UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

New Literature: Oral Indomethacin Spray for Oral Mucositis Pain

Background:

Oral Mucositis (OM) is a common side effect of anti-cancer treatment and is characterized by erythema and ulceration of the GI tract. The MASCC/ISOO Clinical Practice Guidelines for the management of mucositis recommend basic oral care, topical morphine 0.2% mouthwash, and photobiomodulation for the treatment of pain from OM. These guidelines also suggest there is new evidence for the use of topical benzydamine, a non-steroidal anti-inflammatory drug (NSAID), however this drug is not available in the US.

Indomethacin is an NSAID that has analgesic, antipyretic, and anti-inflammatory properties. In the US, indomethacin is available in oral formulations (capsule, ER capsule, suspension), intravenous formulations (solution, preservative-free solution), and as a rectal suppository. All NSAIDs, including indomethacin, have a black box warning for risk of serious cardiovascular thrombotic events (including MI and stroke) and serious gastrointestinal bleeding, ulceration, and perforation.

Importance:

Oral mucositis occurs in more than 70% of patients undergoing anti-cancer treatment for head and neck cancer. Oral mucositis may result in difficulty sleeping, eating, talking, taking oral medications, and can lead to discontinuation of cancer therapy. Palliative care clinicians should be aware of new potential options for treating OM pain.

The Literature:

J Pain Symptom Manage. 2021 Sept 3;62(3):P537-544.

Effects of an indomethacin oral spray on pain due to oral mucositis in cancer patients treated with radiotherapy and chemotherapy (JORTC-PAL04)

Objective: Evaluate the efficacy and safety of indomethacin oral spray to relieve oral mucositis pain caused by anti-cancer treatment

Outcomes:

- Primary:
  - Change in the numerical rating scale of current pain [Brief Pain Inventory (BPI) Item 6] from before to 30 minutes after administration
- Secondary:
  - Number of participants who achieved pain reduction of 25%, 33%, and 50%, 30 minutes after treatment
  - Changes in the rating of current pain before and 15, 60, 120, 180, and 240 minutes after treatment
  - Changes in AUC of current pain rating from 0-60, 0-120, 0-180, and 0-240 minutes
  - Improvement in the Clinical Global Impressions-Improvement (CGI-I) scale

Methods:

- Single-center, double-blind, placebo-controlled, RCT of 0.25% indomethacin oral spray versus placebo in patients with chemotherapy and/or radiation therapy-related OM pain
- NSAIDs, opioids, or other analgesics that were already used regularly could be continued
- Indomethacin spray was compounded by making a 1.25% indomethacin solution, adding a buffered solution, and passing the resultant solution through a membrane filter
- Indomethacin or placebo spray was sprayed four times (0.8 mg indomethacin) and pain intensity was recorded at 15, 30, 60, 120, 180, and 240 minutes after administration
- During the initial 240 minutes, additional doses of study drug, rescue doses of other analgesics, eating, and oral care were not permitted
- Indomethacin oral spray or placebo was used 30 minutes before meals (TID), and as a rescue at times of pain during the 14-day study period

Results: n=60 (40% female, average age = 60.7)

- Mean change in pain intensity between the indomethacin and placebo groups was statistically significant: -1. 26 (95% CI: -1.94 to -0.57) *p<0.01*

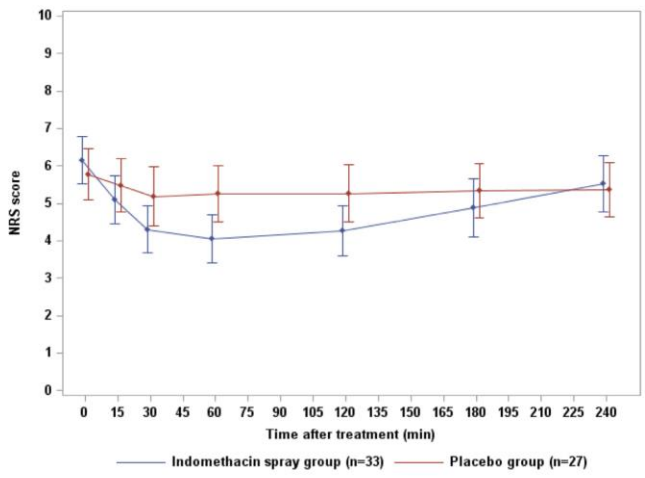

Fig. 2. Changes in mean scores of BPI Item 6 in each group before and after drug administration. Bars indicate 95% confidence intervals in each group.

CLINICAL PEARL:

Indomethacin oral spray (NSAID) may be a safe alternative for treatment of oral mucositis pain, although it may be difficult to obtain

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Results (continued):

- Number of patients that achieved 25% and 33% reduction in pain was significantly higher in the indomethacin group (25%: 67% vs 22%, p<0.01, 33%: 49% vs 19%, *p<0.01*)
- Pain intensity was significantly lower 15, 60, 120, and 180 minutes after treatment (*p<0.05*)
- Percent improvement on the CGI-I was significantly higher in the intervention group compared to placebo (49% vs 11%, *p<0.01*)
- No adverse events reported in the intervention group

Conclusion: Indomethacin oral spray relieved short-term OM pain and may reduce difficulty with eating or having conversations in patients with anti-cancer treatment-related OM

Bottom Line:

- Indomethacin oral spray is safe and provided significant reduction in oral mucositis pain compared to placebo
- Indomethacin oral spray may be a safer alternative to systemic opioids
- Lack of data to support efficacy of indomethacin compared to current guideline-directed therapies, as this was a placebo-controlled trial
- Indomethacin oral spray formulation would not be available for inpatient hospital use, and would need to be compounded at a compounding pharmacy, like Asti's or Hieber's for outpatient use
- Trial procedure (no eating/drinking/oral care for 4 hours after initial indomethacin spray) does not coincide with probable patient use and may not be feasible in the real world.. and we don't know how eating or drinking would impact duration or degree of relief
- Indomethacin spray was shown to relieve pain for up to 3 hours; Patients would likely have to use this spray up to 8 times a day for around the clock relief which may be cumbersome
- Potential for less burning in topical product as it is not compounded in alcohol solution compared to other topical products, like morphine…

CLINICAL PEARL:

Indomethacin oral spray (NSAID) may be a safe alternative for treatment of oral mucositis pain, although it may be difficult to obtain