

Management of Chemotherapy Induced Dysgeusia: An Important Step Towards Nutritional Rehabilitation

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Abstract

Dysgeusia is an alteration in taste and is often associated with ageusia and hypogeusia. It is the most common problem or the side effect noted in almost all cancer patients receiving chemotherapy which severely affects their food intake. So a proper attention should be given to this aspect so as to improve the nutritional needs of these patients. There are also various other factors, which should be considered as risk factors for the development of dysgeusia. The clinician should be aware of all these risk factors and the differential diagnosis so as to be able to diagnose and manage such cases. Although non-pharmacologic management strategies are the one which are routinely recommended, pharmacologic recommendations require more research to alleviate this common side effect.

Key words:

Chemotherapy; Dysgeusia; Malnutrition; Quality of life; Taste alterations

Introduction

Dysgeusia is an alteration in taste and is associated with ageusia, which is the complete lack of taste, and hypogeusia, which is the decrease in taste sensitivity. Although it is one of the most common distressing side effect along with smell changes, fatigue, nausea, vomiting, and hair loss noted in cancer patients receiving chemotherapy [1-5], still enough attention is not given in terms of prior information to the patient, care during the chemotherapy regimen and after effects. Only 17% of patients receive information before initiating chemotherapy [6] and it is so bothersome that patients' rank it second to alopecia [7].

Dysgeusia has a psychosomatic aspect showing complex subjective symptoms. As foods have important symbolic, cultural and religious values beyond nutritional aspects, dysgeusia has shown to affect the psychosocial aspect of life, leading to low quality of life and increased distress [8,9].

Taste disorders affect food selection and contribute to poor meal intake [10-12], thus playing a significant role in the etiology of anorexia in cancer patients [13,14]. DeWys [15] was among the first to implicate taste threshold abnormalities in anorexia development in patients with cancer. This affects the adequate nutrition uptake leading to malnutrition and weight loss [16].

There is also poor response and tolerance to treatment [17,18], further contributing to decrease quality of life (QOL), and poor survival [19]. Nutritional rehabilitation in cancer patients is very essential as a supportive modality as well as in the form of actual therapy. Making them aware of the problem and treating the main

cause or providing them with other alternatives is very essential to improve patient's nutritional rehabilitation program.

Etiopathogenesis

There are various causes of dysgeusia such as progressive malignant disease, comorbidities, and treatment, including cytotoxic chemotherapy and radiotherapy, stomatitis and mucositis, oral thrush, and zinc deficiency [20,21]. Dysfunction of the olfactory sense could also lead to taste changes and diagnoses such as sinusitis and nasal polyps should be considered. Medications such as anti-depressants, anti-hypertensives, anti-emetics and antibiotics may be responsible for taste changes and use of such medications needs to be assessed during clinical evaluation [4].

Chemotherapy (CT) drugs given to cancer patients associated with taste changes include taxanes, cisplatin, carboplatin, cyclophosphamide, doxorubicin, 5-fluorouracil, dacarbazine, nitrogen mustard, cisplatin, vincristine, folinic acid antagonists, platinum agents and methotrexate [20,22-24]. CT agents differ from each other in their impact on taste alterations (TAs), but instead of considering individual drugs impact on taste alterations, chemotherapy regimens impact should be considered as it is more relevant for the clinicians to have information on actually administered regimens than on single agent only [22]. Patients treated with gemcitabine plus a platinum agent reported the lowest levels of TAs [2], as gemcitabine was found to be associated with less severe TAs. Whereas patients receiving irinotecan report significantly more TAs. Irinotecan is administered only in third and higher lines of CT. Patients in this phase of treatment are usually in a condition characterized by debilitation resulting from progressive disease and previous treatments. In addition, there may be an effect of cumulative toxicity caused by previous cytostatic treatments [25].

Pathogenesis

The possible mechanisms are as follows

Direct insult to the taste cell receptors is one suggested theory. Some chemotherapy agents are secreted in saliva and gain direct contact with taste receptors. Patients may experience a metallic or "chemical" taste when chemotherapy is delivered, and this is consistent with drug secretion in saliva [26,27]. It is suggested that cell damage occurs in three ways: 1) a decrease in the number of normal cell receptors, 2) alteration of cell structure or receptor surface changes, and 3) interruption of neural coding. The turnover rate of normal human taste bud cells is 10 days and chemotherapy kills such cells with high turnover rates resulting in taste alteration [4,28-31]. While most taste alterations are transient lasting less than three months after completion of treatment, dysgeusia may persist after drug clearance due to damage to the taste buds [22].

Another probable cause of dysgeusia could be neurotoxicity from systemic chemotherapy. Cranial nerves VII (facial), IX (glossopharyngeal), and X (vagus) control integral sensory functions in the tongue and damage to them has been implicated in taste alterations [26].

Xerostomia or dry mouth is an important symptom to address in all patients receiving chemotherapy, which has been implicated in the development of dysgeusia [32]. Decreased saliva secretion alters the amount of chemicals released by the foods thereby changing the taste. Chemotherapies such as cyclophosphamide, epirubicin/methotrexate, and 5-fluorouracil when used in the adjuvant setting have been implicated in causing xerostomia and a 49.9% prevalence rate of xerostomia has been observed in patients undergoing chemotherapy [33].

The biomedical model and the nursing model has long been used in which the former conceptualizes the symptoms of the patients in which cancer pain control is successfully achieved by using powerful drugs which serve as an archetype, whereas the later better address other aspects such as suffering, distress, and ability to function independently [34,35]. The process of symptom experience involves an individual's perception of a symptom, evaluating its meaning, and then responding either in a positive or a negative way having an impact on daily life. These are thus the indirect indicators of the situational meaning (the person's perception of a new event and their capacity to handle it) of dysgeusia [36]. The evaluation and assessment of these aspects will then highlight the severity, cause, treatability and the effect of the symptom on the person's life. The patient's positive approach towards shaping a situational meaning is mainly dominated by the patient's beliefs and existential meaning which in turn interact with the patients experience and culture [37]. Patient's prior knowledge of the symptoms or psychological conditioning of the patient prior to treatment will thus have a positive impact on the handling of TAs which in turn will also benefit the treatment outcome.

Zinc deficiency has also been associated with taste disorders in some but not all reported studies [38-43]. The possible reasons could be that the drugs that cause hypogeusia have a sulfhydryl group in their structures; this component is known to bind and chelate heavy metal ions like zinc leading to deficiency or there might be low zinc intake [44].

Clinical Implications

TAs often starts at the beginning of CT and do not always cease with its termination, but may persist for weeks or even months beyond active therapy [28,45]. Frequency and intensity of dysgeusia: High prevalences of TAs have been reported in the range of 46%–77% [2]. TAs is more often reported by women and younger participants whereas smokers and older individuals report fewer TAs. The reasons for gender differences could be due to women more readily reporting problems or to differences in prevalence or perception of TSCs and other symptoms [46]. Women also reported more distress and greater impact on daily life from TSCs [2]. Both smokers and elderly patients tend to have elevated taste thresholds (hypogeusia) [2,47,48] therefore CT-induced changes in taste are presumably less noticeable for them. These patients might notice TAs later or less intensely [49].

What changes in taste are noted / how dysgeusia is experienced?

The most frequent complaint is decreased taste sensation [7], taste loss and a tendency toward bad taste perception [50]. The five tastes, sweet, sour, bitter, salty, and umami (savoriness), can all be affected. Most commonly the bitter taste threshold is lowered, while the sweet threshold is increased [22,24] and the salty taste to be altered most often [4]. The patterns and intensity of dysgeusia vary considerably. Some patients prefer sweet foods, while others are able to tolerate more salty foods [22]. Most of the food aversion was to meat, followed by chocolate, fruit, and coffee. Taste sensations are also varied and some patients report chemosensory changes as "saw dust," "toilet paper," and "metal" [7]. One study found no differences in umami taste RT [44] whereas another study found significantly impaired DT of umami taste [51]

There are also individual differences regarding the dysgeusia peaks [7]. Other associated symptoms/problems: it has been suggested that there is an existence of treatment-related symptom clusters [52-56] which states that when chemotherapy stimulates chemoreceptor trigger zones, it causes nausea and vomiting, which in turn has been associated with poor appetite, altered taste, fatigue, changes in smell [36], depressed mood, and dry mouth [23]. 86% of patients with cancer have some degree of subjective chemosensory abnormalities [52].

Sequel of Dysgeusia

Physical changes: Taste disorders are unpleasant experiences, which like any other unsatisfactory event is recorded in the memory as unpleasant (aversive food) experience [53]. These taste signals affect food preference and food intake, playing an important role in anorexia, weight loss and malnutrition disorders in patients with cancer [44].

How nutritional rehabilitation is affected in TAs pts?: Taste detection and recognition thresholds disorders in patients with cancer under chemotherapy treatment could be important factors in malnutrition development [44]. In a study the comparison between patients with upper sweet DT and bitter RT values above the median versus those with values below the median, showed a significant difference with low calorie and nutrient intake leading to weight loss in patients with upper sweet DT and bitter RT values above the median. These findings agree with other reports and confirm that taste disorders not only reduce the patient's quality of life (QOL), but they

may also lead to insufficient eating habits affecting dietary intake and nutritional status [2,7,8,53]. Thus the dysgeusia induced anorexia [35] affects nutritional rehabilitation playing an important role in the etiology of malnutrition and wasting, which affect about 40% of hospitalized patients [55]. Anorexia in cancer patients is also associated with mucositis, dental disease, tumor invasion, vitamin deficiencies, poor oral hygiene, bacterial, viral or fungal oral/nasal cavity infections, postnasal drip, gastroesophageal reflux and volatile compounds in inhaled air [56-58] thus resulting in the cumulative effect of affecting nutritional rehabilitation of these patients [20,59]. The consequences of malnutrition are deleterious. Prolonged morbidity and chemotherapy-induced side effects, decreased response to therapy, and cancer treatment delays can result from nutritional compromise [60].

Psychological changes: Dysgeusia has an impact on patients' daily lives [7,23,61]. Apart from nutritional aspects food and meal situations have important symbolic, cultural, and religious values [2] thus it might be expected to negatively affect psychosocial aspects of life. There might be mood disturbances and decreased social functioning [26,62]. Despite of this, only few patients report to the physician. It is therefore important to better understand and support the patient by psychological counseling.

Reasons for Less Reporting

Haworth and Dluhy [63] motivate the importance of meaning of symptoms in that it often "provides the driving force to initiate the health encounter." Most of the patients give less importance because:

Patients have difficulties envisioning TSCs as "treatable," [36] leading to both staff and patients communicating less about symptoms [64,65]. Dysgeusia also experienced during fever, medication for other reasons, cancers and so on, so patient might think it to be related to cancer which will be relieved with the resolution of cancer. Patients thinking that their experience is trivial, lack of time, or assuming the staff will discover the symptom on their own during physical examination. They have difficulties articulating their problems, [63] they have difficulties expressing their experiences of TSCs due to lack of recognition of the symptom and lack of words to describe their sensations.

Management

Taste alteration varies with each patient and specific suggestions for dysgeusia management must be tailored on an individual basis. Following are the suggestions for the management of dysgeusia.

A] Preventable aspect: The proper care for patients receiving cancer chemotherapy should consist of interventions focused on preventing, minimizing, and alleviating treatment-related symptoms and problems and offering additional support to patients during the treatment phase [34-37]. This can be achieved by (i) patient information of the symptoms before the beginning of the chemotherapy so that they can recognize and report to the physician and (ii) routine assessment by physician which should also involve verbal communication between physician and patients as it has been shown that the response of healthcare staff to patient concerns is of significance [61,66] for how patients interpret their bodily signs [35,67]. Regular reporting of the problem by the patients also helps the physician to provide various treatment options which might help to reduce TAs and associated symptoms.

Thus the physician should also focus on patients' entire symptom panorama during chemotherapy rather than focusing solely on single adverse effect as there is a close relationship between TAs and other adverse effects (nausea, vomiting, depressed mood, appetite loss, and oral problem). This would involve investigation of symptom interactions as well as social and psychological factors that could impact on patients' perceived meaning of the situation.

B] Self care strategies: Self care strategies should be adopted by the patient for dealing with TAs. Many of the suggested recommendations deal with food preparation. Several published studies [6,27] have suggested the following for improving the flavor of foods:

- Consume foods that are cold or at room temperature.
- Avoid the use of metallic silverware.
- Add more seasonings and spices to foods, such as salt, oregano, basil, cinnamon, and ginger.
- Choose protein products with a mild flavor such as chicken, turkey, tofu, dairy products and eggs.
- Add sugar to decrease salty or bitter tastes.
- Reduce consumption of bitter or metallic tasting foods such as coffee, chocolate, and red meat.
- Marinate meats to change the taste.
- Choose frozen fruits such as melon balls, grapes, or oranges.
- Add fats and sauces to foods.
- Choose more bland foods.
- Suck on hard, sugarless candies.
- Drink more water with meals to help with swallowing or rinse away bad taste.
- Eat small meals several times a day.
- Avoiding foods with strong smells [62]
- Also good oral mouth care practices can alleviate some taste alterations.

C] Pharmacological considerations: Zinc supplementation has shown to increase recovery in taste acuity, but another study showed no effect on taste alteration [60,68,69]. This treatment should be used with caution as excessive zinc supplementation can negatively impact the immune system [70].

The amino acid glutamine has also been investigated as a treatment for dysgeusia. Glutamine has shown to improve mucositis and recovery time in patients receiving high-dose chemotherapy [71,72] but does not reduce taste alteration in patients receiving taxane-based chemotherapies [20].

D] Psychological strategies: Certain psychological strategies could also be useful like

- (i) Changing the patient's attitude by making them aware that the TAs are at the expense of curing the cancer by chemotherapy and later having a cancer free state. Patients should also be explained that the TAs is not permanent and they will often revert after the cessation of chemotherapy.
- (ii) Giving up expectations of food and drink and using taste memory help them with taste changes.
- (iii) Remembering how things tasted and using these memories in meal situations might be helpful when dysgeusia occurs.
- (iv) Having someone else prepare the meal would also be effective at reducing food aversion [7]
- (v) Having a variety of food at short intervals might also increase appetite.
- (v) A good meal prior to any social gathering might prevent the patient from feeling depressed.
- (vi) Psychological conditioning of the family members as well so that they support the patient in a more positive

way.(vii) Newer methods could be tried like patients with TAs if possible could meet, form group and share their experiences which might distress them and might prove to be a psychological healer, thus benefitting their nutritional uptake.

Conclusion

Although TAs have been incorporated in the National Cancer Institute Common Toxicity Criteria since 1999 [73], the literature on underlying biological mechanisms, on physical and physiological consequences, and even on prevalence is scarce. And so is the clinicians' awareness of it. Thus it is very important that the physicians are made more aware of this common side effect of chemotherapy, so that they make their patients aware of the problem prior to the treatment and also provide better psychological support to them, as it is clear from the above review that lack of pharmacological strategies should lead to using more of psychological strategies. It therefore seems important that physicians provide active support for patients' own self-care, acting as discussion partners, helping them evaluate different strategies, and encouraging innovative efforts to diminish distress and impact on daily life. Also more research is required for the pharmacological management of dysgeusia which is expected to completely alleviate the problem. Nutritional management of individuals with chemosensory disorders requires a complete clinical and nutritional evaluation with appropriate dietary-intake measurements and expert nutritional counseling. This in turn will prevent malnutrition which is often seen in these patients.

Further Recommendations

Continuing research is required to develop better understanding of the nature, frequency, severity, and duration of taste alterations and their significance in food consumption and malnutrition in patients with cancer under chemotherapy. Thus the patients are needed to be evaluated over a period of time to know the sequence of taste changes, various periods of peaks of dysgeusia, factors contributing to peaks of dysgeusia, and related sequels. This will provide an overall precise insight of variations in taste alterations which will help in educating the patient prior to onset of chemotherapy, various management strategies adopted at various levels of dysgeusia and time to time psychological counseling.

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