MINIMIZATION OF ANOREXIA IN CANCER PATIENTS RECEIVING ABDOMINAL RADIOTHERAPY

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MINIMIZATION OF ANOREXIA IN CANCER PATIENTS RECEIVING ABDOMINAL RADIOTHERAPY

BY

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ABSTRACT

The primary concern of this paper was with the anorexia (loss of appetite) in cancer patients receiving abdominal radiotherapy. It was felt that this anorexia, and the associated weight loss, were partly due to conditioned food aversions resulting from the radiation treatment. Experimental patients were told not to eat breakfast (the meal prior to irradiation) to avoid the development of conditioned food aversions. These patients were expected to lose less weight than control patients who were not given specific instructions regarding food intake prior to morning irradiation. A food preference questionnaire was administered at the beginning of treatment and at two weeks post treatment. No significant differences were found between experimental and control patients on either the food preference measure or on amount of weight loss at two weeks after treatment. There is no substantial diminution of anorexia to be obtained from not eating breakfast prior to X-irradiation treatment.

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INTRODUCTION

Cancer cachexia is malnourishment proceeding to wasting of body tissues, (Campbell, 1981; Kisner & DeWys, 1982) and was reported by Warren (1932) to be the only identifiable cause of death in over 22% of a sample of 500 patients. Cachexia with its resultant malnutrition is characterized by anatomical alterations, anorexia and altered metabolism (Costa, 1977).

This paper is primarily concerned with part of the cachexia problem - anorexia (loss of appetite resulting in decreased food intake). A number of factors (for example, flavour and/or olfactory alterations, radiotherapy, psychological components) may be responsible for the anorexia component of cancer cachexia. Our main concern is with one of these, namely, radiotherapy. A large percentage of patients undergoing high doses of radiation experience significant weight loss during treatment (Donaldson, 1977; 1982). The dominant view, as expressed by Donaldson, seems to be that this anorexia is a direct physiological effect of the treatment. However, the possibility underlying the present work was that it is at least partly due to conditioned food aversions resulting from the radiation treatment. This carries the implication that conditioning principles

may be used to mitigate the anorexia and the consequent weight loss.

No other treatment is known to be as effective at producing conditioned flavour aversions in animals as X-irradiation which is demonstrated by exposing animals to irradiation after they consume a flavoured solution. In rats a single, whole-body, 50 to 100 rad dose of gamma irradiation will produce an aversion to saccharin or sucrose solution consumed as much as 7 to 12 hours earlier (Revusky, 1968; Smith & Roll, 1967). Also, a single 30 rad dose administered together with saccharin drinking will cause the rat to avoid saccharin drinking over a month of continuous availability of both saccharin solution and unflavoured water (Garcia, Kimeldorf & Koelling, 1955).

These powerful flavour aversions depend upon associative learning. The saccharin (or other flavoured substance) must be consumed before the sickness has reached its peak if a learned aversion is to be obtained. In the event that a flavoured substance is consumed after the peak of apomorphine sickness, it may become more highly preferred rather than aversive because its consumption is associated with recuperation from the sickness (Green & Garcia, 1971). Although textbooks treat anorexia as a primary symptom of radiation sickness (Murphy, 1959) a rat will readily consume a novel substance presented at the peak of sickness. This anorexia is specific to what was consumed prior to the sickness (Revusky & Garcia, 1970), indicating conditioning.

It is nearly certain that all mammals exhibit these conditioned flavour aversions (Revusky & Garcia, 1970). Conditioned flavour aversions in humans have been shown through retrospective questionnaires (Garb & Stunkard, 1974). Through experimental studies, Bernstein (1978) demonstrated that children undergoing chemotherapy developed an aversion to the flavour of a novel ice-cream consumed prior to treatment. Indeed, Boland, Mellor & Revusky, (1978) were able to extrapolate from the animal literature on flavour aversions to develop improvements in chemical aversion therapy (CAT) for alcoholics. CAT is the production of therapeutic aversions to alcohol by pairing alcohol consumption with sickness induced by a drug.

Dr. K. Hong (personal communication), head of the radiation/oncology unit at the General Hospital, Health Sciences Complex, St. John's, Newfoundland has noted in his clinical experience that radiation to the abdominal region produces the most intensive sickness. This also seems true in animals as reported by Kimeldorf & Hunt (1965). The main hypothesis of the present study was that patients receiving radiation to the abdomen who did not eat breakfast prior to morning radiation treatment would lose less weight than control patients who were not given specific instructions regarding food intake prior to morning radiation treatment. By extrapolation from previously cited animal work, sickness produced by radiotherapy may be associated with the foods consumed prior to the sickness, but not with foods consumed after the sickness. If so,

administration of radiotherapy while the patient is fasting should diminish the anorexia produced by radiation sickness. Note that this strategy was not intended to eliminate the gastrointestinal upset, but to lower the possibility of conditioned food aversions resulting from that upset. It was felt, therefore, that patients receiving partial-body irradiation, while fasting, would experience less aversions than patients who consumed food prior to irradiation treatment.

In addition, a measure of food preferences was taken to determine whether the aversions formed by the control group were specific to breakfast foods. It was expected that control subjects would develop specific aversions to what was eaten during breakfast, the meal immediately preceding radiation, while the experimental subjects would not.

METHODS

Subjects: The original intention of this study was to use 60 outpatients scheduled for abdominal radiotherapy. However, initially the subjects in the experimental group seemed to be losing weight more rapidly (both at the end of treatment and at the two week follow-up) than were the control group. These findings suggested that the

experimental treatment might be detrimental to the experimental subjects. It turned out that this impression was premature, but at this point no new subjects were added to the experiment. The net result was that there were 14 outpatients who received a full-course of abdominal radiotherapy. Patients receiving chemotherapy along with radiotherapy were excluded.

One control subject chose to terminate treatment upon completion of 63% of the recommended irradiation dosage and was excluded from the experiment. One experimental subject chose to eat breakfast after she had completed 80% of her treatments but was included in the analysis. Prior to the collection of data, it had been decided to include such subjects.

There were six experimental subjects (3 male / 3 female: mean age = 60.16; age range = 56 - 65) and seven control subjects (1 male / 6 female: mean age = 50.14; age range = 32 - 60). Abdominal radiation for all patients ranged from 4000 - 5250 rads (mean dosage = 4280.77) with the number of treatments varying from 18 to 25 (mean = 21.77). Size and location of field for the control group and the experimental group are indicated in Tables 1 and 2 respectively. These tables also include personal data (relevant to this study) on each of the 13 patients who completed treatment.

TABLE 1

Demographic and pertinent treatment variable information relevant to each control subject

Subj. No.	Age	Sex	Field Size (cm)	No. of Rads	No. of Treatments	Abdom. Locat.
1	58	M	15x15	4400	22	lower
3	32	F	15x15	4250	22	lower
5	37	F	16x18	4500	24	lower
8	57	F	15x15	4400	23	lower
10	59	F	20x23	4150	21	lower
12	60	F	15x18	4250	22	lower
14	48	F	15x20	4000	18	lower

TABLE 2

Demographic and pertinent treatment variable information relevant to each experimental subject

Subj. No.	Age	Sex	Field Size (cm)	No. of Rads	No. of Treatments	Abdom. Locat.
2	56	F	15x18	4200	25	lower
4	58	F	15x15	4000	20	lower
6	65	M	15x18	4500	21	lower
7	61	M	13x16	4000	20	lower
9	61	F	15x15	4000	20	lower
11	60	M	14x15	5250	25	lower

Procedure

Upon arrival at the radiation/oncology unit the patient underwent the usual hospital routine after which he/she was interviewed by the experimenter. During this session the patient was asked specific questions about his/her food preferences. The patient was asked to list three foods he preferred for each of breakfast, lunch and dinner. Then the patient was asked to rate the foods on a scale from one to five with "1" being "dislike very much", "5" being "like very much" and "2", "3" and "4" determining points in between "1" and "5" (see appendix A for further details). The sequence of ratings was made in a counterbalanced order based on assignment of the foods to random blocks such that one food from each meal was included in each block. At the two week post irradiation follow-up patients were requested to scale the foods in the same order as they did after treatment so as to detect any food preference changes.

Upon completion of the food preference interview the patient was assigned to one of two predetermined categories. The two categories were based on location of pathology (category 1: upper abdomen; category 2: lower abdomen) using the umbilicus as the center of origin. To qualify as a subject for this research the patient was to receive between 15 and 25 treatments, was to be 75 years of age or

younger (born since Dec. 31, 1906), and have had abdominal cancer to be treated by radiotherapy.

The patients were paired sequentially and one in each pair was randomly assigned to each group. If the patient was assigned to the experimental group he/she was told not to eat breakfast on treatment days and not to eat for two hours after treatment (see appendix B for details). The control group was not given any directions.

Body weights were taken on the day of the first visit, on the morning of the first radiation treatment and on the last day of treatment. A two week and an eight week follow-up were also conducted on the 13 patients who completed radiotherapy (for pertinent information see appendices C and D).

RESULTS

Weight Gain/Loss Results

The histogram in figure 1 indicates the mean body weight in kilograms before treatment, day 1 of treatment, the last day of treatment, two weeks after treatment and eight weeks after treatment for the experimental and the control groups. There was no significant difference in body weights between the two groups on day 1 of treatment (t (11) = 0.32). No significant difference in percentage

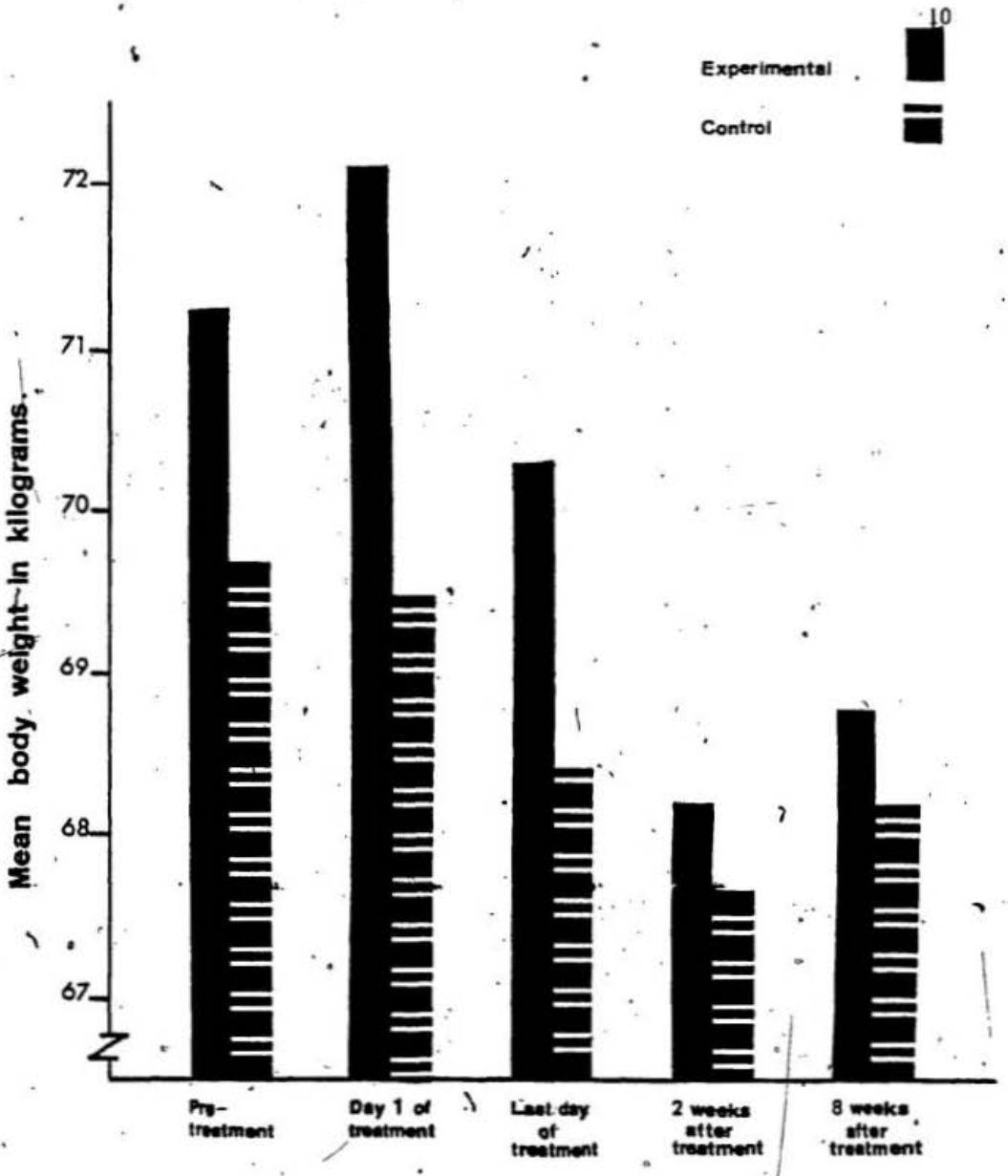

Figure I: Histogram for mean body weight for each group.

weight loss was found between either of the two groups on the last day of treatment (t (11) = 0.11), two weeks after treatment (t (11) = -1.06) or eight weeks after treatment (t (11) = -0.55).

To point to the sensitivity of our analysis 90% confidence intervals (CI) based on the t values for percentage weight loss between the two groups was calculated for the last day of treatment (CI = -0.17 ± 2.02), two weeks after treatment (CI = -1.51 ± 2.06) and eight weeks after treatment (CI = -1.49 ± 3.40). It can be stated from the confidence intervals that if by chance the experimental group weighed more than the control group this difference would be only by .56%. Conversely, if the control group weighed more than the experimental group, the weight difference would be greater by only 3.75%. Also, if the difference between the two groups was more than 0.56%, we were victims of a sampling error that would occur less than 5% of the time by chance. In practice, this means that we excluded the possiblity of a large effect in the predicted direction. In more concrete terms, if fasting prior to irradiation treatment reduces the loss of body weight, this reduction (unless we have an unusual sampling error) is less than 0.56%.

The mean percent loss in body weight for the control group on the last day of treatment was -1.88%, two weeks after treatment was -3.26% and eight weeks after treatment was -2.50%. The mean percent loss in body weight for the experimental group on the last day of treatment

was -1.72%, two weeks after treatment was -4.63% and eight weeks after treatment was -4.20%.

The difference in ages between the two groups (Tables 1 and 2), although not statistically significant, was worrisome. However, an analysis of covariance using age as the covariate did not change the statistical conclusions.

In collating the information obtained in the follow-up questionnaires patients experienced very little nausea and no vomiting. All patients experienced mild to moderate diarrhea.

Diet Preference Results

The mean differences in the ratings for the preferred foods for each meal are shown in Table 3. These negative values indicate that, though the food preference changes are in the right direction, neither the experimental group nor the control group experienced a specific food preference change.

When a repeated measures analysis of variance on the differences between pre/post food preference changes was calculated, no significant differences were found for the meals ($F(2,22) = 0.37$) nor was there a significant difference between the groups ($F(1,11) = 1.04$). What was most important was the groups by meals interaction

which showed no significant effect on food preference changes ($F(2,22) = 0.11$). This indicated, contrary to what was expected, that the experimental group did not show a higher specific preference for breakfast foods than did the control group.

DISCUSSION

This study was based on the assumption that the anorexia suffered by cancer patients was due in part to conditioned flavour aversions. This being the case, an experimental procedure separating radiation from ingestion so as to minimize such aversions ought to be beneficial. Patients requested to fast prior to irradiation treatment were expected to lose less weight than the control patients. However, this expectation was not confirmed as both the experimental group and the control group exhibited approximately equal weight loss at 2 weeks post treatment. It was established by means of confidence intervals, that even if we failed to support our hypothesis due to a sampling error, it would be unlikely that the difference in weight loss in favour of the experimental group could be more than 0.5 kilogram. It is therefore suggested that our experimental manipulation was not useful in ascertaining the development of flavour aversions in the patients we observed.

TABLE 3

Table 3 indicates the mean differences between pre/post treatment measures obtained for breakfast, lunch and dinner on food preference changes for the experimental and the control group

	Breakfast	Lunch	Dinner
Experimental	-2.500	-2.000	-2.167
Control	-1.571	-0.571	-1.571

In analyzing the diet preference questionnaires no significant changes occurred in food preferences for either group for breakfast, lunch or dinner.

On the basis of the animal literature our procedure appeared to be quite plausible because irradiation is known to produce strong flavour aversions (Garcia, Kimeldorf & Koelling, 1955; Revusky, 1968). Also, the abdominal site selected for observation is the site that results in the most intense aversions produced by radiation (Garcia & Kimeldorf, 1960; Kimeldorf & Hunt, 1965). This is why it was felt that, because the control group ate breakfast prior to treatment, it would form stronger food aversions, exhibited as anorexia, than would the experimental group. However, these reasonable extrapolations and assumptions were not supported. It is conceivable that radiation induced anorexia has become less of a problem in the last few years due to improvements in the use of computerized tomography. At present, the radium beams are directed specifically on the neoplasm with much less destruction of normal body tissue than in previous years. This, according to Dr. Hong and Dr. Firme (Radiation/Oncology Unit, General Hospital, personal communications) would minimize abdominal sensitivity and gastrointestinal upset.

It was further suggested by Dr. Firme that the minimal gastrointestinal upset experienced by the patients in this study could

be accounted for in large part by the site irradiated. That is, our patient population received lower abdominal irradiation, which according to Dr. Firme, is less susceptible to radiation sickness than the upper abdomen, the lungs, breasts and/or lymphoma. He also stated that the minimal gastrointestinal upset could be accounted for by the amount, the rate and the volume (per body mass) of the irradiation dosage administered as well as by the precision with which the mapping of the site to be irradiated was done.

Though flavour aversions occur in irradiated animals (Kimeldorf & Hunt, 1965) it is possible that chemical treatments would produce stronger aversions in humans. This appears reasonable as chemotherapy affects the whole body causing severe nausea and vomiting in patients undergoing this type of treatment (Laszlo, et al, 1981). It is therefore speculated that our negative results may be accounted for, in part, by the localization of irradiation which resulted in very little nausea and no vomiting in our patient sample.

Another possible factor responsible for our negative results may have been a minimal difference in food intake between the two groups prior to irradiation treatment. That is, the experimental group did not eat breakfast while the control group ate a very light meal (usually only toast with tea or coffee). Furthermore, these breakfast foods are highly familiar and relatively bland which may have made them less amenable to the production of conditioned food aversions

than the more flavourful and wider variety of foods generally consumed during lunch and dinner. If so, one might expect learned aversions to occur more readily to lunch and dinner foods if they were to be consumed prior to or immediately following afternoon or evening irradiation exposure. This possibility has not been tested.

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APPENDIX A

Diet Interview

1. What three foods do you eat most frequently for breakfast? (be specific)

2. What three foods do you eat most frequently for lunch? (be specific)

3. What three foods do you eat most frequently for dinner? (be specific)

Patient No. ..... Random No. Scale 1. 2. 3. 4. 5.

Breakfast foods:

1. ....

2. ....

3. ....

Lunch foods:

4. ....

5. ....

6. ....

Dinner foods:

7. ....

8. ....

9. ....

APPENDIX B

Patient's Name: .....

Your treatments will begin on .....

.....

Please do not eat any solid foods or drink any beverages for 6 hours before you come for treatment.

Also, do not eat any solid foods or drink any beverages for 2 hours after your treatment.

Water, coffee or tea however, may be taken at any time before or after your treatment.

APPENDIX C

Questions pertaining to the two week follow-up for all subjects.

1.) How are you feeling since you completed your treatment?

2.) Did you feel nauseated or experience any vomiting at any time after your treatment?

3.) Did you suffer from diarrhea any time after your treatment?

4.) Do you ordinarily eat breakfast?

5.) Did you eat breakfast before you had your treatment?

6.) Before you began your treatments you filled out a food preference questionnaire. At that time you listed three foods you preferred for breakfast, lunch and dinner. You were also asked to rate the foods on a scale from one to five with "1" being "dislike very much", "5" being "like very much" and "2", "3" and "4" determining points in between "1" and "5". At this time, I will list the foods which you indicated before your treatments and you are requested to rate them on the same scale of "1" - "5".

Weight was recorded after the interview.

APPENDIX D

Questions pertaining to the eight week follow-up for all subjects.

1.) How are you feeling?

2.) Any problems with nausea, vomiting and/or diarrhea?

3.) How is your appetite?

4.) Are there any foods which you prefer not to eat since you completed treatment eight weeks ago?

5.) What foods are they? *

6.) What do you think is the reason for this? *

7.) Did you eat breakfast before your treatment?

8.) What did you ordinarily eat for breakfast before treatment?

9.) Is there any change in what you eat for breakfast now?

Weight was recorded at the end of the interview.

* Numbers 5 and 6 were only asked if the subject indicated a positive response to number 4.