mucosamin

Sodium hyaluronate + amino acids
glycine, L-proline, L-leucine and L-lysine HCl

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Contents

Mucositis

Definition

Mucositis is a condition characterised by pain, inflammation and ulceration of the body's mucous membrane.[1]

Mucositis occurs when cancer treatments break down the rapidly dividing epithelial cells lining the gastro-intestinal tract (which goes from the mouth to the anus), leaving the mucosal tissue open to ulceration and infection. Mucosal tissue, also known as mucosa or the mucous membrane, lines all body passages that communicate with the air, such as the respiratory and alimentary tracts, and have cells and associated glands that secrete mucus. The part of this lining that covers the mouth, called the oral mucosa, is one of the most sensitive parts of the body and is particularly vulnerable to insult and injury by chemotherapy and radiotherapy; the oral cavity is therefore the most common location for mucositis.[2]

Oral mucositis (OM) is probably the most common, debilitating complication of cancer treatments, particularly chemotherapy and radiotherapy. It can lead to several problems, including pain, nutritional problems through an inability to eat, and increased risk of infection due to open sores in the mucosa. It has a significant negative effect on patients' quality of life and can be dose-limiting (i.e., requiring a reduction in subsequent chemotherapy doses).[2]

For patients with pelvic cancers, targeted radiotherapy can often lead to damage of the vaginal mucosa, known as vulvovaginitis (vaginal mucositis). It can lead to ulceration, pain, dryness and bleeding, often causing considerable discomfort for patients and impacting on their day to day lives.

Similarly, radiotherapy to the pelvic region can result in damage to the rectal mucosa, causing what is known as proctitis (rectal mucositis). This can lead to burning pain sensations, abdominal cramping, tenesmus, urgency, bleeding, diarrhoea and incontinence, which can all have a significant impact on patients' quality of life and daily activities.

Prevalence

It is estimated that around 40% of people receiving chemotherapy will develop some degree of mucositis.[3] OM is seen in 80% of patients receiving very high dose chemotherapy in advance of haematopoietic stem cell transplant (HSCT) (bone marrow transplant).[4]

It is further estimated that up to 97% of people who have radiotherapy for head and neck cancer will develop some form of mucositis, which can include OM.[3]

Up to 90% of paediatric oncology patients may suffer from cancer treatment-induced oral complications.[5]

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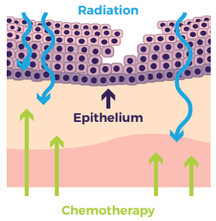
Multiple mechanism model for the development of mucositis

Initiation

The administration of radiation therapy or chemotherapy stimulates the early release of cytokines, thus triggering an acute inflammatory response.[6]

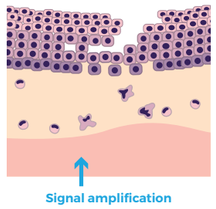


Primary Damage Response

Free radicals cause direct cell death and activate additional secondary messengers that transmit signals from receptors on the cellular surface to the inside of the cell.[7,8]

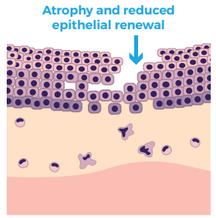
Mitosis of the basal cell layer in the mucosal epithelium is inhibited.[8]

This leads to upregulation of pro-inflammatory cytokines, tissue injury, and apoptosis.[7,8]



Signal Amplification

Upregulation of pro-inflammatory cytokines, produced mainly by macrophages, causes injury to mucosal cells, also activating molecular pathways that amplify mucosal injury.[7]

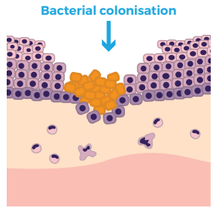


Ulceration

During the ulceration stage, mucosal integrity is broken and nerve endings are exposed, leading to severe pain.

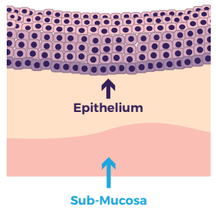
The colonisation of the ulcerated surface by microflora results in the release of toxins into the tissues and subsequent release of further cytokines, causing more tissue damage and leading to a reduction in the number of neutrophils.

The ulcerative stage is considered to be the most symptomatic.[6]



Healing

This phase is characterised by the restoration of the integrity of the epithelium through cellular and tissue differentiation.[7]



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Oral mucositis (OM)

OM is an acute inflammatory and ulcerative complication of the mucosal membrane that commonly occurs during cancer therapy.[9]

- The primary morbidity of OM is the intense pain, which is usually associated with ulcerative lesions.[4] It can also cause dysphagia and impairment of the ability to talk, eat and swallow.[10]
- The inflammation in OM can range from erythema to severe ulceration, and is typically associated with pain and discomfort.[11]
- OM can cause profound psychological distress and impairment of quality of life for cancer patients[9] due to pain and inability to eat solid foods.[6] This can lead to the use of nasogastric tube placement or total parenteral nutrition use.
- OM is one of the more significant side-effects of cancer treatment and can result from systemic chemotherapy, radiation therapy, or a combination of the two.[4]
- The oral mucosa is made up of epithelial cells that regenerate every 7-14 days, making them easily damaged by chemotherapy and radiation therapy. When unable to regenerate, the oral mucosa becomes thinner and ulceration can occur, allowing pathogens entry into the body.[12]
- Chemotherapy-induced OM is regarded as an acute condition, with ulceration normally occurring 1-2 weeks after first treatment, and resolving within 3 weeks of treatment.[13][14] Radiotherapy-induced OM normally occurs around 2 weeks into a 7-week treatment cycle, and resolves 3-4 weeks after treatment has ended.[14][15]
- Cancer therapy induced-OM can have a significant economic impact due to increased healthcare costs such as hospitalisation and anti-infective treatment.[11]

Signs and symptoms of OM include: [2]

- Red, shiny, or swollen mouth and gums
- Blood in the mouth
- Sores in the mouth or on the gums or tongue
- Soreness or pain in the mouth or throat
- Difficulty swallowing or talking
- Feeling of dryness, mild burning, or pain when eating food
- Soft, whitish patches or pus, in the mouth or on the tongue
- Increased mucus production or thicker saliva in the mouth

An extreme case of the condition is called confluent mucositis. In its worst form, the mucous membrane of the patient's entire mouth and tongue can be covered in a white mucus coating up to a millimetre thick. The combination of mucus, excess saliva and pain can make it difficult or even impossible to eat.

Pathogenesis of OM

Historically, it was thought that OM resulted simply from the indiscriminate destruction of rapidly dividing basal epithelial stem cells by chemotherapy or radiotherapy.[15] It is now understood that the pathogenesis is more complex and multifactorial, with a five phase model being the currently accepted explanation for the sequence of events underlying the condition.[8,9,14,15] It is important to note that these events are not wholly linear and often occur simultaneously.[16]

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Factors that increase the likelihood of developing OM[2]

Patients with compromised oral mucous membranes secondary to alcoholism and/or excessive smoking exhibit the most severe mucosal lesions.

Factors that can increase the likelihood of developing mucositis, or that can make it worse if it does occur, include:

- Poor oral hygiene and pre-existing mouth damage
- Smoking or chewing tobacco and drinking alcohol
- Gender (females appear to be more likely than males to develop OM)
- Dehydration
- Low body mass index
- Previous cancer treatment
- Impaired immune status (e.g. diabetes, HIV/AIDS)
- Younger patients tend to be more likely to develop OM than older patients. This appears to be due to the more rapid rate of basal cell turnover noted in children.

Aetiology of OM[2,13]

When caused by chemotherapy, OM is usually due to the low white blood cell count. When caused by radiotherapy, OM is usually due to the necrotic and inflammatory effect of ionising radiation on oral mucosa.

All chemotherapy drugs have the potential to cause OM. Treatments most commonly associated with OM include:

- Anti-metabolites (e.g. fluorouracil, capecitabine, methotrexate)
- Anthracyclines (e.g. epirubicin, doxorubicin)
- All lymphoma or leukaemia patients who have recently had treatment
- Tyrosine kinase inhibitors (such as sunitinib, pazopanib, afantinib) and everolimus
- Radiotherapy to the head and neck region

Measuring the severity of OM[3,17]

OM is usually diagnosed with a description of symptoms and a physical examination. Diagnosis is based on the clinical appearance, location, timing of oral lesions, and use of certain types of therapy known to be associated with OM.

Patients receiving high-dose chemotherapy or radiotherapy will commonly receive regular assessments for mucositis until their risk of developing the condition has passed.

Healthcare professionals use a grading system to determine how serious the symptoms of OM are. There are several grading systems available, including systems presented by the World Health Organisation Oral Toxicity Scale (WHO OTS).

Grade 0	No change
Grade 1	Soreness/erythema
Grade 2	Erythema, ulcers; can eat solids
Grade 3	Ulcers; requires liquid diet only
Grade 4	Alimentation not possible

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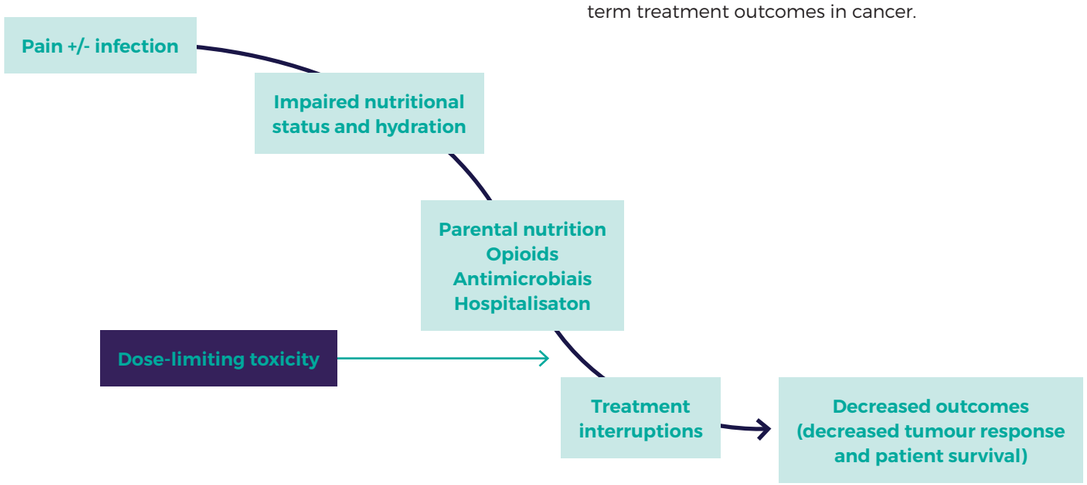
Current guidelines for treating grade 3-4 oral mucositis[18]

- Saline mouthwashes and ice cubes
- Caphosol and other mucosal protectants
- Anti-infective prophylaxis
- Palifermin
- Low-level laser therapy
- Prophylactic insertion of enteral feeding tube
- Referral to the dietitian

What are the implications of Oral Mucositis on the patient experience?[2]

- Oral Mucositis can have a severe impact on patients' Quality of Life and treatment outcomes and can necessitate dose reductions.
- Mucositis induced pain is generally acute in nature, and reaches a peak at 7-8 days after treatment starts. Pain has been reported to be a significant factor in decreased quality of life among cancer patients.
- Oral pain and difficulties in swallowing can lead to problems eating, which in turn can lead to nutritional impairment. In some instances, naso-gastric tube feeding may be necessary.
- Patients with damaged mucosa have an open portal of entry for micro-organisms. In addition, reduced immunity from chemotherapy and radiotherapy makes them more prone to opportunistic infections in the mouth, such as fungal and herpes infections.
- A reduction in chemotherapy dose on the next cycle has been reported to be twice as likely in patients who experience mucositis. This is reported as frequently in grades 1-2 oral mucositis as it is in grade 3 or 4. If cancer treatment doses are decreased, their effectiveness may be limited. Therefore, Oral Mucositis may be associated with overall worsening of long-term treatment outcomes in cancer.



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Vulvovaginitis (vaginal mucositis)

The vaginal mucosa

The vagina is an elastic, muscular canal with a soft, flexible lining that provides lubrication and sensation, and connects the external vagina. The vulva and labia form the entrance, and the cervix of the uterus protrudes into the vagina, forming the interior end.[19]

The vaginal wall consists of three layers:

1. An inner mucous type stratified squamous cell epithelium supported by a thick lamina propria that undergoes hormone-related cyclical changes
2. The muscularis composed of outer longitudinal smooth muscle fibres and inner circular fibres
3. An outer fibrous layer, rich in collagen and elastin, which provides structural support to the vagina[20]

Effect of chemotherapy on the vagina

Chemotherapy can damage the vaginal tissue, which can lead to ulcerations or disruption in the integrity of the mucosa, and increase the risk of infection.[21] Chemotherapy drugs that may cause mucositis can also cause vaginal irritation.[22]

Effect of radiotherapy on the vagina

The vaginal and vulval epithelium are highly sensitive to the effects of pelvic irradiation or pelvic radiotherapy due to rapid cell- turnover.[23]

Radiotherapy to the pelvic region can damage vaginal epithelium, connective tissues and small blood vessels, causing inflammation and cell death prior to resolution. The subsequent reduced blood supply, tissue hypoxia, loss of elastin and collagen deposition leads to thinning of the vaginal mucosa, loss of lubrication, scarring and fibrosis.[24]

Acute effects of pelvic radiation in women

Following pelvic radiation, acute radiation effects include vaginal erythema, moist desquamation and a confluent mucositis. The mucosa may demonstrate severe congestion and submucosal haemorrhage.[23]

Radiation damage to the vaginal mucosa can cause inflammation, leading to pain. In addition, the damaged mucosa may lead to reduced vaginal secretions, causing vaginal dryness and itching.[25]

Significant vaginal, vulval and perineal changes may arise after radiotherapy and cause considerable pain during all phases of sexual interaction in the first months following radiotherapy. The acute effects of pelvic radiotherapy on the vagina may last for 2-3 months following radiotherapy.[23]

Prevalence of vulvovaginitis

Vaginal morbidity and sexual functioning was assessed in a subset of patients[23] (75 patients out of 252) who had post-operative brachytherapy (N=32) or external beam radiation and brachytherapy (N=43). The overall incidence of vaginal stenosis was 54.7% of which most (75%) were confined to the upper third part of the vagina. In addition, vaginal vault scarring was found in 63%, vaginal adhesions in 53%, teleangiectasia in 60%, and mucosal atrophy in 61% with no difference between those who had additional external beam radiation besides brachytherapy.

In a study evaluating the efficacy of cisplatin-based concurrent chemoradiation in squamous cell carcinoma of cervix and the frequency of acute toxicity (n=72),[26] 43% patients were reported to suffer from vaginal mucositis.

When twenty consecutive patients were irradiated with brachytherapy of vaginal intraepithelial neoplasia,[27] mucositis grades 2-3 were reported in 6 (30%) patients.

Current UK guidelines for the acute effects of pelvic radiotherapy

Many current guidelines focus on the treatment of the long term effects of pelvic radiotherapy. However, Macmillan Cancer Support recommends that all women offered pelvic radiotherapy for a gynaecological cancer should receive information on the potential side effects of treatment, including the potential for ovarian or uterine damage caused by pelvic radiotherapy.[28]

There are no specific guidelines for the management of the acute effects of pelvic radiotherapy.

Proctitis (rectal mucositis)

Effect of radiotherapy on the gastrointestinal (GI) tract

The colon and rectum are commonly affected by abdominal and pelvic radiotherapy, because of their anatomical locations within the radiation field of various pelvic cancers.[43] The direct effects of radiation on the bowel mucosa can cause almost every patient to have some manifestation of acute radiation-induced injury of the GI tract in the form of burning pain sensations, abdominal cramping, tenesmus, urgency, bleeding, diarrhoea and incontinence.[44]

Injury to the GI tract due to radiotherapy depends on the type of radiotherapy given, the dose delivered to tissues, the way it is delivered, and how radiation energy dissipates through tissue.[45] Radiation injury of the rectum is attributed to the direct mucosal damage from radiation exposure characterised by inflammation or cell death.[46]

During external beam radiotherapy, ionising radiation enters and exits the body and therefore affects normal tissues surrounding the target tumour.[43]

Radiotherapy initially causes mucosal changes characterised by inflammation or cell death, but subsequently persistent cytokine activation in the submucosa leads to chronic effects such as progressive ischaemia, fibrosis and loss of stem cells. These ischaemic and fibrotic changes potentially cause chronic impairment of GI physiological functions.[47]

Acute changes in GI physiology can occur in any part of the GI tract that is exposed to radiotherapy, leading to clinical or subclinical symptoms.

Acute radiation proctitis

Radiation proctitis is radiation-induced rectal mucositis. It is defined as an inflammatory process of the rectal mucosa that occurs almost immediately, or up to 3 months after the onset of radiotherapy. Symptoms of acute radiation proctitis include burning pain sensations, diarrhoea, nausea, cramps, tenesmus, urgency, mucous discharge and minor bleeding.[48]

Acute radiation proctitis appears oedematous, beefy red, and may have ulceration or sloughing. Microscopically, there is a loss or distortion of the microvillus architecture with hyperaemia, oedema and ulceration. Colonoscopic biopsy of the inflammatory rectal mucosa is not usually recommended due to the increased risk of bleeding and fistula formation.[48]

Acute radiation proctitis is caused by the death of rectal mucosal cells and is confined to the lower 25cm of the large intestine.[49]

Effect of chemotherapy on the GI tract

Cytotoxic chemotherapy agents have a direct effect on the GI mucosa, exerting chemotherapeutic damage to the epithelium, causing inflammation, oedema, ulceration and atrophy.[47][50] Chemotherapy can cause small bowel bacterial overgrowth, bile acid malabsorption and pancreatic insufficiency, leading to chemotherapy-induced GI symptoms. In addition, patients may experience ongoing chronic GI problems with constipation, diarrhoea, flatulence, bloating and pain.[47]

The degree of damage to the mucosa, submucosa and GI stem cells may play a role in the development of chronic problems. In addition, chemotherapy increases the sensitivity of non-cancerous tissues to damage from radiotherapy.[47]

Risk factors for GI radiation injury

Risk factors for GI radiation injury include:

- Radiation techniques: Treatment volume, total dose, fractionation dose and schedules[43]
- Radiation dose is a major determinant of the severity of acute and late normal tissue toxicity[43]
- Radiation dose per fraction and altered fractionation schedules are important factors linked to increased risk of intestinal radiation toxicity[43]
- Treatment field size and intestinal volume irradiated are important factors and a key determinant of radiation toxicity[43]
- Combined modality therapies: Surgery or concurrent chemotherapy[43]
- Surgery could lead to an increased risk of radiation toxicity due to anatomical changes that increase intestinal exposure to radiation[43]
- Combining chemotherapy with radiation has been reported to increase the rate of acute intestinal toxicity[43]
- Medical co-morbidities: Vascular disease, connective tissue disease, inflammatory bowel disease, HIV[43]
- Genetic susceptibility: Single nucleotide polymorphism, ataxia, telangiectasia[43]

Prevalence of GI symptoms and radiation enteritis following cancer treatment

In terms of acute radiation enteritis, almost all patients will experience signs and symptoms.[51]

GI symptoms are the most common of all the chronic physical side effects of cancer treatment and have the greatest impact on quality of life. Yet, the prevalence of GI side effects following cancer treatment is reported to be underestimated.[47]

In 2013, Macmillan Cancer Support estimated that 90,000 people were living with chronic changes in lower GI function following treatment of pelvic cancers.[52] In a UK study, chronic radiation enteritis was reported in up to 20% of patients receiving pelvic radiotherapy.[53] As cancer incidence continues to increase[54] it can be assumed that the number of people affected by GI consequences of cancer and its treatment will also increase.

The prevalence of GI symptoms following chemotherapy is less well reported than the prevalence of GI symptoms induced by pelvic radiotherapy. Some patients will not report GI symptoms, largely due to embarrassment or the belief that nothing can be done.[47]

Current UK Guidelines[13]

Guidance produced using a Delphi process of 60 experts, part-funded by Macmillan Cancer Support, published in 2014 for the management of GI injury due to radiotherapy suggests systematic investigation of symptoms in order to avoid missing other causes.

Sixty experts took part in the Delphi consensus process to develop the guidelines to aid clinical nurse specialists looking after patients with pelvic radiation disease, working in conjunction with a gastroenterologist. The guidelines may also be helpful for general practitioners and generalists investigating and treating the GI symptoms of patients following radiotherapy.

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Mucosamin

Introduction

Regeneration of epithelial tissues and healing of mucosal and cutaneous lesions requires a well-coordinated host response and is linked to proliferation of fibroblasts and their production of collagen and glycosaminoglycans.[29] The speed of these processes depends not only on the patient's general condition (age, infections, drugs taken, systemic diseases) but, above all, on local conditions: vascularisation and availability in situ of glycosaminoglycan precursors of the matrix, that is to say, hyaluronic acid (HA), amino acids (glycine, L-proline, L-leucine and L-lysine) and small leucine-rich proteoglycans (SLRP).[30]

Hyaluronic acid and amino acids

The protective, pain reduction, lesion healing and hydrating properties of Mucosamin derive from the key constituents of the compound.

What role does hyaluronic acid play in Mucosamin?

Sodium hyaluronate is the sodium salt of hyaluronic acid (HA), a key component of connective tissue,[31,32] which has been shown to promote cell differentiation and cell motility.[31,33] Sodium hyaluronate aids in the formation of a barrier that helps to hydrate and protect the mucosa. It is involved in assembly of extracellular matrix (ECM) proteins, where it serves as a scaffold for matrix proteins, exerts an anti-inflammatory effect,[30] and promotes wound healing.[33] Hyaluronic acid increases in concentration during wound healing.[34]

HA may facilitate collagen organisation and contraction during repair.[30] It acts as an antioxidant for inflamed body tissues, protecting body tissue from free radical damage and supporting immune function by inhibiting microbes from moving between, and infiltrating cells.[35]

What role do amino acids play in Mucosamin?

Availability of amino acids, such as those present in Mucosamin support the role of HA in wound repair. The four amino acids present in Mucosamin are involved in favouring wound healing by collagenogenesis and extracellular matrix (ECM) formation. Glycine constitutes one third of the collagen molecule, whilst proline and lysine represent around 23% of collagen chains. Collagen deposition is essential in wound healing and is associated with normal ECM formation. It provides increased strength to the wound and facilitates macrophage and endothelial cell migration. The synthetic collagen precursor amino acids in Mucosamin are intended to promote the formation of collagen, and to improve and accelerate wound closure.

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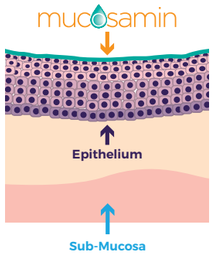
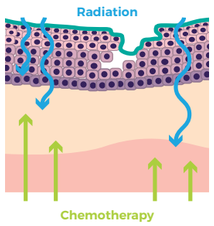
glycine, L-proline, L-leucine and L-lysine HCl

Mode of Action During Mucositis



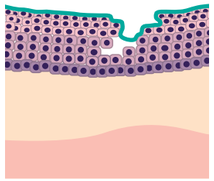
Protection

- Forms a barrier to help protect oral mucosa.[42]



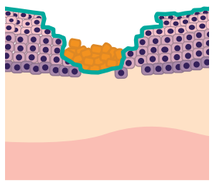
Initiation
(Spray, mouthwash, vaginal cream, rectal gel)

- Modulates tissue hydration and osmotic balance.[30]
- Hydrates and protects the mucosa to reduce the incidence of mucositis.[30]



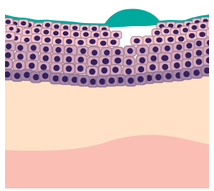
Upregulation/Amplification
(Spray, mouthwash, vaginal cream, rectal gel)

- Reducing the inflammatory infiltrate that can hinder the healing process.[35]
- Alleviates the irritation of the oral cavity caused by mucositis.[32]
- Protects the local mucosa from free radicals[35], to help prevent tissue injury.[36]



Ulceration
(Spray, mouthwash, vaginal cream, rectal gel)

- Creates a film that covers and protects the ulcerated mucosa, to provide pain relief.[32]
- Reduces the pain and burning sensations induced by mucositis.[32]



Healing
(Spray, mouthwash, vaginal cream, rectal gel)

- Mucosamin enhances and promotes epithelial wound repair of the mucosa.[35]

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Summary

HA, made up of repeating units of D-glucuronate and N-acetylglucosamine, is the most important glycosaminoglycan produced by fibroblasts during wound healing and appears to be able to promote cell proliferation, differentiation and motility. HA is naturally biocompatible, biodegradable and non-immunogenic. It acts as an anti-oxidant in inflamed tissues, protecting them from the damage caused by reactive oxygen species and supporting immune function. The viscoelastic matrix of HA constitutes a biocompatible support material suitable for use in surgery as a scaffold for growth of damaged tissue. Thus the principal action of HA is essentially that of a mechanical nature.

Repair of tissue damage that is the result of inflammatory processes, or through the use of radiotherapy and chemotherapy is a complex process. It depends on local conditions such as vascularisation, and on the availability at the site concerned, not only of constituents of the cell matrix (including HA itself), but also of amino acids (glycine, L-proline, L-leucine and L-lysine).

The combination of these amino acids with a base mixture containing hyaluronic acid or sodium hyaluronate, constitutes a means of enriching the damaged area with collagen precursors so as to promote and accelerate healing of mucosal and cutaneous lesions of various etiologies. The action of forming a protective, hydrating film, continues to be performed chiefly by HA. The amino acids support its effects. The excipients contained in such preparations, such as polyvinylpyrrolidone, a water-soluble polymer used in the preparation of the various formulations (gel, spray, cream), are contained in the standard quantities used in numerous medical and cosmetic formulations and are not associated with toxicity; they perform actions of a mechanical nature (hydration and formation of cutaneous films).

The mucosamin range forms a protective layer that, once in place, promotes restoration of the physiological conditions of damaged tissue by maintaining control of the microenvironment. They have no anti-bacterial activity.

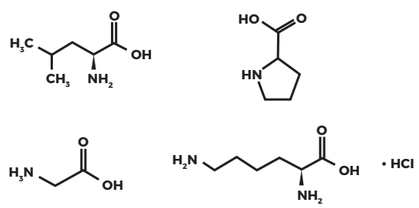
mucosamin
Sodium hyaluronate + amino acids
glycine, L-proline, L-leucine and L-lysine HCl

Product Information

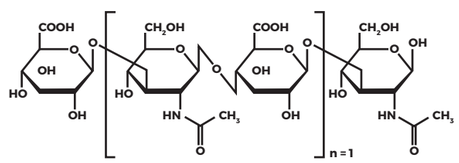
Product name

Mucosamin

Amino acids



Hyaluronic acid



Compositional information

Sodium hyaluronate and synthetic amino acids - glycine, L-Proline, L-Leucine, L-Lysine HCL

Presentations

Mucosamin mouthwash:	Topical oral solution 250mL bottle
Mucosamin Oral Spray:	Topical fluid gel 30mL bottle with spray nozzle
Vaginal cream:	Topical Cream 30g tube plus 6 applicators
Rectal gel:	Topical gel 6 x 7g micro-enemas

Indications

Mucosamin mouthwash:	At start of radiological therapy or chemotherapy to help reduce incidence of oral mucositis; treatment of oral mucositis due to radiotherapy or chemotherapy; ulcerative pathologies of oral cavity (e.g. pemphigus, pemphigoid, erosive lichen planus); recurrent aphthous stomatitis; following surgical operations on tongue and oral mucosa; burning mouth syndrome.
Mucosamin Oral Spray:	Oral mucositis due to radiotherapy or chemotherapy.
Vaginal cream:	Actinic vulvovaginitis caused by radiation treatment of the pelvic region and vulvovaginitis caused during chemotherapy or a combination of both treatments (chemotherapy and radiotherapy)
Rectal gel:	Actinic proctitis caused by radiation treatment of the pelvic region and proctitis caused during chemotherapy, or a combination of both treatments (chemotherapy and radiotherapy)

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Dosing and administration

Mucosamin mouthwash:	Pour 5-10 ml into mouth, distributing product evenly throughout oral cavity and keeping in mouth for at least one minute. Use 3 or 4 times a day. Do not rinse after treatment. For rear sections of oral cavity, product can be gargled. May be diluted with water, according to severity of symptoms
Mucosamin Oral Spray:	Apply uniform layer into oral cavity by repeatedly spraying until the entire affected area is covered, 3 or 4 times a day according to severity of symptoms
Vaginal cream:	Apply vaginal cream, using applicator, once or several times a day, depending on the extent of symptoms, in accordance with medical advice. Please refer to package leaflet for full instructions.
Rectal gel:	Before applying Mucosamin Rectal Gel, the external area should be carefully cleaned. The cap should be removed, the applicator inserted, and the bellows should be pressed to dispense the gel. If necessary, the area can be lubricated with a small amount of Mucosamin Rectal Gel in order to reduce any tenderness and facilitate the entrance of the applicator. The tip of the applicator should be inserted into the affected area and the bellows of the applicator pushed in order to evenly administer Mucosamin Rectal Gel. The applicator is single use so should be disposed of safely after use.

Contraindications / interactions

Known hypersensitivity to ingredients. No reports of side effects or interactions with drugs or medicinal substances. No known secondary effects during pregnancy and breastfeeding; use at physician's discretion.

Other information

The Mucosamin product range are Class IIa/IIb medical devices; CE 0373. Authority for which is held by the manufacturer, Professional Dietetics S.p.A - Milano Italia.

There are no special precautions for the handling of Mucosamin products.

Mucosamin should be stored between 8 and 30 degrees C and kept out of direct sunlight.

mucosamin
Sodium hyaluronate + amino acids
glycine, L-proline, L-leucine and L-lysine HCl

Mucosamin mouthwash and spray [32]

Mucosamin mouthwash and oral spray help in the process of regeneration of the oral mucosa. Both presentations are CE marked class IIa medical devices.

Mucosamin mouthwash is a topical oral solution used to help in the treatment and prevention of OM induced by cancer treatment.

Mucosamin oral spray is a fluid gel used to help in the treatment of OM induced by cancer treatment. The spray formulation allows difficult areas of the mouth to be reached.

Mucosamin mouthwash and Mucosamin oral spray are formulated to help the process of regeneration of the oral mucosa, promote healing of areas of ulceration, and reduce local sensitivity within the mouth.

Mucosamin has multiple effects - it has a predominantly protective action, also helping to hydrate, provide pain relief [31] and promote repair of the oral mucosa. In addition, Mucosamin Mouthwash can be used to help reduce incidence of OM.[36]

When should Mucosamin Mouthwash be used?[36]

Mucosamin Mouthwash should specifically be used:

- At the start of radiological therapy or chemotherapy to help to reduce the incidence of OM[36]
- In the treatment of radiotherapy or chemotherapy induced OM[31]
- In ulcerative pathologies of the oral cavity (e.g. pemphigus, pemphigoid, erosive lichen planus)
- In recurrent aphthous stomatitis
- Following surgical operations on the tongue and oral mucosa[33][40]
- In burning mouth syndrome

When should Mucosamin Spray be used?

Mucosamin Spray should specifically be used:

- To help in the treatment of radiotherapy or chemotherapy induced OM[31][32]

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4 key effects

1 Protection

Mucosamin Mouthwash and Spray

When used at the start of chemotherapy or radiotherapy, Mucosamin hydrates and protects the oral mucosa, in order to help to reduce the incidence of mucositis.[32]

2 Relief from dry mouth

Mucosamin mouthwash & Mucosamin oral spray

Increased levels of hyaluronic acid are associated with fewer symptoms of dry mouth.[38]

3 Pain relief

Mucosamin mouthwash & Mucosamin oral spray

Mucosamin creates a protective film that covers and protects the ulcerated mucosa, quickly reducing the pain and burning sensation induced by oral mucositis.[32]

4 Wound healing

Mucosamin mouthwash & Mucosamin oral spray

Mucosamin creates a protective film that covers and helps to protect the mucosa, helping to promote the wound healing process.[32] [35]

mucosamin
Sodium hyaluronate + amino acids glycine, L-proline, L-leucine and L-lysine HCl

Mucosamin vaginal cream

Mucosamin vaginal cream is a class IIb medical device, made up of the same constituents as Mucosamin mouthwash and oral spray; sodium hyaluronate and four amino acids (glycine, L-proline, L-leucine and L-lysine).

By forming a soothing, protective layer over the mucosa, Mucosamin helps relieve symptoms of neurological injury caused by vulvovaginitis and aids the healing process. The specially designed applicator helps to ensure the entire affected area can be reached.[42]

When should Mucosamin vaginal cream be used?[42]

- Actinic vulvovaginitis caused by radiation treatment in the pelvic region
- Vulvovaginitis caused by chemotherapy
- Use applicator to apply once or several times a day, depending on the severity of symptoms
- Recommended for use throughout the course of treatment

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4 key effects

1 Prevention

When used at the start of chemotherapy or radiotherapy, Mucosamin vaginal cream protects the vaginal mucosa, in order to help to lessen the incidence and severity of vulvovaginitis. [57]

2 Protection

Protects tissue from free radicals to help support mucosal integrity and reduce inflammatory response[36,37]

3 Pain relief

Creates a film to cover exposed nerve endings and helps prevent further inflammation and tissue damage caused by colonisation of microflora[6]

4 Wound healing

Supports epithelial wound repair of the vaginal mucosa[33,35]

mucosamin
Sodium hyaluronate + amino acids
glycine, L-proline, L-leucine and L-lysine HCl

Mucosamin rectal gel

Mucosamin rectal gel is a class IIb medical device made up of the same constituents as the rest of the Mucosamin range; sodium hyaluronate and four amino acids (glycine, L-proline, L-leucine and L-lysine).

By forming a soothing, protective layer over the mucosa, Mucosamin helps relieve symptoms of neurological injury caused by radio or chemotherapy and aids the healing process. The specially designed micro-enema helps to ensure the entire affected area can be reached[42]

When should Mucosamin rectal gel be used?[42]

- Actinic proctitis caused by radiation treatment in the pelvic region
- Proctitis caused by chemotherapy
- Use micro-enema to apply once or several times a day, depending on the severity of symptoms
- Recommended for use from the start and throughout the course of treatment

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4 key effects

1 Prevention

When used at the start of chemotherapy or radiotherapy, Mucosamin rectal gel protects the rectal mucosa, in order to help to lessen the incidence and severity of actinic proctitis. [58]

2 Protection

Protects tissue from free radicals to help support mucosal integrity and reduce inflammatory response[36,37]

3 Pain relief

Creates a film to cover exposed nerve endings and helps prevent further inflammation and tissue damage caused by colonisation of microflora[6]

4 Wound healing

Supports epithelial wound repair of the rectal mucosa[33,35]

mucosamin
Sodium hyaluronate + amino acids
glycine, L-proline, L-leucine and L-lysine HCl

Clinical Studies – Oral mucositis

Colella, G. et al.[31]

Efficacy of a spray compound containing a pool of collagen precursor synthetic amino acids (L-Proline, L-Leucine, L-Lysine and Glycine) combined with sodium hyaluronate to manage chemo/radiotherapy-induced oral mucositis.

Int J Immunopathol Pharmacol. 2010: 23(1): 143-151

Product investigation into the benefits of Mucosamin* spray : A 2-week open-label clinical trial

Study design

This was an open-label clinical trial of 27 patients (Age ≥18 years), investigating the benefits of Mucosamin* in the management of chemotherapy/ radiotherapy-induced oral mucositis (OM).

Patients affected by OM ≥ grade 1 OM, according to the WHO scale, were recruited consecutively in two centres. Each patient was instructed to apply Mucosamin* spray on the OM-associated lesions 3-4 times/day for 14 days, after a meal, keeping it in situ for at least 2 minutes, and avoiding drinking, eating and rinsing the mouth for at least 1 hour.

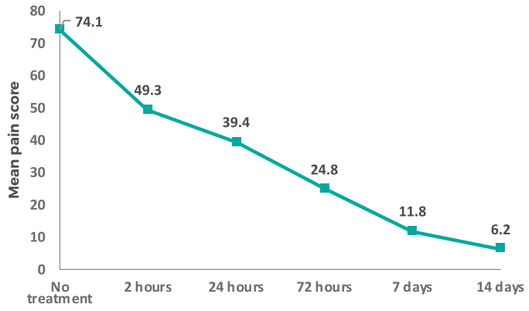
Patients were included who had recent experience (2 weeks) of head and neck radiotherapy for oral, oropharyngeal, nasopharyngeal and/or hypopharyngeal cancers, daily doses of radiotherapy over a 4-6 week period, chemotherapy for haematological malignant neoplasms and/or solid malignant tumours in other areas.

Results

Benefits of Mucosamin* evaluated at study endpoint:

Pain scores evaluated with VAS were significantly reduced after 2 hours of spray administration, compared with baseline measurements ($p<0.0001$, $z=-4.51$). The Wilcoxon's test showed statistically significant differences ($p<0.0001$, $z=-4.51$) for VAS after 24 hours, 72 hours, 7 and 14 days compared with baseline.

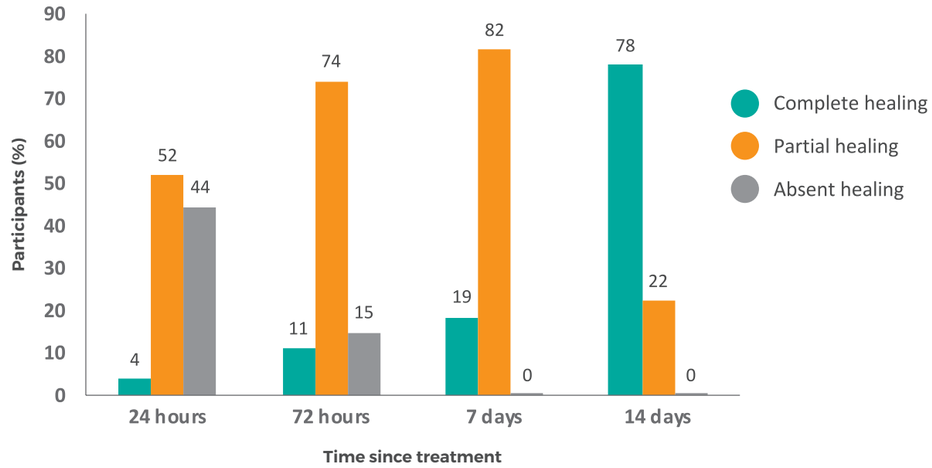
Figure 1: Oral mucositis pain scores assessed with visual analogue scale (VAS) after treatment with Mucosamin*



Mucosamin* was shown to reduce painful symptoms associated with OM after only 2 hours. Significant pain reduction was shown to continue over a two week period.

In terms of the CRI, patient lesions treated with Mucosamin* also significantly improved after 72 hours of treatment ($p=0.0051$; $z=-2.803$) compared with baseline. All patients were reported to comply well with Mucosamin over the study period.

Figure 2: The effect of Mucosamin* on the healing of OM associated lesions.



Additional benefits

The Friedman's test highlighted that during the 2-week observation, all patients significantly improved from baseline ($p<0.0001$) and progressively ameliorated their ability to swallow foods and liquids.

Safety

The compliance of the product was very good, and at the end of the study there were no adverse effects reported.

Conclusion

Mucosamin* was shown to significantly improve oral mucositis after only 72 hours and progressively improve the ability to swallow food and liquids over a two week period.

*Investigated under the brand name, Aminogam

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mucosamin
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glycine, L-proline, L-leucine and L-lysine HCl

Oral mucositis

Favia, G. et al.[33]

Accelerated wound healing of oral soft tissues and angiogenic effect induced by a pool of amino acids combined to sodium hyaluronate (Aminogam).

J Biol Regul Homeost Agents. 2008: 22(2): 109-116.

Properties promoting wound healing in post-surgical wounds – Controlled clinical study

Study design

120 patients (60 for the experimental group and 60 for the control group) were selected.

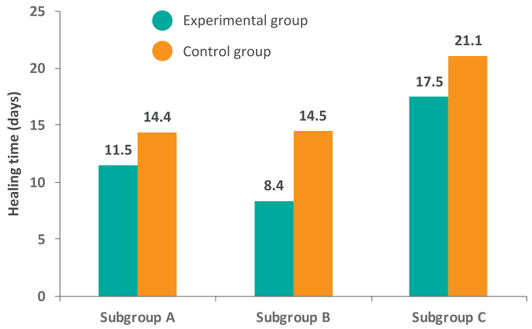
The 60 patients of the experimental group were divided into three subgroups (3 types of oral surgery wounds)

Subgroup A: Dental extraction (n=20)
Subgroup B: Endosseous implant insertion (n=20)
Subgroup C: Diode laser surgery (n=20)

Results

Benefits of Mucosamin evaluated at study endpoint:

Figure 1: Healing time in oral soft tissues following different surgery



Safety

No post-surgical complications seen in any of the experimental groups.

Conclusion

Mucosamin was shown to reduce healing time in oral soft tissues after three different kinds of surgery

*Investigated under the brand name, Aminogam

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Oral mucositis

Cirillo, N.[36]

A hyaluronic acid-based compound inhibits fibroblast senescence induced by oxidative stress in vitro and prevents oral mucositis in vivo.

J of Cell Phys. 2014.

Product investigation into the pre-treatment advantages of Mucosamin spray: Investigative case series.

Study design

This was a case study of 5 patients undergoing radiotherapy, chemotherapy, or both, investigating the benefits of Mucosamin in the management of chemo/radiotherapy-induced OM. Each patient received Mucosamin three times per day starting 4 days before every treatment cycle.

Figure 1: Demographic details, disease and treatment information of patients included in the case series.

Patient	Sex	Age (years)	Disease	Treatment
Case 1	Female	59	Breast cancer	Radical mastectomy plus 6 cycles of chemotherapy
Case 2	Male	63	Squamous cell carcinoma of the tongue	35 cycles of radiotherapy plus 4 cycles of chemotherapy
Case 3	Male	51	Squamous cell carcinoma of the tongue base	35 cycles of radiotherapy and 4 cycles of chemotherapy (treatment stopped at this point due to renal failure)
Case 4	Male	61	Squamous cell carcinoma of the buccal mucosa	36 cycles of post-operative radiotherapy
Case 5	Male	80	Squamous cell carcinoma of the buccal mucosa	36 cycles of post-operative radiotherapy

Results

Benefits of Mucosamin evaluated at study endpoint:

Only one patient (Case 2) reported the transient appearance of grade 1 (mild) OM, which healed completely after 72 hours. No other patients reported the appearance of OM, despite one patient (Case 1) having developed grade 3 OM during cancer treatment 8 years earlier.

Safety

No post-surgical complications seen in any of the experimental groups.

Conclusion

Data from a case-series of patients undergoing radio/chemotherapy strongly suggested that prophylactic use of the hyaluronic acid-based compound in the form of a spray may be effective in preventing the onset or oral mucositis.

mucosamin
Sodium hyaluronate + amino acids glycine, L-proline, L-leucine and L-lysine HCl

Wound healing

Mariggio, M. et al.[30]

Enhancement of fibroblast proliferation, collagen biosynthesis and production of growth factors as a result of combining sodium hyaluronate and amino acids.

Int J Immunopathol Pharmacol. 2009: 22(2):485-492

The effect of Mucosamin on Human foetal lung fibroblasts (MCR-5) - in vitro study

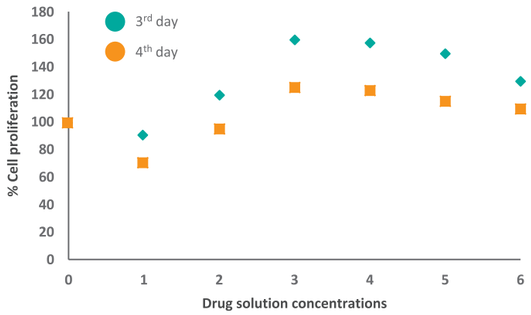
Study design

Fibroblasts play a key role in tissue healing by producing the majority of extracellular matrix (ECM) components, favouring granulation tissue formation and stimulating re-epithelialisation. Hyaluronan is a component of ECM. In this study the biological effects of Mucosamin on cultured Human foetal lung fibroblasts (MRC-5) cells were tested. A mother solution containing 0.665% Hyaluronic acid (HA) and 1% amino acids (AA) was serially diluted in distilled water. To analyse the effects of HA plus amino acids on the cell cycle, the cells were treated with solutions containing different concentrations of AA and HA and incubated for 3 or 4 days.

The MTT assay, a colorimetric assay for assessing cell metabolic activity, was used to evaluate the proliferative activity of HA plus AA on human fibroblasts.

Results:

Figure 1. Proliferative activity of HA + AA on human fibroblasts as evaluated by MTT assay.



The diagram above shows that the combination of HA and AAs enhanced MRC-5 proliferation. This effect was visible by MTT assay after 3 or 4 days of incubation and, in both cases, cell growth induced by HA plus AA was statistically significant vs untreated cells, from concentration of 0.0041% HA + 0.00062% amino acids to a concentration of 0.0332% HA + 0.05% amino acids. Higher HA and amino acid amounts gave a not quite statistically significant result. Four days incubation was less effective in stimulating fibroblast growth than 3 days, probably due to hyaluronan and/or amino acid degradation in culture medium. When the effects of HA plus amino acids on the cell cycle were analysed, MRC-5 cells showed a doubling time of about 2 days.

Reverse transcription-polymerase chain reaction (RT-PCR) carried out on RNA extracted from treated fibroblasts evidenced an increased expression of fibronectin, collagen I and III; three proteins abundant in ECM. After the third day of incubation, expression levels increased, and reached a maximum after the fourth day. Interleukins IL-6 and IL-8 showed an increase after 3 and particularly 4 days of treatment.

Results showed that fibroblasts treated with hyaluronic acid plus amino acid solution increased their proliferative activity, collagen I and collagen III and fibronectin synthesis. HA plus amino acid solution also increased the expression of transforming growth factor beta, connective tissue growth factor; interleukin Il-6 and Il-8 assayed by RT-PCR.

Conclusion:

These results suggested that Mucosamin, involved in several stages of wound healing, as fibroblast proliferation, granulation tissue formation, ECM component deposition and production of cytokines, may be a useful device to favour and accelerate wound closure.

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Haemotopoietic Stem Cell Transplant

Ruggiero T. et al.[41]

Use of sodium hyaluronate and synthetic amino acid precursors of collagen for the symptomatic treatment of mucositis in patients undergoing haematopoietic stem cell transplants.

Journal of Biological Regulators & Homeostatic agents Vol 30, no 3, 889-894 (2016)

Treatment of mucositis in patients undergoing haematopoietic stem cell transplants (HSCT) – case control study vs chlorhexidine

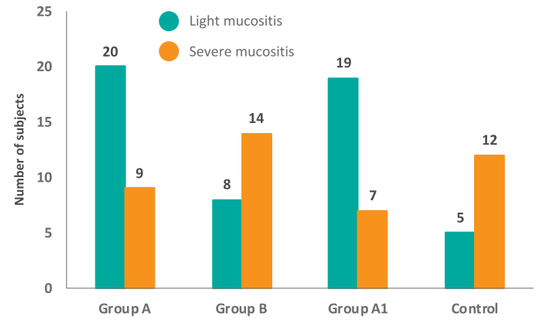
Study design

A total of 68 adult patients (average age 51, range 22-70) due to undergo HSCT for allogenic and autologous transplant were enrolled at the Stem Cell Transplant Unit. The patients were divided into two groups. One group was treated with POHC before HSCT and applications of Mucosamin® during the recovery after transplantation. The second group served as controls, with the usual treatment of Chlorhexidine 0.20% adopted by the department. Thirty-two patients in group A and 28 patients in group B completed the study.

After HSCT symptoms of the patients' mucositis of both groups were evaluated every day. The evaluation included three scores for oral mucositis (OM); a) WHO mucositis scale ranging from 0=no symptoms; 1=soreness, erythema; 2=erythema, ulcers but able to eat solids; ulcers but required liquid diet; 4=oral alimentation not possible; b) Visual analogue scale (VAS) ranging from 0= no pain to 10=worst pain; c) OMAS scale (oral mucositis assessment scale):oral cavity for ulceration 0=no lesion; 1=lesion <1cm2; 2=lesion1 to 3cm2; 3 = lesion>3cm2; oral cavity for erythema; 0=none; 1=not severe; 2=severe.

Results

Figure 1: Evaluation of gravity of oral mucositis related to use of Mucosamin and a session of POHC



Group A: Mucosamin group
Group B: No Mucosamin group
Group A1: Mucosamin and POHC 6 months before HSCT
Control: No mucosamin and POHC 6 months before HSCT

To evaluate whether there is a strengthening of the results with the association between Mucosamin and professional oral health care (POHC), patients in group A who had POHC in the 6 months prior to HSTC (Group A1) were compared to patients who neither used Mucosamin nor had POHC within the 6 months before HSTC (Group CTRL). Patients who had a more recent session of POHC in association with Mucosamin developed significantly lighter OM. Use of OM associated with oral hygiene seems to have a synergy that protects the oral cavity from the highest grades of OM.

Conclusion

The treated patients developed less severe OM, therefore Mucosamin seems to have a protective role against the more severe phases of mucositis. The maximum OM pain, measured with the VAS scale, was higher in patients who did not use Mucosamin. In the treated group OM resolved sooner than in the control group.

mucosamin
Sodium hyaluronate + amino acids glycine, L-proline, L-leucine and L-lysine HCl

Vulvovaginitis (vaginal mucositis)

Girbaudo et al. poster presentation [57]

Evaluation of the use of Mucosamin® vaginal in women treated with VBT after surgery in prevention of vaginal mucositis.

Study design

This prospective randomised study was conducted over a 26-month accrual period. 120 women, from 53 to 80 years, presenting with endometrial carcinoma of stage I, given a surgery and fractionated Vaginal Brachytherapy (VBT) were enrolled.

Inclusion criteria

After surgery, all patients were treated with one course of VBT, 30 Gy in five fraction (6 Gy for fraction), along one week. They were randomly assigned to one of two treatment arms:

60 women were treated with two applications of Mucosamin® vaginal cream per day for one month. For the first week, the preventive treatment was simultaneous to VBT.

The control group comprised 60 patients that did not undergo any treatment during and after VBT.

In the treatment group, Mucosamin vaginal cream was applied to the irradiated vagina twice a day: the first application 1–2 h after the morning radiotherapy session, the second in the evening. The topical treatment was continued over a 4-week period. No concomitant medication was allowed over the whole period of treatment and observation.

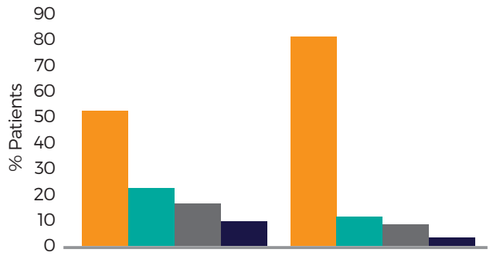
Evaluation parameters

The patients were examined by the physician at the time of admission (Day 0), one month and three months by the same physician. To evaluate the efficacy of hyaluronic acid and amino acid treatment the subjective parameters investigated included the adverse events CTCAE 4.03 scale.

The objective assessment included inflammatory signs, which were inspected by a physician.

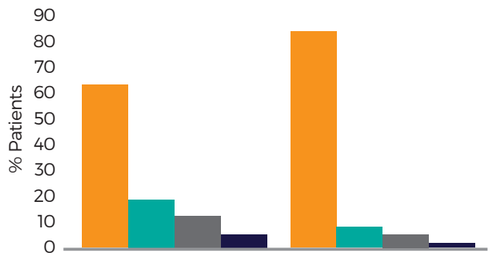
Results:

figure 1. Evaluation of vaginal dryness at 3 months following treatment with VBT



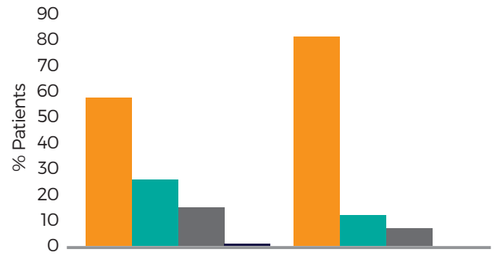
	No treatment (%)	Mucosamin (%)
G0	54	80
G1	23	10
G2	15	7
G3	8	3

figure 2. Evaluation of vaginal structure at 3 months post treatment with VBT



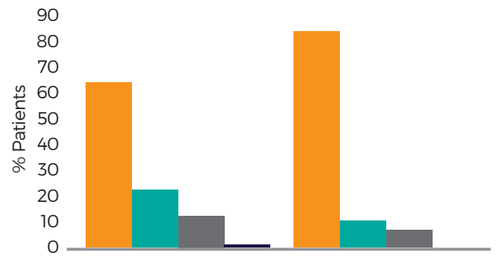
	No treatment (%)	Mucosamin (%)
G0	63	84
G1	18	9
G2	14	5
G3	5	2

figure 3. Evaluation of vaginal inflammation at 3 months post treatment with VBT



	No treatment (%)	Mucosamin (%)
G0	58	81
G1	27	12
G2	14	7
G3	1	0

figure 4. Evaluation of vaginal pain at 3 months post treatment with VBT



	No treatment (%)	Mucosamin (%)
G0	65	83
G1	22	10
G2	12	7
G3	1	0

After the VBT, the treated group showed a statistically significant improvement ($P<0.05$ vs. control) on subjective symptoms of inflammation, vaginal structure, vaginal dryness and pain. The evaluation was performed after 3 months.

Conclusion

The application of Mucosamin® Vaginal Cream on the irradiated vagina during radiation therapy was shown to reduce the severity of mucosal reactions. The results of this prospective study suggest an interesting role of the hyaluronic acid and amino acid cream as supportive treatment to improve compliance and quality of life in patients undergoing radiation therapy.

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Proctitis (rectal mucositis)

Data on file [58]

Clinical data on the use of hyaluronic acid and aminoacids microclysms in the prevention of chronic actinic proctitis in patients undergoing radiotherapy for prostate cancer

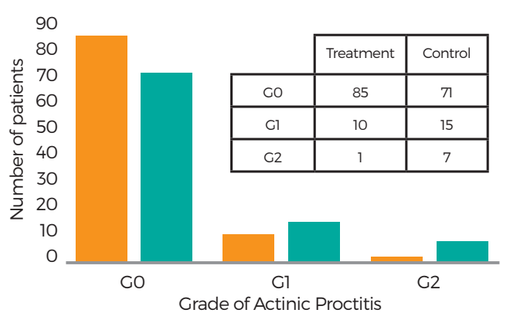
Study design

193 patients undergoing radiation treatment for prostate carcinoma were randomised to treatment with Mucosamin® rectal gel (n = 100) or control with non-topical steroid therapy (n=93).

Mucosamin was applied in the evening from the start of treatment, up until two weeks after cessation of treatment as per the device instructions. All patients had weekly check-ups during the treatment and had a final follow-up 3 weeks after cessation of treatment. Four patients died during the study as a result of disease progression or cardiovascular events.

Results

Figure 1. Comparison of control and treatment of number of patients who experienced late stage actinic proctitis and the grade experienced after an average of 24-month follow-up.



	Treatment	Control
G0	85	71
G1	10	15
G2	1	7

Considering an average follow-up of 24 months, the treatment group experienced significantly fewer G0, 1 and 2 toxicities ($p<0.05$) compared with the control group and more G0 rectal toxicities were experienced in the treatment group (85 vs 71).

Conclusions

Compared with oral steroidal treatment, Mucosamin rectal gel was significantly more effective and reduced the number of incidences of actinic proctitis (inflammation of the lining of the rectum).

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Prescribing Information

Mucosamin® mouthwash (Sodium hyaluronate and synthetic amino acids - glycine, L-Proline, L-Leucine, L-Lysine HCL) oral solution Prescribing Information

Presentation: Topical oral solution (Sodium hyaluronate and synthetic amino acids - glycine, L-Proline, L-Leucine, L-Lysine HCL). **Indications:** At start of radiological therapy or chemotherapy to help reduce incidence of oral mucositis; treatment of oral mucositis due to radiotherapy or chemotherapy; ulcerative pathologies of oral cavity (e.g. pemphigus, pemphigoid, erosive lichen planus); recurrent aphthous stomatitis; following surgical operations on tongue and oral mucosa; burning mouth syndrome. **Dosage and method of use:** Pour 5-10 ml into mouth, distributing product evenly throughout oral cavity and keeping in mouth for at least one minute. Use 3 or 4 times a day. Do not rinse after treatment. For rear sections of oral cavity, product can be gargled. May be diluted with water, according to severity of symptoms. **Contraindications:** Known hypersensitivity to ingredients. No reports of side effects or interactions with drugs or medicinal substances. No known secondary effects during pregnancy and breastfeeding; use at physician's discretion. **Legal category:** Class IIa Medical Device. **Cost:** £19 for 250ml bottle. **CE number:** CE 0373. **Manufacturer:** Professional Dietetics S.p.A. - Via Ciro Menotti, 1/A – 20129 Milan - Italy **Distributor:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire GU32 3QG, UK. **Date last reviewed:** September 2018. **Version number:** 1010461476 v 1.0.

Mucosamin® spray (Sodium hyaluronate and synthetic amino acids - glycine, L-Proline, L-Leucine, L-Lysine HCL) oral solution Prescribing Information

Presentation: Topical fluid gel (Sodium hyaluronate and synthetic amino acids - glycine, L-Proline, L-Leucine, L-Lysine HCL). **Indications:** Oral mucositis due to radiotherapy or chemotherapy. **Dosage and method of use:** Apply uniform layer into oral cavity by repeatedly spraying until the entire affected area is covered, 3 or 4 times a day according to severity of symptoms. **Contraindications:** Known hypersensitivity to ingredients. No reports of side effects or interactions with drugs or medicinal substances. No known secondary effects during pregnancy and breastfeeding; use at physician's discretion. **Legal category:** Class IIa Medical Device. **Cost:** £19 for 30ml bottle with spray nozzle. **CE number:** CE 0373 **Manufacturer:** Professional Dietetics S.p.A. - Via Ciro Menotti, 1/A – 20129 Milan – Italy. **Distributor:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire GU32 3QG, UK. **Date last reviewed:** September 2018. **Version number:** 1010462477 v 1.0.

Mucosamin® vaginal cream (Sodium hyaluronate and synthetic amino acids - glycine, L-Proline, L-Leucine, L-Lysine HCL) Prescribing Information

Presentation: Vaginal cream (Sodium hyaluronate and synthetic amino acids - glycine, L-Proline, L-Leucine, L-Lysine HCL). **Indications:** Actinic vulvovaginitis caused by radiation treatment of the pelvic region and vulvovaginitis caused during chemotherapy or a combination of both treatments (chemotherapy and radiotherapy). **Dosage and method of use:** Apply vaginal cream, using applicator, once or several times a day, depending on the extent of symptoms, in accordance with medical advice. Please refer to package leaflet for full instructions. **Contraindications:** Known hypersensitivity to ingredients. No reports of side effects or interactions with drugs or medicinal substances. During pregnancy and breastfeeding; use at physician's discretion. **Legal category:** Class IIb Medical Device. **Cost:** £27.50 for 30g tube with six 5g single-use applicators. **CE number:** CE 0373 **Legal Manufacturer:** Professional Dietetics S.p.A. - Via Ciro Menotti, 1/A – 20129 Milan – Italy. **Distributor:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire GU32 3QG, UK. **Date last reviewed:** October 2019. **Version number:** 1010461482 v 3.0

Mucosamin® Rectal Gel (Sodium hyaluronate and synthetic amino acids - glycine, L-Proline, L-Leucine, L-Lysine HCL) Prescribing Information

Presentation: Rectal Gel (Sodium hyaluronate and synthetic amino acids - glycine, L-Proline, L-Leucine, L-Lysine HCL). **Indications:** Actinic proctitis caused by radiation treatment of the pelvic region and proctitis caused during chemotherapy or a combination of both treatments (chemotherapy and radiotherapy). **Dosage and method of use:** Apply Rectal Gel, using applicator, once or several times a day, depending on the extent of symptoms, in accordance with medical advice. Please refer to package leaflet for full instructions. **Contraindications:** Known hypersensitivity to ingredients. No reports of side effects or interactions with drugs or medicinal substances. During pregnancy and breastfeeding; use at physician's discretion. **Legal category:** Class IIb Medical Device. **Cost:** £27.50 for six 7g single-use micro-enemas. **CE number:** CE 0373 **Legal Manufacturer:** Professional Dietetics S.p.A. - Via Ciro Menotti, 1/A – 20129 Milan – Italy. **Distributor:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire GU32 3QG, UK. **Date last reviewed:** July 2019. **Version number:** 1010461577 v 2.0

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Aspire Pharma Ltd on 01730 231148.

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