



Chemotherapy induced oral mucositis: prevention is possible

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Abstract

Oral mucositis (OM) is a frequent side-effect of antineoplastic treatments. Patients usually describe the first symptom as burning sensation in the mouth and swelling, erythema or ulceration and pain will follow.

These will place them at a higher risk of infection, might impair significantly their nutritional status and worsen their quality of life. Consequently, OM might lead to noncompliance with the oncological treatment with a negative impact on survival. Numerous treatments have been used to alleviate OM and improve patient's nutritional status, but so far, no definite therapy has demonstrated the ability to prevent it.

We have recently published a prospective study in patients with breast cancer undergoing treatment with neoadjuvant or adjuvant intent. Patients received either FEC (5 fluorouracil, epirubicin and cyclophosphamide) or Docetaxel. Our results showed a significant reduction in the rate of OM grade 2-3 with a especial mouthwash containing steroids, antifungal and saline. Patients were instructed on the correct use based on the chronology and duration of the previous episode of OM. Although further evaluation is warranted, we have been widely using this especial mouthwash in our patients.

We present here the case of a male diagnosed with colorectal cancer, who has been receiving palliative treatment with FOLFOX and Panitumumab. He struggled with OM after the first cycle and after using the special mouthwash, he found a significant benefit with the following treatments.

Introduction

Oral mucositis (OM) is a frequent side-effect of systemic chemotherapy (CM) and radiotherapy for cancer (1-3).

In patients receiving conventional CM, OM has been described in 20-40% of the cases (4).

Chemotherapeutic agents target rapidly dividing cells such as the oral mucosa lining and this leads to

atrophy and ulcers. OM usually starts 5 to 10 days after the treatment administration and patients usually describe the first symptom as burning sensation in mouth. Later, swelling, erythema or ulceration and pain will develop.

These will place patients at higher risk of infection, might impair significantly their nutritional status and worsen their quality of life (4,5).

Consequently, OM might lead to noncompliance with the oncological treatment as it may become a dose-limiting toxicity, requiring CM dose reductions or delays or even definite interruptions.

There are numerous treatments to alleviate the symptoms caused by OM and improve patient's nutritional status, but so far no definite therapy has demonstrated the ability to prevent it and it is expected that the intensity of OM worsens with further cycles of CM (1,2,6).

Our institution has recently published a prospective study evaluating the role of a specific mouthwash consisted of a combination of 100 mL of water, 5 mg of soluble prednisolone, 2 drops of nystatin and 2.300 mg of salt (1 teaspoon) in breast cancer patients undergoing neoadjuvant or adjuvant treatment who had developed OM grade 2 or 3 with the previous cycle (7).

We found a significant reduction in the rate of OM grade 2-3 with following cycles in those patients after using this especial mouthwash, with no need for CM dose reduction for most patients. Although further evaluation is warranted, we have been widely using this especial mouthwash in our patients.

We present here the case of a male diagnosed with colorectal cancer, who has been receiving palliative treatment with FOLFOX and Panitumumab. He struggled with OM after the first cycle and after using the special mouthwash, he found a significant benefit with following cycles.

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Case Report(s)

A male 55 years old, diagnosed with sigmoid adenocarcinoma underwent oncological surgery. The histopathological diagnosis showed a pT3N0 tumour with extramural vascular invasion. The patient received adjuvant treatment with Capecitabine for 6 months.

After an interval free of disease of 2 years, a surveillance CT scan showed liver metastases. The patient started a treatment with FOLFIRI and Bevacizumab achieving good response and underwent liver metastasectomy.

Three years later, another surveillance CT showed a solitary peritoneal nodule and a liver lesion. Both locations were considered resectable and the patient was subjected to another surgery.

Nine months after, the disease progressed significantly in liver and peritoneum although the patient was asymptomatic. He started a treatment with FOLFOX (5-fluorouracil and Oxaliplatin) and Panitumumab.

After the first cycle, he developed sickness grade 1 and OM grade 2-3 which impacted on his nutritional status negatively. We increased the dose of antiemetics and discussed with him about using the special mouthwash to prevent OM with its uncertainties, versus reducing the dose of CM. He was happy to try the mouthwash for the second cycle. We established the chronology for the OM after the first cycle and its duration. Then we recommended him to start this special mouthwash 3 days before the expected OM would appear and to continue it at least for 3 days after the expected duration (based on the first cycle).

In his next pre-chemotherapy visit, he confirmed that he had not developed any OM at all and was able to continue eating properly.

He continued to receive full dose of the CM for further 3 months without any significant issues. Then he started to feel more fatigued, with more significant diarrhoea and anorexia, although manageable and OM appeared again but grade 1-2. The dose of steroids in the mouthwash was doubled and was able to continue for another 6 weeks without major issues. Later, the dose of CM was reduced due to several cumulative side-effects, but OM was manageable, being only grade 1.

The patient has shown partial response to treatment and continues to receive maintenance therapy with Panitumumab.

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Discussion

Patients with advanced colorectal cancer benefit from CM in terms of survival and quality of life [8-12].

Fluoropyrimidines are the most common agents used [9] and phase III studies have shown that combinations with irinotecan or oxaliplatin improve response rates and survival [13-15].

Panitumumab is a fully human anti-epidermal growth factor receptor (EGFR) monoclonal antibody that improves survival in KRAS wild-type metastatic colorectal cancer. The study by Douillard *et al* showed that Panitumumab added to FOLFOX4 significantly improved progression-free survival (PFS) compared to FOLFOX4 in patients with KRAS exon 2 wild type tumours (16).

A trial evaluating the efficacy and safety of panitumumab plus FOLFIRI compared with FOLFIRI alone in second line demonstrated that the combination significantly improved PFS but showed that one of the most common adverse events was OM (51%). Grade 3 or 4 OM affected 8% of the patients receiving Panitumumab plus FOLFIRI versus 3% on FOLFIRI alone (17).

A phase II study of Panitumumab in combination with FOLFOX or FOLFIRI as first line in wild-type metastatic colorectal cancer, has shown good results with grade 3 or above OM in 10.5% of the patients (18).

As mentioned before OM is a clinically important adverse-event which sometimes become a dose-limiting toxicity of cancer treatment. Stomatitis lesions are painful, may deteriorate nutrition and patient's quality of life and eventually may oblige to reduce CM dose with its potential negative effects on final results.

The pathogenesis of OM is complex although inflammatory cytokines and reactive oxygen species seem to play a key role (7,19).

Current management of OM is focused on alleviating the pain and improving nutritional status.

Several strategies have been used to try prevention but unfortunately, the available results are heterogeneous and inconclusive (19,20).

As we had a very good experience in our institution with this special mouthwash (nicely called "the recipe" by our patients) in the breast cancer population, we decided to use it widely in patients with other primary tumours (7).

The case we present here showed a significant benefit

with this mouthwash after a first episode of OM grade 2-3. Without any intervention to prevent this, it is expected that the intensity of OM with the second episode would have been higher and this adverse event would have been a dose limiting toxicity.

Our patient was able to continue with full dose CM for further months without any dose reduction. Then, although OM appeared, the grade was manageable and by increasing the dose of steroids in the mouthwash, he was able to continue for longer without any CM dose change.

The patient showed a partial response to the treatment which impacts positively on his prognosis and as OM was prevented, his quality of life was significantly better while receiving active treatment.Â

Conclusion

This case shows good results in terms of prevention or reduction in intensity of OM induced by CM.

Although we need further evaluation, so far our results are positive enough as to continue to recommend this recipe in those patients who have developed OM with first cycle, to prevent further episodes and to be able to maintain CM dose.Â

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