International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Role of Human Placental Extract (Placentrex®) as a Biostimulant in Reducing Chemotherapy-Induced Toxicities in Carcinoma Breast

Dr. N. I. Hebsur[1], Dr. Ayshath Mufeeda[2], Dr. S, Y. Mulkipatil[3], Dr. Ananya Hebsur[4], Dr. Vinayak R. B[5]. , Dr. Sukumar[6], Dr. Amit Rafi[7]

[1]Professor, Department of General Surgery, Karnataka medical College And Research Institute(KMCRI), Hubballi, Karnataka, India
[2]Post graduate Student, Department of General Surgery, Karnataka medical College And Research Institute(KMCRI), Hubballi, Karnataka, India
[3]Associate Professor, Department of General Surgery, Karnataka medical College And Research Institute(KMCRI), Hubballi, Karnataka, India
[4] Third year MBBS student, Siddhartha medical college , Tumkur, Karnataka, India
[5]Assistant Professor, Department of General Surgery, Karnataka medical College And Research Institute(KMCRI), Hubballi, Karnataka, India
[6,7]Post graduate Students, , Department of General Surgery, Karnataka medical College And Research Institute(KMCRI), Hubballi, Karnataka, India

OPEN ACCESS

Corresponding Author:

Dr Ayshath Mufeeda
Post graduate Student, Department of General Surgery, Karnataka medical College And Research Institute(KMCRI), Hubballi, Karnataka, India

Received: 14-06-2026
Accepted: 25-06-2026
Available online: 20-07-2026

ABSTRACT

Background: Chemotherapy is integral to the management of carcinoma breast, but its non-selective cytotoxicity on rapidly proliferating normal cells produces dose-limiting toxicities — most notably mucositis, leukopenia, and generalised fatigue and myalgia. These complications impair quality of life and frequently mandate dose reduction, treatment delay, or discontinuation, thereby compromising oncological outcomes. Human placental extract (Placentrex), a biogenic stimulator containing peptides, nucleotides, enzymes, vitamins, and growth factors, has well-documented anti-inflammatory, immunomodulatory, antioxidant, and tissue-regenerative actions, yet its role in mitigating chemotherapy toxicity in breast cancer is poorly defined.

Aim: To evaluate the efficacy of Placentrex administered prior to each chemotherapy cycle in reducing the incidence and severity of chemotherapy-induced mucositis, leukopenia, and fibromyalgia-like symptoms in patients with carcinoma breast.

Methods: A prospective comparative interventional study was conducted over 18 months in KMCRI a tertiary care teaching hospital. One hundred and twenty histologically proven, chemotherapy-naïve carcinoma breast patients aged 18–70 years with ECOG performance status 0–2 were allocated to two groups of 60 each. The study group received Inj. Placentrex 2 mL intramuscularly prior to each cycle, while the control group received standard chemotherapy alone. Both groups received a uniform regimen of four cycles of doxorubicin–cyclophosphamide (AC) followed by four cycles of paclitaxel. Mucositis was graded by the WHO Oral Toxicity Scale, leukopenia by CTCAE v5.0 using total leukocyte count, and fibromyalgia-like symptoms were assessed clinically. Statistical analysis used the Chi-square test and Student t-test in SPSS, with $p < 0.05$ considered significant.

Results: Moderate-to-severe mucositis (Grade $\geq$ 2) occurred in 33.3% of the Placentrex group versus 60.0% of controls ($p = 0.006$). Leukopenia (TLC < 4000 cells/mm³) was observed in 20.0% versus 53.3% ($p < 0.001$), with mean TLC at cycle 8 of 4800 versus 3000 cells/mm³. Fibromyalgia-like symptoms occurred in 33.3% versus 66.7% ($p < 0.001$). All differences were highly statistically significant.

Conclusion: Placentrex, administered prior to chemotherapy, produced a clinically meaningful and statistically significant reduction in mucositis, leukopenia, and

fibromyalgia-like symptoms in patients with carcinoma breast. It appears to be a safe, inexpensive, and broad-spectrum adjunct that may improve treatment tolerance and compliance. Larger randomised controlled trials are warranted to confirm these findings.

Keywords: *Placentrex; human placental extract; carcinoma breast; chemotherapy; mucositis; leukopenia; supportive oncology; biostimulant.*

INTRODUCTION

Carcinoma breast is the most frequently diagnosed malignancy and the leading cause of cancer-related death among women worldwide, with GLOBOCAN 2020 estimating 2.26 million new cases and 685,000 deaths annually.[1] Its management is multimodal — combining surgery, chemotherapy, radiotherapy, hormonal, and targeted therapy — with systemic chemotherapy occupying a central role in both neoadjuvant and adjuvant settings.

Although effective, conventional cytotoxic agents act non-selectively on rapidly dividing cells, producing predictable injury to the gastrointestinal mucosa, bone marrow, hair follicles, and gonads. The resulting toxicity profile is a principal determinant of treatment tolerability and is, in many patients, the rate-limiting step that prevents delivery of the full planned dose.

Chemotherapy-Induced Mucositis

Mucositis affects up to 40% of patients receiving standard-dose chemotherapy and approaches 100% with high-dose conditioning regimens. Its pathobiology, as elaborated by Sonis, proceeds through five overlapping phases — initiation, primary damage response, signal amplification, ulceration, and healing — driven by reactive oxygen species, NF-κB activation, and pro-inflammatory cytokine release.[2] Clinically it manifests as oral pain, dysphagia, and an increased risk of secondary bacteraemia.

Chemotherapy-Induced Leukopenia

Myelosuppression — particularly neutropenia — remains the most common dose-limiting toxicity of cytotoxic chemotherapy. Febrile neutropenia carries a case-fatality rate of 5–10% and is the leading non-malignant cause of hospitalisation in oncology practice.[3] Granulocyte colony-stimulating factor support, although effective, is expensive and not universally accessible in resource-limited settings.

Fibromyalgia-Like Symptoms

Cancer-related fatigue, diffuse myalgia, and tenderness affect up to 80% of patients on chemotherapy and persist beyond treatment in a substantial minority. Mechanisms include systemic inflammation, mitochondrial dysfunction, hypothalamic–pituitary–adrenal axis dysregulation, and central sensitisation.[4] Effective pharmacological options are limited and the syndrome is often under-recognised.

Rationale for Placentrex

Human placental extract (Placentrex®, Albert David Ltd., India) is an aqueous, deproteinised extract derived from fresh-term human placenta. It is a complex biological preparation containing peptides, nucleotides, amino acids, enzymes, water-soluble vitamins, steroids, fatty acids, and growth factors, and acts as a biogenic stimulator with documented anti-inflammatory, immunomodulatory, antioxidant, and tissue-regenerative effects.[5] Its principal proposed actions include:

- **Promotion of angiogenesis and epithelial regeneration** through fibroblast growth factor and epidermal growth factor activity;
- **Reduction of oxidative stress** via free-radical scavenging by short-chain peptides and uracil derivatives;
- **Immunomodulation** through cytokine balance and stimulation of haematopoietic progenitors;
- **Enhancement of cellular metabolism** by supplying coenzymes and trace nucleotides.

Placentrex has been extensively used in radiation-induced mucositis of head and neck cancers,[6] non-healing ulcers, and pelvic inflammatory disease. However, its role in systemic chemotherapy-induced toxicities — particularly in carcinoma breast — has remained largely unexplored. The present study seeks to address this gap by formally evaluating whether prophylactic Placentrex reduces the principal toxicities encountered during anthracycline–taxane based chemotherapy.

AIM AND OBJECTIVES

Aim

To evaluate the role of Inj. Placentrex as a biostimulant in reducing chemotherapy-induced toxicities in patients with carcinoma breast.

Objectives

- To compare the incidence and severity of oral mucositis between patients receiving Placentrex and those not receiving it.
- To assess the incidence and grade of leukopenia in both groups across successive chemotherapy cycles.
- To evaluate the occurrence of fibromyalgia-like symptoms — generalised body pain, fatigue, and tenderness — in both groups.
- To assess treatment compliance, including the need for dose reduction, treatment delay, or supportive interventions.

MATERIALS AND METHODS

Study Design and Setting

A prospective comparative interventional study was conducted in the Department of General Surgery of Karnataka Medical College and Research Institute, a tertiary care teaching hospital over a period of 24 months. Written informed consent was obtained from all participants.

Study Population

One hundred and twenty consecutive patients with histologically confirmed carcinoma breast planned for chemotherapy were enrolled and allocated into two parallel groups of 60 patients each:

- **Study group (n = 60):** received Inj. Placentrex 2 mL intramuscularly 30 minutes prior to each chemotherapy cycle, in addition to standard chemotherapy.
- **Control group (n = 60):** received standard chemotherapy alone, without Placentrex.

Eligibility Criteria

Inclusion Criteria

- Histologically proven carcinoma of the breast.
- Patients planned for neoadjuvant or adjuvant chemotherapy.
- Age 18–70 years, both sexes.
- ECOG performance status 0–2.
- Baseline total leukocyte count ≥ 4000 cells/mm³ and adequate hepatic and renal function

Exclusion criteria

- Pre-existing leukopenia or other haematological disorders.
- Active oral or systemic infection at enrolment.
- Prior chemotherapy or radiotherapy for any malignancy.
- Known autoimmune disorders or chronic pain syndromes (including pre-existing fibromyalgia).
- Severe comorbid illness — uncontrolled diabetes, advanced cardiac, hepatic, or renal disease, Pregnancy, lactation, or known hypersensitivity to Placentrex.

Chemotherapy Protocol

To eliminate treatment-related bias, both groups received an identical chemotherapy regimen consisting of:

- **Four cycles of AC:** doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m² intravenously every 21 days;
- **Followed by four cycles of paclitaxel:** 175 mg/m² intravenously every 21 days.

Standard pre-medication (5-HT3 antagonist, dexamethasone, and H1/H2 blockers as appropriate) was administered uniformly. No prophylactic granulocyte colony-stimulating factor was used in either group at baseline; it was reserved for documented Grade 3/4 neutropenia.

Outcome Measures

1. Mucositis

Oral mucositis was graded after every cycle by clinical examination using the WHO Oral Toxicity Scale (Table 1).

Table 1. WHO Oral Mucositis Grading Scale

Grade	Clinical Features
Grade 0	No mucositis
Grade 1	Soreness with or without erythema
Grade 2	Erythema and ulcers; patient can swallow solid food
Grade 3	Ulcers requiring liquid diet only
Grade 4	Severe mucositis; oral alimentation not possible

2. Leukopenia

Total leukocyte count (TLC) was measured at baseline and on day 10 ± 1 after each chemotherapy cycle (nadir window). Leukopenia was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 (Table 2).

Although absolute neutrophil count is the preferred clinical parameter, TLC was used uniformly across all cycles for operational consistency.

Table 2. CTCAE v5.0 Grading of Leukopenia (Total Leukocyte Count)

Grade	TLC (cells/mm³)	Clinical Interpretation
Grade 1 — Mild	3000 to < 4000	Mild decrease; usually asymptomatic
Grade 2 — Moderate	2000 to < 3000	Increased risk of infection
Grade 3 — Severe	1000 to < 2000	High infection risk; requires intervention
Grade 4 — Life-threatening	< 1000	Very high risk; urgent management required
Grade 5	—	Death attributable to adverse event

3. Fibromyalgia-Like Symptoms

Patients were assessed at each visit for the triad of generalised body pain, fatigue, and tenderness at standard reference points. A composite clinical impression of the presence of two or more of these symptoms persisting for more than seven days post-cycle was recorded as positive.

Data Collection and Statistical Analysis

Demographic, clinical, and laboratory data were recorded on a structured proforma after every cycle and at the end of treatment. Data were entered in Microsoft Excel and analysed using SPSS v23.0 (IBM Corp., Armonk, NY). Categorical variables were expressed as frequencies and percentages and compared using the Chi-square test (Fisher's exact test where applicable); continuous variables were expressed as mean ± standard deviation and compared using the unpaired Student t-test. A two-tailed p value < 0.05 was considered statistically significant.

RESULTS

All 120 enrolled patients completed the full chemotherapy course. The two groups were comparable in age distribution, stage at presentation, and chemotherapy regimen, eliminating major sources of allocation bias.

Mucositis

The incidence and severity of oral mucositis were markedly lower in the Placentrex group. Forty percent of patients in the study group remained free of mucositis (Grade 0) and a further 26.7% experienced only mild involvement (Grade 1). In contrast, only 16.7% of controls had Grade 0 disease, with the majority shifted into Grade 2 or higher categories. The full grade-wise distribution is presented in Table 3.

Table 3. Grade-wise Distribution of Oral Mucositis (WHO Scale)

WHO Grade	Placentrex (n = 60)	%	Control (n = 60)	%
Grade 0	24	40.0%	10	16.7%
Grade 1	16	26.7%	14	23.3%
Grade 2	12	20.0%	18	30.0%
Grade 3	6	10.0%	12	20.0%
Grade 4	2	3.3%	6	10.0%
Total	60	100%	60	100%

Figure 1. Grade-wise Distribution of Oral Mucositis (WHO Scale)

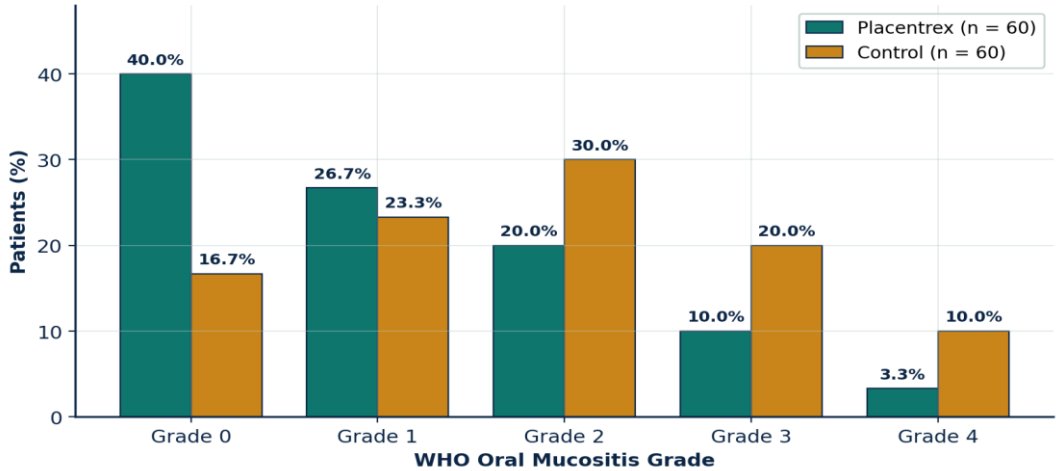

Figure 1. Grade-wise comparison of oral mucositis between study groups. The Placentrex group shows a marked rightward shift towards milder grades, with 40% remaining mucositis-free versus 16.7% in controls.

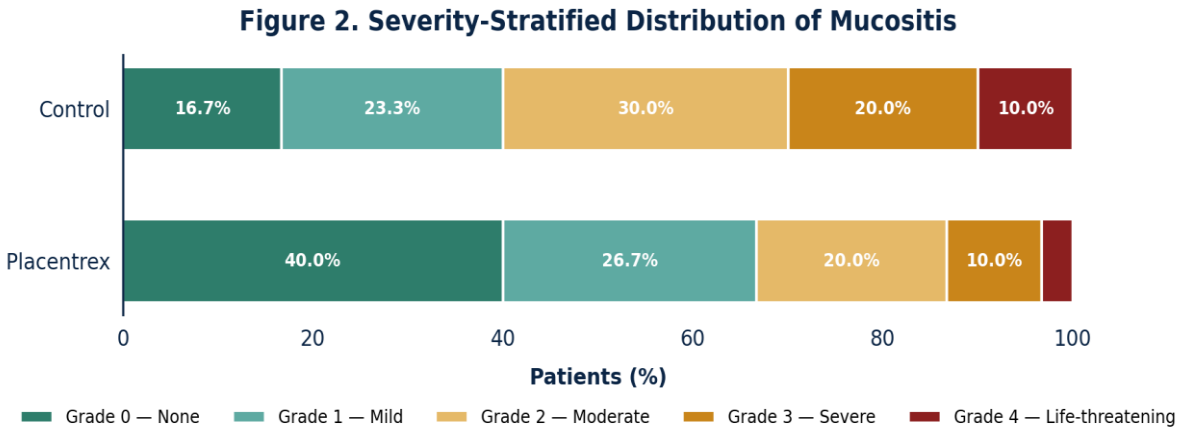

Figure 2. Severity-stratified distribution of oral mucositis. The combined Grade 0–1 (no/mild) burden is 66.7% in the Placentrex group versus 40.0% in controls; conversely, the Grade 3–4 burden is reduced from 30.0% to 13.3%.

Considered as a binary outcome, moderate-to-severe mucositis (Grade ≥ 2) occurred in 20 of 60 (33.3%) patients in the Placentrex group versus 36 of 60 (60.0%) in the control group ($p = 0.006$) — a relative risk reduction of approximately 44%.

Leukopenia and TLC Trends

Leukopenia (TLC < 4000 cells/mm³) occurred in only 12 of 60 (20.0%) patients in the Placentrex group, compared with 32 of 60 (53.3%) in the control group ($p < 0.001$). The protective effect was progressive: both groups demonstrated a decline in mean TLC across successive cycles, but the slope was substantially shallower in the Placentrex group. By cycle 8, the control group approached a critical mean of 3000 cells/mm³, whereas the Placentrex group maintained a clinically safer mean of 4800 cells/mm³ (Table 4).

Table 4. Mean Total Leukocyte Count (cells/mm³) Across Chemotherapy Cycles

Cycle	Regimen	Placentrex Group	Control Group
Cycle 1	AC	6200	5900
Cycle 2	AC	5800	4800
Cycle 3	AC	5500	4200
Cycle 4	AC	5300	3900
Cycle 5	Paclitaxel	5100	3600
Cycle 6	Paclitaxel	5000	3400
Cycle 7	Paclitaxel	4900	3200
Cycle 8	Paclitaxel	4800	3000

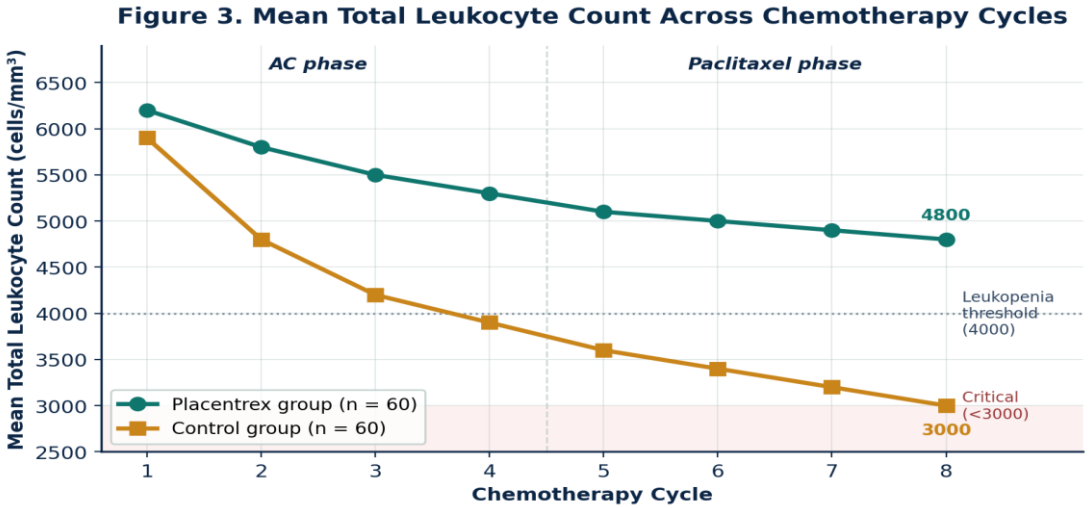

Figure 3. Mean total leukocyte count across eight chemotherapy cycles. The control group shows a progressive decline that breaches the leukopenia threshold (4000 cells/mm³) by cycle 4 and approaches the critical band (<3000 cells/mm³) by cycle 8, whereas the Placentrex group maintains counts well above threshold throughout.

Fibromyalgia-Like Symptoms

Fibromyalgia-like symptoms — defined by the persistent triad of body pain, fatigue, and tenderness — were reported by 20 of 60 (33.3%) patients in the Placentrex group, compared with 40 of 60 (66.7%) in the control group ($p < 0.001$). Patients in the Placentrex group also reported a subjectively faster return to baseline functional status between cycles.

Summary of Principal Outcomes

Table 5. Comparison of Chemotherapy-Induced Toxicities Between Groups

Parameter	Placentrex (n = 60)	Control (n = 60)	p value	Significance
Mucositis (Grade ≥ 2)	20 (33.3%)	36 (60.0%)	0.006	Significant
Leukopenia (TLC < 4000)	12 (20.0%)	32 (53.3%)	< 0.001	Highly significant
Fibromyalgia-like symptoms	20 (33.3%)	40 (66.7%)	< 0.001	Highly significant

Figure 4. Incidence of Principal Chemotherapy-Induced Toxicities

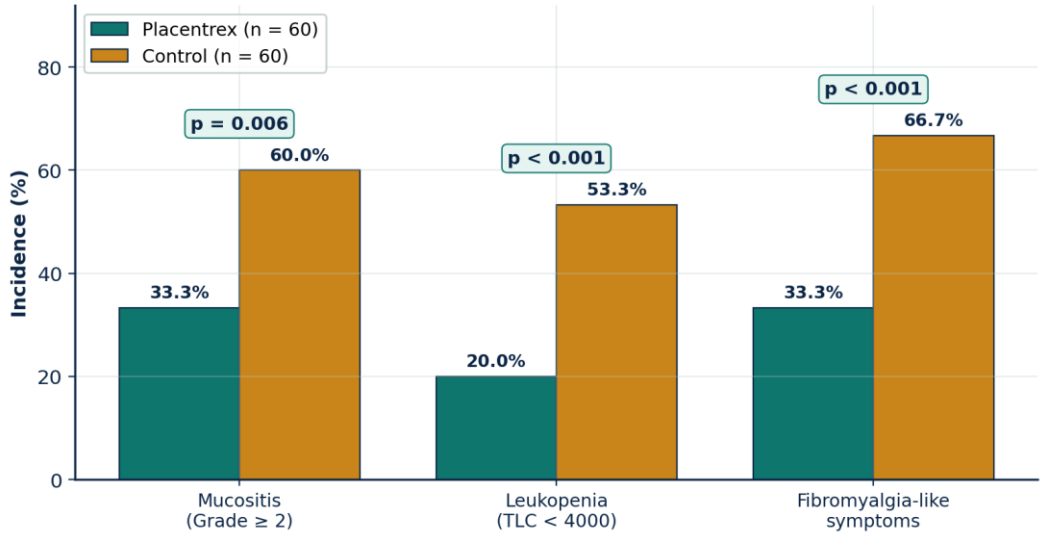

Figure 4. Incidence of the three principal chemotherapy-induced toxicities. All three differences reach statistical significance, with the Placentrex group showing roughly half the incidence of mucositis (Grade ≥ 2), leukopenia, and fibromyalgia-like symptoms compared with controls.

Key Finding

Across all three principal toxicities — mucositis, leukopenia, and fibromyalgia-like symptoms — patients receiving prophylactic Placentrex demonstrated a statistically significant reduction in both incidence and severity, with a consistent shift towards milder grades and better preservation of leukocyte counts across successive cycles.

DISCUSSION

Toxicity-related interruption of chemotherapy is a well-recognised determinant of inferior oncological outcome in carcinoma breast. The present study addresses this problem by formally evaluating Placentrex — a biologically rational, inexpensive, and widely available agent — as a prophylactic adjunct, and demonstrates a consistent benefit across three clinically important toxicity domains.

Mucositis

Grade ≥ 2 mucositis was reduced from 60.0% in controls to 33.3% in the Placentrex group ($p = 0.006$), with a parallel shift of the entire distribution towards milder grades. This pattern is biologically consistent with the five-phase model of mucositis described by Sonis,[2] in which oxidative stress, NF-κB activation, and pro-inflammatory cytokine release drive epithelial injury. The peptide, nucleotide, and growth-factor components of Placentrex plausibly attenuate each of these steps — scavenging reactive oxygen species, dampening cytokine amplification, and accelerating epithelial regeneration. Our findings extend the work of Kaushal et al.,[6] who demonstrated reduced radiation-induced mucositis in head and neck cancers with Placentrex, and that of Kondaveeti et al.,[7] who reported benefit in chemoradiation-induced mucositis. Although the precipitating insult differs — ionising radiation versus systemic cytotoxic chemotherapy — the downstream injury pathway converges on the same inflammatory and oxidative cascade, supporting biological plausibility for the present results.

Leukopenia and Bone Marrow Preservation

The cycle-wise TLC trajectory is, in our view, the most clinically informative single observation of this study. The control group followed the expected pattern of progressive marrow suppression characteristic of anthracycline–taxane sequences, with mean TLC approaching the critical 3000 cells/mm³ threshold by cycle 8 — a level at which empirical

dose reduction or G-CSF support is often required.[3] The Placentrex group, in contrast, maintained means above 4800 cells/mm³ throughout, suggesting a genuine bone-marrow-sparing effect rather than a transient post-dose recovery phenomenon.

The proposed mechanism is dual. First, the nucleotide and peptide fractions of placental extract may serve as substrates and signals for haematopoietic progenitor proliferation. Second, the immunomodulatory action — restoring a balanced Th1/Th2 cytokine milieu — may reduce marrow-suppressive inflammatory cytokine load. These effects are concordant with experimental literature on placental preparations in myelosuppressed animal models.

Fibromyalgia-Like Symptoms

The halving of fibromyalgia-like symptoms (66.7% to 33.3%, $p < 0.001$) is clinically meaningful. Cancer-related fatigue and diffuse musculoskeletal pain are increasingly recognised as cytokine-mediated phenomena, with circulating IL-6 and TNF-α as principal drivers.[4] The anti-inflammatory and antioxidant properties of Placentrex offer a coherent mechanistic explanation. The functional implication — patients feeling better between cycles — has direct consequences for adherence and quality of life.

Clinical Significance

The simultaneous improvement across mucosal, haematological, and systemic symptom domains is the principal clinical message of this study. Most pharmacological adjuncts in supportive oncology target a single toxicity — palifermin for mucositis, G-CSF for neutropenia, methylphenidate or modafinil for fatigue — at considerable cost. Placentrex appears, in contrast, to function as a broad-spectrum biological adjuvant that addresses multiple toxicities through overlapping anti-inflammatory and regenerative mechanisms. In a resource-limited setting, this combination of low cost, parenteral simplicity, and multi-domain efficacy is particularly attractive.

Better tolerated chemotherapy translates, predictably, into improved dose intensity. Although the present study was not powered to detect a survival difference, the literature consistently links preserved dose intensity to improved disease-free survival in carcinoma breast, providing an indirect long-term rationale for any intervention that meaningfully reduces toxicity.

Comparison with Existing Literature

Published evidence on placental extracts in oncology has been dominated by radiation-induced mucositis in head and neck cancers.[5,6] Comparative data in systemic chemotherapy — and specifically in carcinoma breast — are sparse. To our knowledge, the present work is among the first to evaluate Placentrex across mucosal, haematological, and constitutional toxicity domains in a uniformly treated breast cancer cohort. The direction and magnitude of benefit observed are concordant with extrapolation from the radiation-mucositis literature.

Limitations

- Although the present sample ($n = 120$) is larger than most prior single-centre reports, it remains modest for detecting smaller subgroup effects.
- Single-centre design, restricting external validity.
- Absence of randomisation and blinding, with attendant risk of allocation and observer bias.
- Use of total leukocyte count rather than absolute neutrophil count, which is the preferred biomarker of infection risk.
- No formal quality-of-life or patient-reported outcome instrument (e.g. EORTC QLQ-C30) was used.
- Short follow-up; survival and recurrence outcomes were not assessed.

Future Directions

These limitations frame the agenda for further work. Adequately powered randomised, double-blind, placebo-controlled trials — ideally multicentric — are needed to confirm the magnitude of effect. Future studies should incorporate absolute neutrophil count, validated patient-reported outcome measures, and an exploratory panel of inflammatory cytokines (IL-6, TNF-α, CRP) and oxidative-stress markers to clarify mechanism. A pharmacoeconomic analysis comparing Placentrex with conventional supportive agents would further inform health-system uptake.

CONCLUSION

In this prospective comparative observational study, prophylactic administration of human placental extract (Placentrex) prior to each chemotherapy cycle produced a statistically significant and clinically meaningful reduction in the principal toxicities of anthracycline–taxane chemotherapy for carcinoma breast. Moderate-to-severe mucositis was nearly halved, leukopenia was reduced from 53.3% to 20.0% with preservation of leukocyte counts across all eight cycles, and fibromyalgia-like symptoms were reduced from 66.7% to 33.3% — each difference reaching statistical significance.

The simultaneous -enefit across mucosal, haematological, and constitutional domains positions Placentrex as a broad-spectrum supportive agent rather than a single-target intervention. Its low cost, simple intramuscular administration, and favourable safety profile make it particularly suited to resource-limited oncology practice, where comprehensive supportive care with multiple targeted agents is often impractical.

Although the present findings cannot, in the absence of randomisation and long-term follow-up, establish Placentrex as standard supportive therapy, they provide a coherent biological and clinical rationale for larger randomised trials. Pending such confirmation, Placentrex emerges as a safe, accessible, and promising adjunct that may meaningfully improve the tolerability and completion of curative-intent chemotherapy in carcinoma breast.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–249.
2. Sonis ST. The pathobiology of mucositis. Nat Rev Cancer. 2004;4(4):277–284.
3. Crawford J, Dale DC, Lyman GH. Chemotherapy-induced neutropenia: risks, consequences, and new directions for its management. Cancer. 2004;100(2):228–237.
4. Bower JE. Cancer-related fatigue — mechanisms, risk factors, and treatments. Nat Rev Clin Oncol. 2014;11(10):597–609.
5. Bhandari V, Gupta RS. Human placental extract: a review of its therapeutic applications. Int J Pharm Sci Res. 2017;8(10):4154–4162.
6. Kaushal V, Verma AK, Pandey RM. Clinical evaluation of placentrex in radiation-induced mucositis. Int J Tissue React. 2001;23(3):105–110.
7. Kondaveeti SS, Reddy PR, Kumar V. Therapeutic benefit of placentrex in chemoradiation-induced mucositis. Asian Pac J Cancer Prev. 2013;14(10):6107–6110.
8. Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 20th ed. New York: McGraw-Hill; 2018.
9. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) v5.0. U.S. Department of Health and Human Services; 2017.
10. World Health Organization. WHO Handbook for Reporting Results of Cancer Treatment. Geneva: WHO Offset Publication No. 48; 1979.