radiologic Techniques that spare normal tissue are one of the most effective ways to reduce mucositis and toxicity (Trotti et al., 2003). However another recent study on 100 patients who were diagnosed with head and neck tumors, Benzydamine oral rinse was found to be effective, safe, and well tolerated for prophylactic treatment of radiation-induced oral mucositis (Kazemian, Kamian, Aghili, Hashemi, & Haddad, 2009)

At present, there is no standard therapy for OM. Therefore, new treatment methods were investigated including good oral hygiene, mouthwashes, alternative natural agents and others. The review revealed clinical trials that evaluated vitamin ( E ), plants extract Traumeel S Glycerine Payayor, Transforming Growth factor TGF-beta , Benzydamine, Chlorhexidine, Cryotherapy, Glutamine, laser, Debridement approach, and chewing gum and fluoride mouthwashes, with topical application of Miconazole.

These therapies aim either to increase comfort or to remove debris from the oral cavity to decrease the risk of further ulceration and infection (Kennedy & Diamond, 1997). Obtaining cultures from oral lesions is useful in appropriate management of lesions and thereby possibly preventing systemic spread (Anirudhan, Bakhshi et al., 2008). In this context Benzydamine, Chlorhexidine, Cryotherapy, and Glutamine have been reported as effective and acceptable methods in prevention of OM in children.

### Basic oral care

Several mucositis studies compound the interventional agent with basic oral care which indicate the importance of oral hygiene in preventing or decreasing severity of OM (Abramoff et al., 2008; Chen, Wang, Cheng, & Chang, 2004; Hogan, 2009; McGuire, Correa, Johnson, & Wienandts, 2006; Rheingans, 2008; Vokurka et al., 2005). A few oral care protocols were examined in the pediatric setting; the focus was on patient and family education, instruction on tooth brushing, and use of rinses effectively. Four studies demonstrate the benefit of using oral care protocols in comparison with general oral care. (Chen et al, 2004; Cheng et al, 2002; Cheng et al, 2004; Kwong, 2004). Considering the benefit of basic oral care versus the benefit from the interventional agents, investigators are consistent in reporting that the positive result may be due to a subject's commitment and practice of daily mouth care throughout the study period. Therefore oral care is a highly recommended practice and should be one of the nurse's routine actions.

### Benzydamine and Chlorhexidine

Literature review demonstrated that the use of Benzydamine, and Chlorhexidine rinses have beneficial effects on mucositis in pediatric populations (Cheng, Molassiotis, & Chang, 2002; Cheng et al., 2001). Small sample size or non-random allocation to group trials means therapeutic benefit needs to be

confirmed. Studies have demonstrated that the use of two concentrations of Chlorhexidine (0.12 %OR 0.2%) along with 0.12% Chlorhexidine mouth rinse in young children diagnosed with Acute Lymphoblastic Leukemia might decrease the incidence of oral mucositis and ulceration (Costa, Fernandes, Quinder, de Souza, & Pinto, 2003). Another study on fourteen child who used 0.2 % Chlorhexidine reported the same beneficial results (Cheng et al., 2002). Benzylamine hydrochloride which contains anti-inflammatory, pain relieving and antimicrobial actions can be used prophylactically to prevent mucositis (Cheng, Chang, & Yuen, 2004). The results provide that Chlorhexidine is more helpful than Benzylamine in reducing mucositis. From a patient's perspective both agents are acceptable and tolerable in children, but Chlorhexidine is more preferable (Cheng, 2004). Comparing Benzylamine with natural agents, Glycerine Payayor (herbal product) was found to be superior in preventing and relieving radiation-induced OM than Benzylamine hydrochloride (Putwatana et al., 2009).

### Glutamine

Glutamine is a non-essential amino acid required for body growth. Studies tested Glutamine as a prophylactic treatment if used orally, as a topical rinse or parental formulation. Storey, in 2007 reviewed the role of glutamine in pediatric bone marrow transplants and reported that even the studies conducted on glutamine supplements were inconsistent and conflicting. Researchers found that it is still promising in maintaining and healing mucosal tissue. Different glutamine doses, dosing in travel, duration and administration routes play a major role on the degree of glutamine efficacy in reducing OM (Storey, 2007). Three studies reported that Glutamine reduced duration and severity of oral mucositis in children (Aquino et al., 2005; Kuskonmaz et al., 2008; Sonis, 2006).

A study that evaluated glutamine supplements in 120 children reported a benefit of 2gm twice daily as preventable and interventional therapy that should be considered for children under hematopoietic stem-cell transplantation HSCT (Kuskonmaz et al., 2008; Sonis, 2006). A randomized study was conducted to determine if enteral glutamine, 0.65 g /kg daily for 7 days, is effective in reducing the incidence and severity of mucositis in seventy-six children undergoing treatment for pediatric malignancy. Results revealed that high-dose enteral glutamine did not reduce the incidence and severity of oral mucositis (Ward et al., 2009).

### Cryotherapy

Evidence from randomized trials suggest that the use of Cryotherapy by ice cups for five minutes before chemotherapy and maintained during infusion of chemotherapy improves OM (Karagozoglu & Filiz Ulusoy, 2005). Another study proved that the use of ice cold water every ten minutes for three hours during chemotherapy infusion improves OM in patients who receive high dose Cytrabine and irradiation as a treatment regimen. In the hematopoietic stem-cell transplantation (HSCT) population ice water can remove Cytrabine directly from the oral cavity and decrease drug absorption by vasoconstriction. Ice -water reduces blood flow and reduces the amount of drug distributed to mucosal tissue (Mori et al., 2008). The combination of Cryotherapy with other agents might maximize the effectiveness of reduction of mucosal toxicity in patients with malignancy who undergo high-dose chemotherapy (Sato et al., 2006). This finding was contradictory, with a large study on 130 patients including children. The study reported that Cryotherapy during MTX administration does not reduce oral mucositis in patients undergoing bone marrow transplant (Gori et al., 2007). The cheapness of this approach and its positive results on several regimens except MTX can encourage its use in the clinical setting.

### Vitamin (E)

The efficacy of vitamin (E) was studied as prophylaxis against chemotherapy-induced mucositis in children. The results of the studies on vitamin "E" were conflicting. One study by (El-Housseiny, Saleh, El-Masry, & Allam, 2007b) looked at the administration of topical vitamin "E" versus systemic administration in 80 children. The study concluded that topical application of 100 mg vitamin "E" twice daily is a more effective measure for the treatment of chemotherapy-induced oral mucositis than systemic administration of vitamin "E". Another study has not demonstrated the beneficial effect of topical vitamin "E. Researchers performed a series of controlled trials on 16 children and 45 post chemotherapy cycles randomly assigned to receive either topical vitamin E (800 mg) or placebo. The study found no difference in mucositis scores because topical vitamin E does not reduce doxorubicin-induced oral mucositis in children. (Sung et al., 2007).

### Laser therapy

Two out of three studies that tested laser therapy in children provide evidence suggesting that children should benefit from this easy, highly accepted method. In a previous study, sixty patients diagnosed with leukemia or lymphoma, and solid tumors were randomized in the laser group and in the control group. Results showed no beneficial effect of low-energy laser (Cruz et al., 2007). A recent study showed evidence that Low-level Infrared laser therapy in addition to oral care can decrease the duration of OM (Abramoff et al., 2008). Furthermore, other researchers applied Laser to every OM lesions for five consecutive days, confirming promising results of low-energy laser that was observed in randomized trials in adult studies. The success of laser may encourage pediatric oncologists to use laser therapy as a first-line option in children with chemotherapy induced OM (Kuhn et al., 2009). Traumeel S plant extracts and mineral agents, that have anti-

inflammatory properties may reduce the severity and duration of OM in children undergoing bone marrow transplantation (Oberbaum et al., 2001).

### **Povidone-iodine**

Antiseptic agent Povidone-iodine mouthwash was studied in three clinical studies in the adult population. Recently there was no evidence for the child population. The results of Povidone-iodine mouthwash were not in total agreement. Alcohol-free Povidone-iodine mouthwash was found to be effective in patients treated by radiotherapy. Patients were instructed to rinse with 10 ml of the mouthwash, twice a day, for a period of 6 weeks. Chlorhexidine (0.12%), Povidone-iodine (1%), or salt/soda (Madan, Sequeira, Shenoy, & Shetty, 2008). These results were consistent with other studies conducted by colleagues. Mouth wash was performed 3 days a week after dinner for esophageal cancer patients. Researchers found that incidence of mucositis was significantly reduced (Yoneda et al., 2007). In contrast with another finding from a randomized trial on 132 patients receiving autologous peripheral stem cell transplantation, the study comparing Povidone-iodine with normal saline proved that no significant difference was found between the groups in respect of OM characteristics. (Vokurka et al., 2005)

### **Growth factor therapy**

Growth factor therapy (KGF1) is approved by FDA as current medication for OM (Redding, 2005). KGF is mainly Palifermin; a recombinant form of the human keratinocyte growth factor that seems to be effective in preventing oral mucositis in patients with hematological malignancies receiving conditioning radio-chemotherapy (Awada, Genot, & Klastersky, 2005; Barasch, Epstein, & Tilashalski, 2009). Although clinical studies tested the adult population in addition to a small number of children there is a need to evaluate Palifermin benefits and related adverse reactions on children

under cancer treatment. Based on a report of one study that tested Transforming growth factor TGF-beta (2) in childhood-cancer patients, the potential benefit of TGF-beta (2) on OM was not proved (de Koning et al., 2007)

### **Fluoride mouthwashes**

It was believed that Miconazole could impact oral mucositis by significantly suppressing fungal organisms since fungal organisms were the common isolated organism from oral mucosal lesions followed by bacterial organisms (Anirudhan, Bakhshi et al., 2008). A controlled clinical trial evaluated five children diagnosed with Acute Lymphoblastic Leukemia (ALL) for twelve months. The study reported that use of non-alcoholic 0.05% fluoride mouthwashes, with topical application of Miconazole-antifungal oral gel, have no significant effect on oral complications (Rojas de Morales et al., 2001).

### **Other approaches**

#### **Debridement**

Depending on the classical theory of Kennedy & Diamond in which the removal of debris will enhance healing and prevent spreading of infection, recent RCT has showed a novel approach of debridement for forty children complaining of severe mucositis. A total of 20 children who received debridement showed a reduction in the severity of mucositis (Cubkcu, 2007).

#### **Chewing gum**

Gandemer and his colleagues conducted a multi center trial, to test the effectiveness of increased salivary flow by chewing gum in prevention of OM in children. The trial resulted in no effect for such a technique in reducing OM (Gandemer et al., 2007).

### **Conclusion**

Finally, several mucositis studies compound the interventional agent with basic oral care which indicates the importance of oral hygiene in preventing or decreasing severity of OM. Regardless of the benefit

and frequency of these practices the patient's individual preference and tolerance of solutions offered should be considered. Topical approaches and rinses may be sufficient during the early and pre phases of ulcerative mucositis, but there is a great need for effective treatment in the active ulceration phase of mucositis. In a stage-based intervention model future preventive and treatment strategies will likely include the use of multiple agent' interventions. Usually oral care is connected with discomfort and pain, thus some children neglect oral care even if they are aware of its importance. Nurses should consider the benefit of basic oral care versus the discomfort associated with oral care. Nurses should apply different strategies to enhance the patient's comfort prior to basic oral care, use flexible arrangement for doing mouth care, using a soft tooth brush, and allowing enough time to perform this task, can effectively enhance children's compliance to oral care practices.

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