Improved weight and nutritional status after mouth rinse with calcium phosphate solution at stem cell transplantation: An intervention study

Author: Kerstin Lugnet
Supervisor: Annearin Svanberg

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Examinator: Praneed Lundberg
SAMMANFATTNING

Bakgrund:
Oral mukosit (OM) är en toxisk biverkan efter högdos cytostatikabehandling (HDC) och hematopoietisk stemcellstransplantation (HSCT). OM orsakar kliniska komplikationer samt negativa följer för patienten, som längre sjukhusvistelse, oral smärta, viktförlust och parenteral nutrition (PN).

Syfte:
Att undersöka om det föreligger skillnad i viktförändring och nutritionsstatus hos patienter som använder munsköljmedlet, Caphosol® i tillägg till standardbehandling i jämförelse med standardbehandling vid behandling med HDC och HSCT.

Metod:
En randomiserad kontrollerad öppen studie där patienter > 16 år (n=40), behandlades med HDC, inför HSCT på Akademiska universitetssjukhuset, Uppsala. Patienterna randomiserades, 1:1, till oral standardbehandling och munsköljmedlet Caphosol® (EXP n=20) eller oral standardbehandling (KTR n=20). OM, oral smärta, viktförlust och dagar av PN registrerades och analyserades från baseline till 21 dagar efter avslutad HDC.

Resultat:
Caphosol® hade ingen signifikant betydelse för viktförändringar mellan EXP- och KTR-grupperna. OM-smärta debuterade senare i EXP än i KTR-gruppen. KTR gruppen använde mer PN jämfört med EXP-gruppen.

Konklusion:
Caphosol® hade obetydlig inverkan på förekomst, duration och svårighetsgrad av OM under HCT vid HSCT och därmed liten effekt på nutrition och vikt. Det föreläg ingen fördel att addera Caphosol® till oral standardbehandling.

Nyckelord:
 Viktförändring, nutrition, munsköljmedel, kalcium fosfat lösning, hematopoietisk stamcellstransplantation.
ABSTRACT

Background:
Oral mucositis (OM) is a result of cytotoxic effects of high dose chemotherapy (HDCT) administered before hematopoietic stem cell transplantation (HSCT). It is a source of negative consequences for the patient, such as longer hospitalization, oral pain, weight loss, and use of parenteral nutrition (PN).

Objective:
To investigate whether there is differences in weight changes and nutritional status in patients receiving mouth rinse, Caphosol®, in addition to standard oral care (OC) compared to standard OC for HDCT and HSCT.

Method:
A randomized, controlled open study with patients > 16 years, treated with HDCT before HSCT at Akademiska University Hospital, Uppsala, Sweden. Patients randomized 1:1 to standard OC and Caphosol® (EXP, n=20) or standard OC (CTR n = 20). Oral pain, weight loss and days of PN was recorded and analysed from baseline to day 21 post HDCT.

Result:
Caphosol® had no significant impact on weight changes between EXP and CTR groups. OM-pain peaked later in the EXP group than in CTR. No significance in weight change between settings. CTR group had higher use of PN compared to EXP.

Conclusion:
Caphosol® had little effect on frequency, duration and severity of OM and thereby little effect on nutrition and weight. There was no advantage to add Caphosol® to standard OC.

Keywords:
Weight change, nutrition oral, mouth rinse, calcium phosphate solution, hematopoietic stem cell transplantation.
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### ABBREVIATION

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<td>ALL</td>
<td>Acute lymphoid leukemia</td>
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<td>AML</td>
<td>Acute myeloid leukaemia</td>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CLL</td>
<td>Chronic lymphoid leukemia</td>
</tr>
<tr>
<td>CML</td>
<td>Chronic myeloid leukemia</td>
</tr>
<tr>
<td>CMML</td>
<td>Chronic myelomonocytic leukemia</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyrbonucleic acid</td>
</tr>
<tr>
<td>GI</td>
<td>Gastrointestinal tract</td>
</tr>
<tr>
<td>GVHD</td>
<td>Graft versus host diseases</td>
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<tr>
<td>HSCT</td>
<td>Hematopoietic stem cell transplantation</td>
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<tr>
<td>HDCT</td>
<td>High dose chemotherapy</td>
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<tr>
<td>IV</td>
<td>Intravenous</td>
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<tr>
<td>Kcal</td>
<td>Kilocalories</td>
</tr>
<tr>
<td>MDS</td>
<td>Myelodysplastic syndrome</td>
</tr>
<tr>
<td>OC</td>
<td>Oral cryotherapy</td>
</tr>
<tr>
<td>OM</td>
<td>Oral mucositis</td>
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<tr>
<td>PN</td>
<td>Parenteral nutrition</td>
</tr>
<tr>
<td>TBI</td>
<td>Total body irradiation</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual analog scale</td>
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<td>WHO</td>
<td>World Health Organization</td>
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1 INTRODUCTION

1.1 History

A cancer diagnosis is associated with actual risk of dying. Many people recover, but not all. Historically, tumors and their treatment are described in early Chinese and Indian writings. It is also mentioned in the Egyptian papyrus rolls from 2000 BC (Einhorn & Gustavsson-Kadak. 1998).

1.2 Anticancer treatment

Anti-cancer treatment, surgical, chemo- and radiation therapy, are becoming more and more effective, but are also associated with short and long-term side effects (Sonis et al., 2004). Common short term side effects include nausea, vomiting, abnormal smell and taste, diarrhea and/or constipation, infection and oral mucositis (OM) (Hansson, Henriksson & Peterson 1998). OM is an inflammation of the oral mucosa caused by chemo- and/or radio therapy, which causes erythema (redness) and ulcers (Sonis et al., 2004; Tervit & Phillips, 2006; Dickinson & Porter, 2006) and is one of the main complications in non-surgical cancer treatment. It can provide a dose-limiting toxicity when using some chemotherapy drugs, radiation to the head-neck region or radio-chemotherapy in combination (Sonis et al. 2004, Alterio et al. 2007).

Furthermore, cracked lips, difficulty to swallow, bleeding, and xerostomia (subjectively perceived dry mouth) caused by OM, may lead to pain (Tervit & Phillips, 2006) and inability to eat and drink (Orrevall Granberg, 1995). Failure to ingest may lead to malnutrition, which is a deficiency, excess or imbalance of energy and other nutrients (Huhmannn & Cunningham 2005).

1.3 Nutritional status

Optimal nutritional status is prerequisite for good health. Imbalance between intake and output of nutrients affects the nutritional status (Socialstyrelsen [SoS], 2000). Historically, food has been important to humans. It fulfills physical as well as emotional and psychological needs and symbolizes life. In the Old Testament (Gen: 11) mentions what is good for man to eat or not to eat (Bibeln, 1994). Hippocrates (400 BC) thought that lean and restrictive diets always are dangerous in chronic and acute diseases (Vinnars & Hammarqvist, 2004). More than 20 % of the patients in European hospitals are malnourished and more are at risk for malnutrition (Agerberg, 2009). Nutrition interventions need to be highlighted. The sick
individual's nutrition must be considered in the same way as other medical treatment and therefore be included to the same requirements for investigation, diagnosis, treatment plan and monitoring / documentation (SoS, 2000).

According to resolution by Council of Europe (ResAP 2003) all patients, admitted to hospital, should be screened in regard to malnutrition. Patients with signs of malnutrition should be further investigated, nutritional needs be calculated and an individualized nutritional plan established. The nutritional plan should be documented in the patient journal, followed up and reported to receiving care instance (Europarådets resolution, 2003).

1.4 Theoretical framework; The Neuman’s system model

Disease is defined as any condition that impairs body functions (Collin, 2003). Part of health care interventions within public health and health promotion is disease prevention which can be divided into different levels; primary- an intervention before a reaction and/or a disease occurs, secondary- an early detection of a symptom/disease and treatment of a symptom/disease and tertiary prevention- an existing disease and to minimize further deteriorating of that existing disease (Pellmar & Wramner, 2007).

Neuman’s model describes three levels of prevention; primary, secondary and tertiary. Primary prevention is an intervention that takes place before a reaction occurs to maintain well-being. An intervention may start when a risk factor or possible stressor is suspected or identified (Freese & Lawson, 2010; Reed 1995). The goal of secondary prevention is to protect the humans’ primary well-being (Lindell & Olsson, 1993). Tertiary prevention focuses on readjustment toward optimal system stability. It is used to maintain level of well-being after completion of treatment. The intervention is aimed to help the patient to achieve or maintain optimal level of well-being after completion of treatment (Reed, 1995). Primary, secondary, and tertiary prevention are used to achieve, maintain, and preserve a system in balance.

The model has a theoretical structure, a visual illustration, for thoughts about nurses and patients and their relations. The basic idea of the model is a dynamic interaction between the individual and their adaptation to the environment. Key concepts in the model are individual, environment, health and nursing care (Lindell & Olsson, 1993). Stress reactions and systemic response loops are two main mechanisms in the model. Neuman’s system model has a wholistic (mind, body and spirit) approach, which means all aspects of a person are considered. At first is the physiological aspect, which is the body function and structure. Then, the psychological component which is mental processes, and third, socio-cultural.
Further mentions the developmental aspect, which is age and maturity, and finally, the spiritual aspect. All of the aspects interacts with environmental stressors (infection, pain, nausea, fear), both internal and external. Tension-producing stimuli that have possibility to disturb system stability, which result in a positive or negative experience are called stressors (Freese & Lawson, 2010). Nursing must have a preventive nature, i.e. intervene before the disease occurs (Lindell & Olsson, 1993) and the nursing staff's role in the act is helping the patient to achieve or maintain well-being (Freese & Lawson, 2010). Thus, the prophylactic administration of mouth rinse, Caphosol® for HSCT patients, fortifies the flexible line of defense, thereby protecting the normal line of defense from the stressor OM. The normal line of defense includes the human's constant development over time with regard to factors such as intelligence, ability to act, conception of life, and ability to express the problem (Lindell & Olsson, 1993). It is necessary to improve the flexible line of defense through primary prevention strategies, to help a person to maintain well-being by stress prevention through health promotion strategies (Freese & Lawson, 2010; Reed 1995).

2 BACKGROUND

Every human being is derived from only one cell (the fertilized egg), so does the tumor cell. In order to developed into a cancer cell, the cell need to disable a number of adjustable genes through mutations. One of these adjustable genes is the gene for apoptosis. Apoptosis is programmed cell death, which is the built-in ability to weed out the worn out or no longer needed cells i.e.” a suicidal gene”, which the cancer cell doesn’t have (Klein & Friberg, 1998). A tumor can either be malignant or benign. Malignant tumors are capable to send tumor cells to other organs in the body to form a metastasis (Linder & Collins, 1998).

2.1 Anti cancer treatments

Anti cancer treatments can either be surgical, radiation therapy, medical (chemotherapy) or a combination of these.

The purpose of chemotherapy is to destroy the fast growing cancer cell and/or slow down progression of the disease (Hansson, Henriksson & Peterson, 1998; Cancerfonden, 2012). The origin of chemotherapy is a result from research of industrial gases during the period between the two world wars (Hansson et al., 1998). Chemotherapy affects the cells in several ways. One important line of attack is to damage the deoxyribonucleicacid (DNA)-genes in nucleus. Another action is to affect the cells’ transport system and the molecules that are essential to
cells survival. The main result is the same, the death of the cell, i.e. apoptosis (Hansson et al., 1998; Cancerfonden, 2012).
Surgical treatment is the oldest and the most common method to treat solid cancer diseases. It has for a long time been the only option and is still the basic treatment in many solid tumor diseases. The aim of surgical cancer treatment is to remove all cancer cells (Hafström, 1998; Cancerfonden, 2012).
Radiation therapy is a clinical specialist field. Radiation therapy consists of ionizing radiation. Ionization is a generation of electrically charged particles and radiation is the energy transportation. Ionizing radiation gives rise to free radicals in the tissue and cause damage in the genome to cause cell death (Littbrand & Turesson, 1998; Cancerfonden, 2012). Total body irradiation (TBI) is given to some patients prior to hematopoietic stem cell transplantation (HSCT), to eradicate tumor cells, by acting on parts of the body which the chemotherapy will not reach (Cule & Butters 2006).

2.2 Hematopoietic stem cell transplantation (HSCT)
Patients with high-risk myelodysplastic syndromes (MDS), certain types of leukemia and lymphomas, may be treated with high-dose chemotherapy (HDCT) and HSCT. In these cases, the aim is to cure. For patients with multiple myeloma, the purpose is to alleviate and prolong life (Gahrton, Hagberg, Hellström-Lindberg, Kimby & Mellstedt, 1998).
Treatment consists of HDCT, which will eradicate the malignant cells, and when required in combination with total body irradiation (TBI). After HDCT and TBI, an infusion with stem cells, either autologous (uses the patient’s own cells) or allogeneic (from a relative or unknown donor), is given to the patient as an intravenous infusion or injection into a central vein (Hansson et al., 1998). The purpose of HSCT is to replace malignant blood stem cells to restore hematopoiesis (formation of red and white blood cells and platelets) and the immunological function (Gahrton et al., 1998; Richardson & Atkinson, 2006).
A post transplant side effect is graft versus host disease, GVHD, when white blood cells in the graft (the tissue) identify the host (patient) as "foreign" and the transplanted cells then attack the patient’s body cells (Bross et al., 1984).

2.3 Side effects of chemotherapy / TBI
Chemotherapy and radiation therapy exterminates not only the malignant cells, but also affects the healthy cells, hence the side effects. Common dose-limiting side effects of chemotherapy are inflammations in the gastrointestinal (GI) tract, across the continuum of
oral and gastrointestinal mucosa, from the mouth to the anus. Other side effect that may appear from anticancer-treatment is nausea, vomiting, diarrhea, constipation and infection (Hansson et al., 1998). Stem cell transplant recipients are vulnerable to infection during the period of treatment because of neutropenia (reduced immunity) (Hansson et al., 1998; Gahrton et al., 1998). Adverse reactions from anticancer-treatment might lead to reduced efficacy of treatment, treatment delay, and in severe cases even death (Tervit & Phillips, 2006).

2.4 Oral mucositis
The presence of OM may be seen in 90-100% of the HSCT patients (Elting, Cooksley, Chambers & Cantor, 2003; Filicko, Lazarus & Flomenberg, 2003) and 40% of the patients undergoing chemotherapy treatment for malignant diseases (Panahi, et al., 2010). OM is an inflammation of the oral mucosa, which causes erythema (redness) and ulcers. In addition, cracked lips, bleeding, xerostomia (subjectively perceived dry mouth) and difficulty to swallow may be observed (Sonis et al., 2004; Tervit & Phillips, 2006; Dickinson & Porter, 2006). OM is a painful experience which may lead to inability to eat and drink, in turn, a need for intravenous analgesic (morphine drip) and parenteral nutrition (PN) may arise (Stiff, 2001; Sonis et al., 2001). The onset of mucosal injure in OM generally occurs 5-7 days after the start of chemotherapy treatment and continues approximately 7-10 days (Duncan & Grant, 2003) and takes 2-3 weeks to heal (Figure 1).

Figure 1. Stages of OM ref. Sonis et al., 2004
2.5 **Nutritional status**

The nutritional status is the balance between the ingestion of nutrients by the human being and the spending of these in the process of growth, reproduction, and health maintenance. Nutritional status includes clinical examination, current and previous weight, weight loss, and weight change over time, and biochemical analysis (Grodner, Long & DeYong, 2004). A patient’s nutritional status can be affected by OM, as the oral pain linked to the condition often prevents patient from eating solid food, and every so often even from swallowing (Sheean, 2005).

2.6 **Malnutrition, cancer cachexia and its impact**

Malnutrition is defined as a deficiency, excess or imbalance of energy and other nutrients (Grodner et al., 2004; Mercandante, 1996; Abrahamsson, Andersson, Becker & Nilsson, 2008). Various factors have been implicated in the occurrence of malnutrition, but it is multifaceted and unclear. Haematological cancers and its treatment give symptoms such as reduced or loss of appetite and difficulties to eat, caused by the condition of oral cavity and function of the GI-tract. Furthermore, the underlying risk of malnutrition needs to be considered; that is illness or disability, surgery, pain, wounds or drug treatment (Mehmet, 2006).

Reduced intake or absorption of calories may depend on altered diet (hospital stay) or appetite (medical products, for example chemotherapy), reduced gastrointestinal absorption of nutrients due to chemotherapy-induced oral mucositis and stomatitis, hormone-induced metabolic changes, or cytokines (cell local neurotransmitters) released as a result of cancer-related immune activation (Mayenfeldt, 2005). Malnutrition may cause cancer cachexia, a syndrome of progressive weight loss and muscle weakness (Evans et al., 2008; Fearon, 2008), which also includes anorexia, insulin resistance and inflammation (Bozzetti & Mariani, 2009). Cancer cachexia is a life-threatening syndrome present in approximately half of all cancer patients (Bussola et al., 2007), which might cause 20 % mortality (Gordon, Green & Goggin, 2005).

The consequence of malnutrition is an increased risk of infection, impaired wound healing and impaired muscular function. Malnutrition is a significant prognostic factor, an indicator for poor response to treatment and shortened survival (Wilson, 2000; Huhmannn & Cunningham, 2005; Bosaeus, Daneryd & Lundholm, 2002). It also affects the quality of life of patients (Davies, 2005; Bussola et al., 2007).
Maintaining and/or improving nutritional status is essential during the HSCT-treatment. A previous study by Svanberg et al., (2010) to prevent oral mucositis using cryotherapy, i.e. cooling of the oral mucosa with ice chips proved to have positive effect on OM. The positive effect was inter alia milder and shorter period of OM. A similar trend was shown in an unpublished study with a mouth rinse, Caphosol®. The mouth rinse is a supersaturated electrolyte solution, containing calcium phosphate. Calcium promotes tissue repair (Sonis et al., 2004) and phosphate helps maintain dental structure, pH balance and reducing the risk of bacterial overgrowth in the oral cavity (Sonis, 2009). The mouth rinse, Caphosol®, enhanced protection of oral mucosa against OM after treatment with high-dose chemotherapy before HSCT (Papas et al., 2003). The HSCT patients with weight loss has poorer prognosis than weight stable patients (Bozetti et al., 2009). In a well nourished patient, it takes less time for stem cells to find their place in the marrow, to begin producing new blood stem cells, compared to a malnourished (Muscaritol et al., 2002) It would be of interest to investigate if it would be possible to prevent OM and hereby maintain weight and nutritional status in HSCT patients.

3 AIM
The aim of the present study was to evaluate whether the development of mucositis severity has an impact on the discrepancy in weight change and nutritional status in patients receiving mouth rinse, Caphosol® in addition to standard treatment in comparison to the standard treatment during treatment with HDCT and HSCT.

4 METHOD
4.1 Design
The study was a randomized, controlled, open study (the intervention was known among both patients and nursing staff). Patients were randomized to standard treatment or standard treatment and Caphosol® during HDCT medication and HSCT.

4.2 Inclusion criteria
Qualified to participate in the study were patients >16 years of age with hematological/oncological disease, able to communicate in Swedish, scheduled for HSCT, at Akademiska University Hospital in Uppsala. Participation was voluntary and might end at any
time without explanation. Patients who decided to participate gave their written consent and were randomly assigned to the EXP or the CTR group.

4.3 Sample

Fifty-two patients were asked to participate in the study and 40 gave their consent. The patients were randomized into two groups: EXP (n = 20) and CTR (n = 20). No significant difference was found regarding gender or age nor diagnoses and treatment between the EXP and CTR groups (Table 1).

![Table 1](image)

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>EXP (n=20)</th>
<th>CTR (n=20)</th>
<th>TOTAL</th>
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<tr>
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<td>9</td>
<td>8</td>
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<tr>
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<td>49.6 (21-65)</td>
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<tr>
<td>AML</td>
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<td>8</td>
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</tr>
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<td>ALL</td>
<td>4</td>
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</tr>
<tr>
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<td>RICT</td>
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4.4 Procedure

The study was performed at the hematology ward, Uppsala University Hospital, Sweden during the period September 2010 to December 2011.

The patients received written information (Appendix 1) and were informed verbally about the randomized, controlled, open intervention study and its confidentiality as the basis of decision about to participate or not. The day after admitted to the ward, but before the start of chemotherapy treatment, a written consent (Appendix 2) or decline to participate was
collected by the research nurse or the nurse in charge. The participant was able to renounce participation at any time without having to give any reasons.

Randomization was performed by a non-patient responsible nurse by drawing of pre-marked cards. Patients were coded with a number and the code list was kept by the research nurse in a locked room. CTR-group received clinic standard oral care, which includes cryotherapy (cooling the oral mucosa by sucking on ice-chips) during chemotherapy infusion. EXP - group received cryotherapy and in addition, Caphosol®, oral rinse, 30 ml, four times a day, starting at the initiation of chemotherapy (day 0) and ended 21 days after start of chemotherapy. All patients cared for oral hygiene according to ward's routine of oral care.

4.4.1 Oral care
Before start of high-dose chemotherapy, the patient was examined by a dentist to rule out dental problem. During hospitalization the patient cared for her/his oral hygiene by brushing teeth with extra-soft toothbrush, which was changed daily and special mild toothpaste (toothpaste with effective protection against harmful bacteria). The patient was instructed to rinse the mouth two to three times per day with water or sodium chloride. Patients should not use dental floss or toothpicks. Nursing Staff assisted with oral care as needed and hygienist / dentist was consulted as required.

4.4.2 Instrument
Visual analog scale (VAS) was used to record oral pain. It is a one-to-eleven-point scale describing pain from zero to ten, where zero is no pain and ten is unbearable pain (Figure 2) (Wewers & Lowe, 1990).

![Figure 2. VAS-scale.](Wagner, Hospital for special surgery (2009))
The World Health Organization scale was used to measure the degree of oral mucositis (OM) (Figure 3). It is a five-point scale which describes the severity of blisters and ulceration of the oral mucosa. The scale range from zero; no oral problems to four; severe blistering and ulcers of the oral mucosa, when only the tablets is possible to be swallowed, otherwise nothing else per os (by mouth) (Bellm, 2000; Sonis et al., 2004).

**Figure 3. The World Health Organization (WHO) scale.**

**4.4.3 Measurement**

The patients’ height, weight and BMI was measured and calculated at admission and discharge. During treatment, daily weight on patient-bound scale was performed according to routine at the ward. Dietary registration (Appendix 1) was recorded twice a week as routine (or daily on medical indication) and plotted as graphs in nutritional monitoring form (Appendix 2). The effect of the intervention versus standard was monitored daily, measuring oral pain by using VAS-scale and WHO-scale to estimate OM. The measurements were recorded in medical record.

Information used in the present study regarding days with parenteral nutrition (PN), height, weight, body mass index (BMI= kg/m²), Visual Analog Scale (VAS) and World Health Organization (WHO) scale was collected from the patient’s medical record.

**4.5 Data analysis**

The analysis was made on an intention-to-treat basis. Data used in the intervention study, collected from medical records were analyzed, using the statistic program Statistical Package for the Social Sciences (SPSS). The statistical analyzes which were used was the independent t-test, differences between groups, weight change, BMI and use of PN. Chi² test was used to
see correlation in nutrition consumption between the groups, and VAS versus WHO (Djurfeldt, Larsson & Star Hagen, 2008). A $p < 0.05$ was regarded as statistically significant. Data was presented in tables and graphs made in Microsoft Office Excel 2007.

### 4.6 Ethical considerations

Participation in the study was voluntary and based on the autonomy principle of informed consent. The patient made the decision to participate in the study with full knowledge and without the influence of others' interests (Malmsten, 2007).

Data were treated according to The Personal Data Act (Personuppgiftlagen [PuL], 1998:204). Act (Svensk författningssamling [SFS] 2003:460) concerning the ethical review of research involving humans. It concludes that the review must be made if a study involves sensitive personal data, physical intervention in the research person, interventions that intend to damage the person physically or mentally, research of biological material or interference deceased person.

Mouth rinse, Caphosol®, is a medical device and was used in addition to the wards standard oral care in HSCT and all patients who participated in the study received a currently evidence-based adequate treatment for OM.

Ethical permission for the study was obtained, reference number 2010/134 (Appendix 5) and a written permission was obtained from the clinic's director (Appendix 6).

### 5 RESULT

#### 5.1 Weight change

There was no significance in weight change (Independent t-test) between the settings (mean 6.45 %). In CTR lost three patients (patient 3, 5 and 14) more than 10 % of their bodyweight (Figure 1). The first patient, a male, had nausea, mucositis and constipation due to opioid infusion. The second case, a female, had GVHD in the intestines, which lead to malabsorption and weight loss. The last patient, also a female, had weight loss due to diarrhoea and nausea, and therefore low calorie intake and calorie absorption. A patient in the EXP, a female who lost 13 % of the body weight, even though she reached the calories she needed. The other patient in EXP, a male, who lost ten percent of body weight, also had GVHD in the intestines.
5.2 Calories needed

Both groups needed approximately the same amount of calories at start of the treatment (EXP mean 1840 kcal compared to 1880 in CTR group) (figure 2). The EXP has a large calorie intake at start of the treatment, and then drops to approximately the same level as CTR, and both groups follow each other with a lower calorie intake than needed throughout the intervention (baseline -21 days); however the CTR has a slightly lower calorie intake than EXP-group (measuring points 2-7 in figure 1). BMI didn’t show any differences between the groups, BMI at admission was 25 in EXP group and 24 in CTR, and at discharge 24 and 23 respectively (Independent t-test).
5.3 Nutrition

The Chi²-test showed no difference in PN use between the groups; however there was an additional half day-dose of PN used in the CTR than EXP-group. The mean PN-use in EXP-group was 9.05 compared to 9.55 in CTR.

Figure 3 exemplify the distribution of day-doses of PN among the patients and the groups. Patient 3, 4 and 8 did not fulfill the project and are noted as one day doses PN each in the figure. PN use is strikingly higher at patient number five, otherwise is the PN-use similar (figure 3).

![Total Use PN](image)

Figure 3 exemplify how the day-doses of PN are spread among the patients and the groups.

Totally, there were no differences between the groups in PN use, but the CTR group had a higher use of PN alone compared to EXP group which used more use of mixed nutrition (PO plus PN and PN)(figure 4).
5.4 Mucositis and pain

Oral mucositis (WHO-score) had a later onset in EXP compared to CTR group. OM-pain (VAS-score) started later in the EXP than in CTR group. The EXP group had a higher VAS-score at the end of the period (day 19) than CTR group (Figure 5).

Figure 5. *Days during intervention 1=day 0, 2=day 5, 3=day 8, 4=day 9, 5=day 10, 6=day 11, 7=day 12, 8=day 13, 9=day 14, 10= day 16, 11=day 19, 12=day 21.
6 DISCUSSION

6.1 Result discussion

Svanberg et al. (2007, 2010) previously showed a significant effect of OC on the severity of OM, the use of opioids and PN and on nutritional status in this group of patients. In efforts to further alleviate oral mucositis, a combination of various means may be of significance. The main result of the present study did not show that Caphosol® had any significant effect on OM, nutritional status or weight reduction, although a tendency was notified as a reduction of PN use in EXP compared to CTR group. Despite the negative result there was a small tendency in benefit for the Caphosol® group concerning oral pain VAS-grading and mucositis score. That is in line with Papas et al (2003) who showed in a study that patients treated with HCT in connection with HCST and the use of Caphosol® mouth rinse had fewer days of mucositis, lower grade of ulceration, and fewer days of oral pain.

In the present study the majorities of HCST patients had a good nutritional status at start of treatment, BMI of 24 in CTR and 25 in EXP group, and a satisfactory calorie intake at baseline, but the calorie intake deteriorates during the treatment, which is in line with a study by Bozetti & Mariani (2009). Due to low calorie intake and reduced physical activity, not only viceran and lean body mass reduces, but also muscles atrophy (shrink) ocures (Itano & Taoka1998). This progressive weight reduction may lead to cancer cachexia (Evans et al.; 2008, Feron, 2008) which is a life threatening syndrome and present in half of all cancer patients (Bussola et al., 2007). It is of great importance to prevent weight reduction in this patient category due to malnutrition and cachexia which often occur and are indicators of poor prognosis and, per se, accountable for excess morbidity and mortality (Bozzetti et al. 2009). Neuman’s model highlights the importance to start an intervention (primary prevention) when a risk factor or possible stressor is suspected or identified (Freese & Lawson, 2010; Reed 1995), in this case a potential weight reduction.

The result in this study (Figure 1.) illustrates the individual weight changes and shows the peeks of weight for the individual (mean weight reduction in both groups was 6, 45 %). The weight change was expected as a side effect of HSCT treatment, nausea, mucositis, and constipation due to opioid infusion and GVHD in the intestines. The reason for weight loss and change in nutritional status among these patients was reduced ingestion or absorption of calories as a consequence of the side effects. OM is well known to interfere with eating, chewing and swallowing which might necessitate PN (Feldman & Dixon, 2000). Other reasons might be a change in diet or appetite, reduced gastrointestinal (GI) absorption,
hormone induced metabolic changes or cytokines released caused by cancer related immune activation (Mayenfeldt 2005). In the present study, several patients in both groups were able to eat and/or drink, but insufficient intake and therefore received PN as a complement to maintain satisfactory calorie intake. The CTR group used more PN as only nutrition than EXP group. In the EXP group three patients didn’t use PN at all compared to four in the CTR. The reason could be that Caphosol® has had some influence on OM and therefore could the patient eat. Related finding was seen in a Caphosol- study from Markiewizs at al. (2012), where none of the EXP-patients used PN during HSCT-treatment.

In this study, oral mucositis (WHO- score) had a later first appearance in EXP group compared to CTR. The WHO scale mixes both functional outcomes (capability to eat) with objective mucosal alteration (ulceration and redness) in order to measure the score. The inspection of the oral cavity was carried out by the nurse of the day, which meant the evaluation could have been interpreted in a personal way and the evaluation of the oral cavity would differ from day to day, although there was WHO- template to follow. Same with the functional outcome, if the patient expresses a negative capability to eat, the nurse might out of “convenience” start PN.

EXP group had a higher VAS-score at the end of the period (day 19), however the CTR had an overall higher scoring, which was in line with a pilot study from McGuire et al. (1998). Comparable findings was seen in a study from Vera-Llonch et al.(2007) where the worst OM grade was positively linked with the total days of oral ulceration. The VAS scores fell accordingly to pain intensity due to the OM.

The incidence and severity of HSCT regimen-induced OM remains a big and important unmet need in the management of patients with hematoloy maligancies. Not only does mucositis cause great symptomatic suffering, it also predisposes to systemic and local infection and has a marked effect on a number of healthcare outcomes. Reduction of the symptomatic suffering of treatment for the HSCT-patients can also be called secondary prevention, which is described in Neuman’s model, as the protection of the humans’ primary well-being (Lindell & Olsson, 1993).

There are guidelines to support the intervention of well-being; among others are the national guidelines (SoS, 2000). One of these guidelines express nutrition interventions; Nutrition need to be highlighted, which mean the sick individual's nutrition must be thought of the same way as other medical treatment and therefore be included to the same obligation for examination, diagnosis, treatment plan and monitoring / documentation. The obligation for nursing in HSCT patient is to help the patient to be able to achieve as good wellbeing as possible in the
situation the patient is in, which in this case is to minimize problems due to OM. To predict future problems such as OM, low nutritional intake, through available preventive methods (Caphosol, cryotherapy), and if a problem occurs (OM, low nutritional intake) assist the patient with relief (analgesia, nutritional support). The pain connected with OM can stop patients from eating, drinking, or taking oral medications and lead to malnutrition. The result of malnutrition is an increased risk of infection, impaired wound healing and reduced muscular function, as well as a significant predictive factor, a marker for poor response to remedy and shortened survival (Wilson, 2000; Huhmannn & Cunningham, 2005; Bosaeus, Daneryd & Lundholm, 2002). It also affects the patients’ quality of life (Davies, 2005; Bussola et al., 2007). If any of the factors occurs, a tertiary prevention may be used as Neuman describes. The tertiary prevention intervention is intended to help the patient to restore or preserve optimal level of well-being after completion of HSCT-treatment (Reed, 1995).

6.2 Method discussion

Fifty-two patients were asked to participate in the study and 40 gave their consent. Twelve patients withdrew of unknown reason. Patients were randomized into two groups, with 20 participants in each group (Table 1). Three patients did not fulfill the intervention. They used Caphosol® between 0 and 60 hour and withdrew from using the medical devise because of nausea, smell and taste. They were all men and all developed severe mucositis with need of intravenous opioids.

The study was a small (n=40), randomized, controlled, open intervention study. It was neither blinded nor placebo. It is difficult to reach significance with few numbers of participants, but a trend may be observed. To see an effect of, or analyze the method of procedure, and discover relationships between variable, a larger selection of participants is needed (Polit & Beck, 2008).

Randomization often includes a homogeneous group. In order to increase the control of randomized studies, several repeated studies need to be done in order to achieve generalised results. There is always a risk that processing error can arise from the collected material. A problem could be whether the author of the study interprets the result out of expectation to the intervention. To reach the best result of a study, it needs to be both blinded and randomised. (Polit & Beck, 2008).

Weaknesses and threats to internal validity in this study are because it is an open study, which means that all those involved in the study knows who gets the intervention or not.
Furthermore, the study was conducted over a relatively long period of time, 16 months, with a lot of staff involved and new employee in intervention. The more persons involved the higher risk that error may occur (Polit & Beck, 2008).

In addition, the measuring instrument can be interpreted differently from person to person, despite the fact that there are guidelines to follow, and pictures of the different stages of OM. WHO-scores verified strong correlations with the symptoms and therefore have a good reability and validity (Sonis et al. 1999).

Pain is a subjective experience and does not always match up to the degree of tissue damage (Werner & Strang, 2003). VAS is a one-dimensional instrument which should not be used alone within pain-assessment and is sensitive to pharmacological and non-pharmacological interventions that affect pain experience. The instrument is effective to visualize and document pain, as well as daily variations and therapeutic effects. (Werner & Strang, 2003; Price, et al. 1983). Absolute VAS value should not direct pain treatment, but it is the patients that determine if the analgesia is sufficient (Werner & Strang, 2003).

Weight measurement and BMI has restrictions, and should be taken into consideration when nutrition status is evaluated. BMI: s breaking points are arbitrary and based on young, healthy male adult and are probably not appropriate for patients with cancer due to the effect of the disease. Estimation and calculation of weight change over time may be a better indicator on nutritional status. A rapid weight drop points to a more severe malnutrition (Ottery, 1995; Nitenberg & Raynard, 2000).

6.3 Primary prevention and Neuman’s model

Neuman’s model sees the human as a whole which is in continuously, energetic interaction with the surroundings. Prevention is the most important nursing intervention to reach a balance and stability in a system. Nursing staff identifies a risk factor/stressor; in this study the risk of getting OM, primary prevention was to initiate the use of mouth rinse to maintaining system stability. Secondary prevention applies whenever a stress reaction occurs and the normal level of well-being was disturbed with other identifiable external symptoms, which in this study was to treat existing symptoms in the oral cavity, minimizing the effect of OM and thereby reducing risk of weight loss.
6.4 Practical clinical significance

Promotion of health care has a responsibility to provide information on methods to prevent illness and injury (aim 6, Folkhälsoinstitutet (FHI), 2012); in this case the injury of OM and initiation of mouth rinse as a primary prevention.

Impaired nutritional status is a consequence of the oral side effects of HSCT, thus malnutrition (Meyenfeldt, 2005), which may cause measurable adverse effect on the body and its function. By improving the patient's nutritional status through reducing chemotherapy side effects of OM by means like oral mouth rinse (Caphosol®) (Markiewicz et al.,2012) or cryotherapy (Svanberg 2010), and thereby enhance immune function, survival and quality of life for the patient (Davies, 2005, Horsley et al 2005). Early interventions may be beneficial to the patient and for health care by reducing complications and shorter hospital stay (Davies, 2005; Bussola, 2007, Horsley et al 2005), which has been seen in previous studies to prevent oral mucositis by using cryotherapy, i.e. cooling of the oral mucosa have been performed at the Haematology ward, 50 C, at Uppsala University Hospital. Oral cryotherapy (OC) proved to have positive effect on OM; less days in hospital, reduction in need of PN parenteral (intravenous) nutrition and better nutritional status among HSCT patients (Svanberg, Öhrn & Birgegård, 2010). Cryotherapy is now included as standard treatment at the haematology ward at Uppsala University Hospital, Sweden.

6.5 Proposal for further studies

In order to investigate if Caphosol® mouth rinse in addition to oral cryotherapy had an impact on OM and hereby nutrition and weight, it is desirable to do a larger, multicenter study were more participants are included during the hospitalization period, to be able to reach significance. It would be of interested to investigate why some patient get no or little OM, what is keeping their oral mucosa in better shape than others; “the healthy factors “and if a poorer nutritional status at start of HDCT has an impact on OM, weight loss and treatment outcome.

7 CONCLUSION

Caphosol® mouth rinse seems to have little influence on duration and severity of OM during chemotherapy in HSCT, thereby little effect on nutrition and weight. No advantage to add Caphosol® to oral standard care was seen.
Nursing must be proactive instead of reactive; a preventive nature, i.e. get involved before a problem occurs. The nursing staff’s role in the act is helping the patient to prevent weight loss and to keep nutritional status by using best known practice and evidence based care.
8 REFERENCES


Horsley, P., Bauer, J. & Gallagher, B. (2005). Poor nutritional status prior to peripheral blood stem cell transplantation is associated with increased length of hospital stay. Bone Marrow Transplantation, 35, 1113-1116.


