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Research Article

Prevalence and Temporal Course of Chemotherapy-Induced Ageusia and Anosmia in Breast, Colorectal, and Lung Cancer Patients: A Prospective O0bservational Study

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ABSTRACT

Background: Taste and smell disturbances are common but under-recognized consequences of cancer chemotherapy. This study describes the prevalence and 12-week temporal course of chemotherapy-induced ageusia and anosmia across four regimens used for breast, colorectal, and lung cancer.

Methods: In this prospective observational study conducted in the Department of Medical Oncology, King George Hospital, Visakhapatnam, India, 100 adults undergoing chemotherapy (trastuzumab or adriamycin for breast cancer; capecitabine for colorectal cancer; paclitaxel for lung cancer) were enrolled and followed for 12 weeks. Taste and smell symptoms were assessed with the Chemotherapy-Induced Taste Alteration Scale (CiTAS) and the Self-Administered Odor Questionnaire (SAOQ) at intervals coinciding with chemotherapy cycles.

Results: Ageusia and anosmia were each reported by all 100 patients (100%; 95% exact CI 96.4–100%). The cohort was 51% male and 49% female; sex was completely or almost completely confounded with regimen (both breast-cancer regimens were 100% female, the lung-cancer regimen 100% male, and the colorectal-cancer regimen 81% male). Female patients were significantly older than male patients (53.6±13.9 vs 46.2±12.2 years, p=0.005). Across all four regimens, most patients' symptoms were first documented within weeks 1–5 of treatment (59.1–65.5% for ageusia, 54.6–68.2% for anosmia), with progressively fewer patients documented in later windows — except for capecitabine, for which the proportion recorded at weeks 11–15 (22.2%) exceeded that at weeks 6–10 (18.5%). Planned analyses of CiTAS/SAOQ severity scores and EORTC QLQ-C30 quality-of-life domains could not be verified against the scoring procedures specified for these instruments and are not reported (see Limitations).

Conclusion: In this single-center cohort, chemotherapy-induced ageusia and anosmia were universal, and their timing differed somewhat by regimen, with a possible late-phase increase in anosmia under capecitabine that warrants confirmation. Because sex, cancer type, and regimen were almost entirely confounded and several planned quality-of-life analyses could not be validated, these findings should be treated as descriptive and hypothesis-generating. Larger, multi-center studies with independently verified instrument scoring are needed.

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Introduction

Cytotoxic and targeted chemotherapy agents damage rapidly dividing epithelial cell populations, including the taste bud and olfactory epithelial cells that normally turn over every 10–14 days; disruption of this turnover is one proposed mechanism for chemotherapy-associated taste and smell disorders [1,2]. Reported prevalence estimates for chemotherapy-induced taste alteration vary widely in the literature, from under 20% to over 70%, depending on the population studied, the regimen used, and the measurement instrument [2,3]. Smell disturbances have been studied less often than taste disturbances but appear to follow a broadly similar course [1]. Both symptoms are consistently associated with reduced appetite, unintended weight loss, and lower self-reported quality of life among cancer patients [3,4], and chemosensory dysfunction more broadly is known to alter food-related behavior even outside the oncology setting [6]. Despite this burden, taste and smell dysfunction remains under-recognized in routine oncology care relative to more visible toxicities such as nausea or peripheral neuropathy [5].

Most existing studies of chemotherapy-induced taste and smell disturbance are cross-sectional or focus on a single tumor type or regimen [2,3]. Comparative, prospective data spanning multiple regimens and tumor types are comparatively scarce. This study describes the prevalence, and the 12-week timing, of ageusia and anosmia in patients receiving four regimens commonly used for breast, colorectal, and lung cancer at a single tertiary oncology center in India.

Materials and Methods

Study design and setting

This was a prospective observational study conducted in the Department of Medical Oncology, King George Hospital, Visakhapatnam, India, with a 12-week follow-up period per patient.

Ethics approval

The study protocol was reviewed and approved by the Institutional Ethics Committee, King George Hospital (Reg. No. ECR/197/Inst/KGH/2013/RR-20). Written informed consent was obtained from all participants in English or Telugu prior to enrollment.

Participants

Inclusion criteria were: adult patients (≥18 years) undergoing chemotherapy; histopathologically confirmed breast, lung, or colorectal cancer; ability to provide informed consent; and availability for follow-up assessments. Exclusion criteria were: not undergoing chemotherapy; pre-existing taste or smell disorder unrelated to chemotherapy; significant cognitive impairment or communication barriers precluding study participation; and pregnancy or breastfeeding.

Sample size was estimated using Cochran's formula, assuming a population proportion of 0.5, an acceptable margin of error of 9.8%, and a 95% confidence level, yielding a target of 100 participants. One hundred patients were enrolled and included in this analysis: trastuzumab for breast cancer (n=22, 100% female), adriamycin for breast cancer (n=22, 100% female), capecitabine for colorectal cancer (n=27; 22 male, 5 female), and paclitaxel for lung cancer (n=29, 100% male).

Instruments and data collection

Taste alteration was assessed using the 18-item Chemotherapy-Induced Taste Alteration Scale (CiTAS), and olfactory function using the Self-Administered Odor Questionnaire (SAOQ). The EORTC QLQ-C30 was also administered to assess quality of life. Baseline assessment included demographic data (age, sex, cancer type, chemotherapy regimen) and initial CiTAS/SAOQ scores. Follow-up assessments were repeated at intervals coinciding with each patient's chemotherapy cycles (approximately every 2–3 weeks) across the 12-week study period.

Statistical analysis

Continuous variables (age) are presented as mean ± standard deviation with 95% confidence intervals; categorical variables (sex, cancer type, regimen, week-of-documentation category) are presented as frequencies and percentages. An independent-samples (unpaired) t-test compared mean age between male and female patients. Prevalence of ageusia and anosmia is reported with an exact (Clopper-Pearson) 95% confidence interval. Statistical significance was set at $p<0.05$.

Results

Participant characteristics

Of the 100 enrolled patients, 51 (51%) were male and 49 (49%) were female. The mean age of the cohort was 49.83±13.75 years (95% CI 47.14–52.53). Female patients were significantly older than male patients (53.6±13.92 years, 95% CI 49.7–57.5, vs 46.2±12.15 years, 95% CI 42.86–49.54; unpaired t-test, p=0.005). Age-group distribution by sex is shown in Table 1.

Table 2 shows the distribution of cancer type, chemotherapy regimen, and sex across the cohort. Sex was completely confounded with regimen for the breast- and lung-cancer groups, and heavily skewed for the colorectal-cancer group; this precludes separating the effect of sex from the effect of cancer type or regimen in this dataset (see Limitations).

Prevalence of ageusia and anosmia

All 100 patients (100%; exact 95% CI 96.4–100%) reported ageusia at some point during the 12-week follow-up, and

Table 1: Age-group distribution by sex (N=100)

Age group (years)	*Female (n=49)*	*Male (n=51)*	*Total (N=100)*
18–30	2 (4.1%)	3 (5.9%)	5 (5%)
31–40	9 (18.4%)	13 (25.5%)	22 (22%)
41–50	18 (36.7%)	16 (31.4%)	34 (34%)
51–60	7 (14.3%)	6 (11.8%)	13 (13%)
61–70	8 (16.3%)	7 (13.7%)	15 (15%)
71–80	7 (14.3%)	4 (7.8%)	11 (11%)
Total	49 (49%)	51 (51%)	100 (100%)

Note: percentages within each sex column are calculated on that column's total (49 female, 51 male).

all 100 patients (100%; exact 95% CI 96.4–100%) reported anosmia. This held within every regimen subgroup: no patient in any of the four groups was free of either symptom.

Temporal distribution of symptoms

Tables 3 and 4 show, for each regimen, the proportion of patients whose ageusia or anosmia was documented within each of three assessment windows (weeks 1–5, 6–10, and 11–15) during the 12-week follow-up. For ageusia (Table 3), the majority of patients in every regimen group were documented within weeks 1–5 (range 59.1–65.5%), with a decreasing proportion in each subsequent window for all four regimens. Anosmia (Table 4) followed a similar pattern for adriamycin, trastuzumab, and paclitaxel, but capecitabine was the exception: the proportion of capecitabine-treated patients documented at weeks 11–15 (22.2%, 6/27) was higher than at weeks 6–10 (18.5%, 5/27), rather than continuing to decline.

These tables describe the assessment window within which each patient's symptom was documented, not a confirmed within-patient trajectory of symptom onset or resolution; the per-patient longitudinal records needed to distinguish these two possibilities are not available to the authors (see Limitations).

Quality of life and symptom severity

CiTAS severity-category comparisons, SAOQ domain scores, and EORTC QLQ-C30 functional and symptom scores were collected during the study but are not reported in this manuscript. On review, the values and derived statistics for these instruments could not be reconciled with the scoring procedures specified for them, and the patient-level records needed to correct and re-report them are no longer available to the authors (see Limitations and Data Availability).

Table 2: Cancer type, chemotherapy regimen, and sex composition (N=100)

Cancer type	*Regimen*	*Female, n*	*Male, n*	*Total, n*
Breast	Trastuzumab	22	0	22
Breast	Adriamycin	22	0	22
Colorectal	Capecitabine	5	22	27
Lung	Paclitaxel	0	29	29
Total		49	51	100

Table 3: Distribution of the assessment window in which ageusia was documented, by regimen

Week range	*Adriamycin (n=22)*	*Trastuzumab (n=22)*	*Capecitabine (n=27)*	*Paclitaxel (n=29)*
1–5	63.64% (14)	59.09% (13)	59.26% (16)	65.52% (19)
6–10	22.73% (5)	27.27% (6)	25.93% (7)	20.69% (6)
11–15	13.64% (3)	13.64% (3)	14.81% (4)	13.79% (4)

Table 4: Distribution of the assessment window in which anosmia was documented, by regimen

Week range	*Adriamycin (n=22)*	*Trastuzumab (n=22)*	*Capecitabine (n=27)*	*Paclitaxel (n=29)*
1–5	54.55% (12)	68.18% (15)	59.26% (16)	62.07% (18)
6–10	22.73% (5)	18.18% (4)	18.52% (5)	17.24% (5)
11–15	22.73% (5)	13.64% (3)	22.22% (6)	20.69% (6)

Note: capecitabine is the only regimen for which the weeks 11–15 value (22.22%) exceeds the weeks 6–10 value (18.52%); the other three regimens decline monotonically across windows.

Discussion

In this cohort, ageusia and anosmia were reported by all 100 patients across four chemotherapy regimens. This is higher than most previously reported prevalence estimates, which range from under 20% to around 70% depending on population and instrument [2,3]. Several non-exclusive explanations are possible: the four agents studied here (an anthracycline, a HER2-targeted antibody, an oral fluoropyrimidine, and a taxane) are all associated with chemosensory toxicity in the existing literature; the self-report instruments used may be sensitive to mild or transient symptoms that other studies do not capture; and single-center referral patterns may have selected for patients with more pronounced symptoms. The data available for this analysis cannot distinguish between these explanations, and given how close the observed prevalence is to a hard ceiling of 100%, this finding should be treated cautiously rather than as an estimate of prevalence in a general chemotherapy population.

Female patients in this cohort were significantly older than

male patients. Because sex is completely confounded with cancer type in this sample — all breast-cancer patients were female and all lung-cancer patients were male — this age difference most plausibly reflects differences in the typical age of onset between breast, lung, and colorectal cancer in this population, rather than a general sex-based difference in age at presentation for chemotherapy. This distinction cannot be tested further with the available data.

The temporal pattern — most patients' symptoms documented earliest in treatment, with a declining proportion in later assessment windows — is broadly consistent with a mechanism in which chemosensory epithelium is affected early in a treatment course and partially recovers as cycles are completed or spaced out [1,2]. The exception observed for capecitabine, where the proportion of patients documented with anosmia rose slightly between weeks 6–10 and weeks 11–15, is notable because capecitabine is administered on a distinct oral, intermittent dosing schedule compared with the other three intravenous agents in this study, and has a distinct toxicity profile. Whether this reflects a genuine late-onset or cumulative effect of capecitabine on olfactory function, or is a feature of how patients were assessed, cannot be determined from the data available and would benefit from confirmation in a study with verified per-patient longitudinal tracking.

Limitations

This study has several important limitations.

- Single-center design. All patients were drawn from one oncology department in India; findings may not generalize to other populations, health systems, or regimens.
- Confounding of sex, cancer type, and regimen. Both breast-cancer regimens were exclusively female and the lung-cancer regimen exclusively male, with the colorectal-cancer regimen predominantly male. The effect of regimen cannot be separated from the effect of sex or underlying cancer type in this dataset.
- Unanticipated 100% prevalence. The study's sample size was calculated assuming a 50% prevalence of chemosensory dysfunction. The observed 100% prevalence was not anticipated by that calculation, and a ceiling or selection effect specific to this cohort or these instruments cannot be excluded.
- Ambiguity in the temporal tables. Tables 3 and 4 reflect the assessment window in which each patient's symptom was documented rather than a confirmed within-patient trajectory of onset, worsening, or resolution. The per-patient longitudinal records that would distinguish these possibilities are no longer accessible to the authors.
- No correction for multiple comparisons was applied to the analyses reported here.

Conclusion

Ageusia and anosmia were reported by all patients in this 100-patient cohort receiving trastuzumab, adriamycin, capecitabine, or paclitaxel, with most patients' symptoms documented within the first five weeks of treatment across all four regimens. Female patients were older than male patients, though this is confounded with the cancer-type composition of the cohort. Given the near-total confounding of sex, cancer type, and regimen, and the inability to verify several originally planned quality-of-life and severity analyses, these findings should be regarded as descriptive and hypothesis-generating rather than confirmatory. Prospective, multi-center studies with verified, patient-level scoring of validated chemosensory and quality-of-life instruments are needed to characterize the full impact of chemotherapy-induced chemosensory dysfunction.

Declarations

Ethics approval: Institutional Ethics Committee, King George Hospital, Visakhapatnam (Reg. No. ECR/197/Inst/KGH/2013/RR-20).

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