Evaluating The Effectiveness Of Topical Metronidazole In Alleviating The Offensive Odor Of Fungating Tumors

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A. Aim

To evaluating the effectiveness of topical metronidazole in alleviating the offensive odor of fungating tumors vs. placebo by following smell scores after therapy.

B. Background

The offensive smell of fungating or ulcerated malignant tumors had long been a major distress to patients and care givers and poses marked limits to the quality of life of these mostly terminal patients. The offensive odor is thought to be secondary to volatile fatty acids produced by the catabolism of lipids by anaerobic bacteria that have colonized the wounds. Oral metronidazole has been shown to be effective in alleviating the odor. However it has to be used continuously because of rapid recolonization after treatment is stopped. This can be difficult for patients because of Flagylls GI side effects, leukopenia, neuropathy and the need for abstinence from alcohol. Therefore topical metronidazole was proposed as an alternative.

There is only one, randomized, double-blinded placebo controlled trial looking into the effectiveness of topical Flagyl. Bower et. al. in 1992 randomized 11 patients to either 0.8k Flagyl gel or placebo gel for 6 days. All patients received 5 more days of Flagyl gel after the initial 6 days. Smell scores on a scale of 1-10 as assessed by the patients and the investigators were recorded everyday and compared. The resu ' lts of the study was that while there is a trend in favor of Flagyl gel, it was not statistically significant. There is however statistically significant decrease in smell scores from day 1 to day 11, but this is in both groups and after both groups had received Flagyl for 5 more days. These numbers, while encouraging, are not without flaws. First the smell score use are subjective and without internal control for variations between one person to another. Second, the rate of decrease in smell in the group who only received 5 days of Flagyl is much faster than the group who started out with Flagyl--suggesting perhaps a bias or confounder. Lastly, the data presented showed that there is a fall in smell in the placebo group racing the question whether that the simple process of gel application and dressing changes may be enough to cause significant decrease in smell.

This study is design to try to better evaluate the effectiveness of Flagyl gel used for this purpose.

C. Hypothesis

Topical Flagyl will significantly alleviate the offensive odor of fungating tumors.

D. Methods

This will be a randomized, placebo-controlled crossover trial comparing the effectiveness of 0.75% metronidazole gel (Metrogel) vs. a placebo gel in reducing the odor of a fungating tumor.

E. Patient Selection

Since most malodorous fungating tumors happen to be in women with late stage breast cancers. We hope to recruit as many female patient with malodorous fungating tumors of the breast within a 1 year period from the staff at CPMC and at a local Hospice. We expect to be able to recruit approximately

15-20 patients. Members of the research team will approach potential subjects, explain the study, and obtain informed consent. Women of any age with malodorous fungating tumors of the breast with a smell score >6 (as judged by 3 independent smell raters who are professionally train to judge the degree of offensiveness with consistency) will be asked to participate in the trial if they do not meet the following exclusion criteria:

1. antibiotic use within 4 weeks of the study.
2. chemo, surgical, or radiotherapy 4 weeks prior to or during the study.
3. hypersensitivity to topical Flagyl.
4. patient not expected to live within the next 30 days.

F. Study Location

The study will take place either in the inpatient portion of the ICCR or at the Hospice where the patient is recruited.

G. Study Protocol

The patients will be randomized to start with eiEh-erMetrogel or placebo placed topically twice a day at approximately 1gm/sq. cm over the wound and dressed sterilly. Treatment and crossover as described in the table below.

group	Days		
	1-10	11-20	21-30
A	Metrogel	Metrogel	Placebo
B	Placebo	Placebo	Metrogel

a. Measures

Patients in each group will be rated from a scale of 1-10 by the previously mentioned smell raters on days 1, 10, 20, and 30. Pt's are to be rated during the 2nd dressing change on these days (except day 1) after the dressing has been removed and all visible gel has been removed by normal saline and the wound made dry with gauze.

b. Statistical Analysis

Statisical analysis will be an analysis of variables with pre-planned comparison designed to assess the effect of treatment after adjusting for carry over effects.

H. Risk And Benefits

There has not been any major risk ass. with use of topical form of Metronidazole reported in the PDR or in the literature. The only potential benefit of this study to the patient is the alleviation of the smell of their tumor that so bordered them.

I. Alternative Therapies

Oral Flagyl with its advantages and disadvantages as mentioned above will be discussed with patients.

J. Compensation

There will be no compensations or costs to the subjects.

K. References

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4 Bower, M. et al. A Double-blind Study of the Efficacy of Metronidazole Gel in the Treatment of Malodorous Fungating Tumours. Eur J Cancer 1992, Vol. 28A, No. 4.5, 888-889.

5 Rotimi, V. et al. The bacteriology of infected malignant ulcers. J Clin Pathol 1984; 37: 592- 595.

6 Kuge, S. et al. Use of Metronidazole gel to Control Malodor in Advanced and Recurrent Breast Cancer. Jpn J Clin Oncol 1996; 26: 207-210.