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Megestrol Acetate in Cancer Cachexia: A Prospective Observational Study at a Tertiary Care Centre

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Abstract: ***Background*: Cancer cachexia is a complex syndrome involving weight loss, muscle wasting, and metabolic changes that impair patient quality of life and treatment efficacy. Megestrol Acetate, a synthetic progestin, has been used as an appetite stimulant in such patients. This study aims to evaluate the efficacy and safety of Megestrol Acetate in cancer cachexia in a real-world clinical setting. *Objectives*: To assess changes in appetite, body weight, and functional status among cancer patients receiving Megestrol Acetate and to monitor the associated adverse effects. *Methods*: This was a prospective observational study conducted at a tertiary care center. Cancer patients diagnosed with cachexia were initiated on Megestrol Acetate. Data were collected on baseline and post-treatment parameters including Visual Analogue Scale for appetite score, weight, (ECOG) performance status, and adverse events. *Results*: Among 105 patients enrolled, a significant proportion showed improvement in appetite and weight gain after Megestrol Acetate therapy ($p < 0.05$). Improvement in ECOG performance status was also observed in a subset of patients. Common adverse events observed were fatigue (25.7%), edema (20%), hyperglycemia (20%), and thromboembolism (6.7%). Grade 3–4 toxicities were less frequent but notable. *Conclusion*: Megestrol Acetate appears to be beneficial in improving appetite and nutritional status in cancer cachexia, with an acceptable safety profile. Regular monitoring is essential to manage potential adverse effects.***

Keywords: Cancer cachexia, Megestrol Acetate, Appetite, Weight gain, Adverse effect

1. Introduction

As per the American Society of Clinical Oncology guidelines (2015): cancer cachexia is defined through a consensus definition of weight loss of >5% of body weight in the past 6 months or >2%–5% loss of body weight in patients with body mass index of <20 kg/m2 or loss of skeletal muscle mass. (1)

Cancer-related anorexia/cachexia syndrome (CACS) is a multisystem syndrome, characterized by anorexia, weight loss, loss of skeletal muscle and body fats, systemic inflammation, and functional decline of cancer patients. Cancer cachexia affects 50%–80% patients in the advanced stage and is responsible for 20% of cancer-related deaths. (1)

The exact etiology of cancer cachexia is multifactorial and not fully understood. Certain types of cancers such as lung, esophagus, pancreases, and head-and-neck cancers are at a higher risk to experience cancer cachexia than patients with breast cancers and sarcomas. (2)

Managing cancer cachexia is challenging because of multiple reasons such as differences in predisposition of cancer types, underlying multiple pathophysiological processes, and concomitant disease process among cancer patients. A number of randomized clinical trials involving variety of agents have been done, but no single gold standard or Food and Drug Administration approved agent exists for cachexia management. (1,2)

MA is a synthetic progestin which acts on hormone-dependent tumoral cells, though its antitumoral mechanisms remain unclear. The inhibiting effects of growth in the cell cycle are not phase-specific, but its activity appears to reach a peak in the G1 phase of cell division. Although the mechanisms by which MA improves appetite are not well understood, most hypotheses suggest that it is likely to be due to its action on cytokines, and its inhibiting effect on TNF from acting on fatty cells and their products. (3)

In 2005, a systematic review was published, which proves strong evidence in favor of progestins such as megestrol acetate (MA) and short course of corticosteroids as appetite stimulant in cancer patients. (2)

MA is primarily used as an appetite stimulant in a number of conditions and also used as an antineoplastic agent in the treatment of endometrial, breast, and prostate cancers. It can substantially increase appetite in most individuals when given in relatively high doses, even in patients with advanced stages of cancer, hence is often used to boost appetite and induce weight gain in patients with cancer-associated cachexia. (3)

With this background, the study aims to prospectively evaluate the effectiveness of Megestrol acetate in improving appetite, weight, and overall outcomes in patients with cancer cachexia at our tertiary care centre.

This study addresses a critical gap in the management of cancer cachexia by evaluating a widely used but underdocumented agent—Megestrol Acetate in a real-world clinical setting.

Aims and Objectives

1) Primary Objective
- To assess weight gain and appetite improvement in patients treated with Megestrol Acetate at a tertiary care centre in Central India.

2) Secondary Objectives
- To assess improvements in quality of life (QOL) among patients undergoing treatment with Megestrol Acetate.
- To determine the safety and tolerability of Megestrol Acetate based on the CTCAE toxicity grading criteria.

2. Material and Methods

Study Design
This is a **prospective observational study** conducted at Department of Radiation Oncology at a tertiary care centre in Central India.

Study Population and Sample Size
The study population includes adult patients with histologically confirmed advanced or metastatic malignancies who exhibit clinical features of cancer cachexia and are eligible for Megestrol acetate therapy as part of routine supportive care. All eligible patients treated between April 2025 to July 2025 will be included. The estimated sample size is 104 patients.

Inclusion Criteria for Study:
a) Patients aged >18 years with histologically confirmed advanced cancer at any site
b) Patients with an expected life expectancy of at least 12 weeks
c) Patients with an Eastern Cooperative Oncology Group (ECOG) performance status of 0-3.
d) loss of >5% preillness body weight in the previous 3 months
e) Patients who provide informed consent to participate in the study.

Exclusion Criteria for Study:
a) Patients with history of hypertension and diabetes mellitus
b) Patients with mechanical obstruction to feeding.
c) Patients with high doses of corticosteroids and clinically bulky ascites.
d) Patients on medications that significantly alter body metabolism or weight.

Ethical considerations
Approval was taken from the Institutional Ethics Committee (IEC).
- Title and synopsis approved from Board of Research Studies (BORS), MUHS, Nashik.
- Informed written consent in subject's vernacular language was taken after apprising them of the nature and purpose of study.

3. Data Collection Parameters

a) Baseline Demographic and Clinical Data
The following variables were recorded at baseline:
- Age
- Gender
- ECOG Performance Status
- Stage of disease
- Weight (kg) and BMI
- Nutritional status
- Appetite score (e.g., Visual Analog Scale [VAS])

b) Follow-up and Monitoring
Patients were followed up at regular intervals (baseline score, 4 weeks score and 12 weeks score). At each visit, the following were assessed:
- Weight
- Appetite score (VAS)
- Any adverse events or complications

c) Adverse Events Assessment
Adverse events were assessed and graded according to **CTCAE version 5.0**. The following adverse effects were specifically monitored:
- Thromboembolism
- Oedema
- Hyperglycaemia
- Hypertension
- Gastrointestinal symptoms (nausea, diarrhoea)
- Fatigue
- Mood changes

Endpoints

a) Primary Endpoints:
- **Change in Body Weight** – measured from baseline to 4 weeks and 12 weeks.
- **Appetite Improvement** – assessed using a Visual Analog Scale (VAS) from baseline to follow-up.

b) Secondary Endpoints:
- **Incidence and severity of adverse events** as per CTCAE v5.0.
- **Overall quality of life (if measured)** using EORTC QLQ-C30 or another validated tool.
- **Treatment adherence and tolerability** of Megestrol acetate.

Statistical Analysis
Data were analysed using Microsoft Excel 2019 and SPSS (version as applicable).

1) Primary Endpoint Analysis
a) **Weight Gain:**
- Mean weight change from baseline at 4 and 12 weeks.
- Proportion of patients achieving ≥5% weight gain.

b) Appetite Improvement:
- Change in appetite score (VAS) from baseline at each follow-up.

2) Secondary Endpoint Analysis
a) **Quality of Life (QoL) Scores**
- If collected, analysed using EORTC QLQ-C30 or other validated tools.

b) Adverse Events
- Frequency and severity summarized using proportions.

3) Statistical Methods:
- **Continuous variables**: Presented as **mean ± standard deviation** (SD).
- **Categorical variables**: Summarized using **frequency and percentage**.
- **P-value <0.05** considered statistically significant.

4. Results

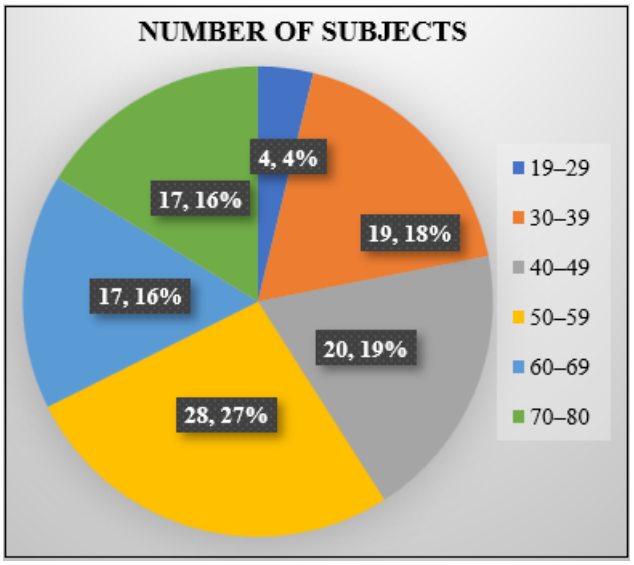

Figure 1: The above figure shows the distribution of study subjects according to their age. In the present study, a total of 105 subjects were included. Majority of the study participants, 28 (26.7%), belonged to the age group of 50–59 years, followed by 20 (19.0%) participants in the 40–49 years age group. The 30–39 years age group included 19 (18.1%) participants, while both the 60–69 years and 70–80 years age groups had 17 (16.2%) participants each. Only 4 (3.8%) subjects belonged to the youngest age group of 19–29 years. This distribution indicates that most of the study participants were in the age range of 40–59 years.

Table 1: Distribution of study subjects according to Gender

Gender	Number of Subjects	Percentage
Male	48	45.70%
Female	57	54.30%
Total	105	100%

Table 01: The above table shows the distribution of study subjects according to their gender. Out of a total of 105 patients enrolled in the study, 57 (54.3%) were female, while 48 (45.7%) were male. This indicates a slight female predominance among the study population.

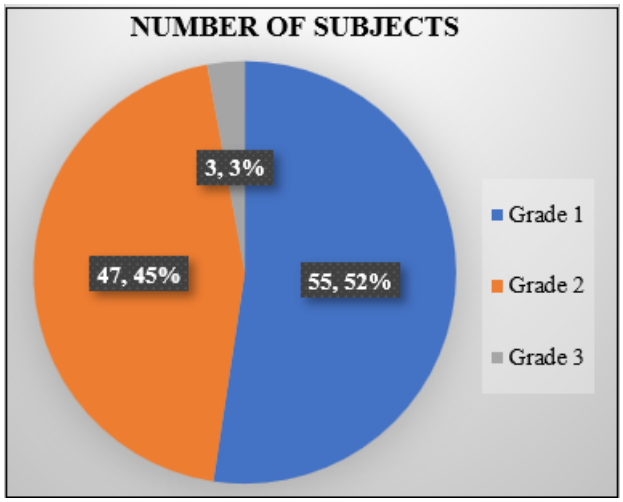

Figure 2: Distribution of study subjects according to ECOG

Figure 02: The above figure shows the distribution of study subjects according to their ECOG (Eastern Cooperative Oncology Group) performance status. Majority of the study participants, 55 (52.4%), had an ECOG Grade 1 performance status, followed by 47 (44.8%) participants with Grade 2 status. Only 3 (2.8%) subjects had an ECOG Grade 3 performance status. This distribution indicates that most of the study participants had relatively good functional status at the time of assessment.

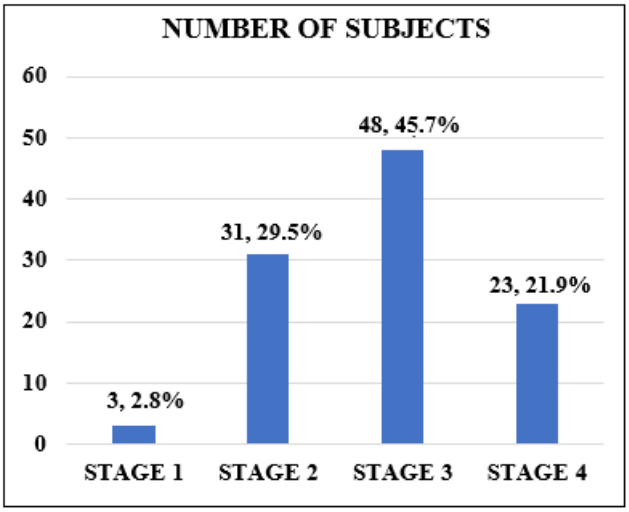

Figure 3: Distribution of study subjects according to Stage of disease

Figure 03: The above table shows the distribution of study subjects according to the stage of disease. Majority of the study participants, 48 (45.7%), were in Stage 3 of the disease, followed by 31 (29.5%) participants in Stage 2. A total of 23 (21.9%) subjects were in Stage 4, while only 3 (2.8%) participants were in Stage 1. This suggests that most participants were diagnosed at advanced disease stages.

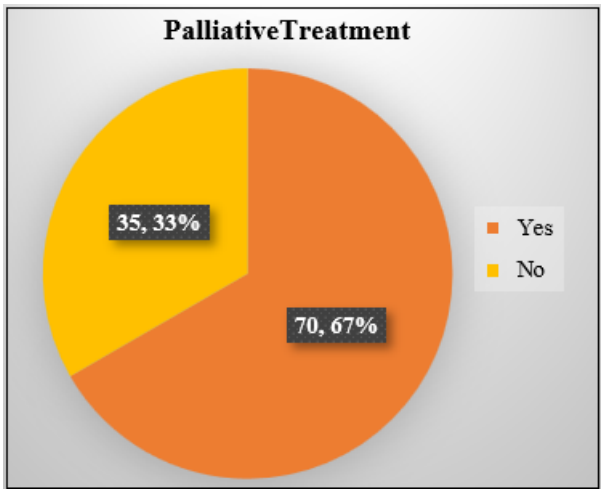

Figure 4: Distribution of study subjects according to Palliative Treatment

Figure 04: The above figure shows the distribution of study subjects based on whether they received palliative chemotherapy. Out of 105 study participants, 70 (66.7%) participants received palliative chemotherapy and 35 (33.3%) did not receive it.

Table 2: Assessment of End- points before and after treatment

End Points	Before Treatment	After Treatment	P- value
Body weight (kg)	44.08 + 9.80	45.09 + 9.84	< 0.00001
Appetite	2.1 ± 0.6	4.0 ± 0.8	<0.001
EORTC QLQ - 30	52.6 ± 11.8	67.4 ± 12.3	<0.001

Table 02: The above table shows the comparison of various end points before and after treatment among the study subjects. In the present study, a statistically significant improvement was observed in all measured parameters following treatment. The mean body weight increased from 44.08 ± 9.80 kg to 45.09 ± 9.84 kg ($p < 0.00001$). Appetite scores improved from 2.1 ± 0.6 to 4.0 ± 0.8 ($p < 0.001$). Similarly, the quality of life as assessed by the EORTC QLQ-C30 questionnaire improved from a mean score of 52.6 ± 11.8 to 67.4 ± 12.3 ($p < 0.001$). These findings indicate a significant positive impact of treatment on physical and functional well-being of the patients.

Table 03: Distribution of study subjects according to Assessment of toxicities

Toxicity	Grade 1–2	Grade 3–4	P
Thromboembolism	5 (4.8%)	2 (1.9%)	0.041*
Edema	15 (14.3%)	6 (5.7%)	0.050*
Hyperglycemia	14 (13.3%)	7 (6.7%)	0.063
Fatigue	18 (17.1%)	9 (8.6%)	0.072
Nausea	12 (11.4%)	2 (1.9%)	0.030*
Diarrhea	6 (5.7%)	3 (2.9%)	0.295
Mood Changes	4 (3.8%)	2 (1.9%)	0.492

Table 03: The above table shows the distribution of study subjects according to treatment-related toxicities. In the present study, the most common toxicities observed were fatigue in 27 (25.7%) subjects (Grade 1–2: 18, Grade 3–4: 9), followed by oedema in 21 (20.0%) subjects (Grade 1–2: 15, Grade 3–4: 6), and hyperglycemia in 21 (20.0%) subjects (Grade 1–2: 14, Grade 3–4: 7). Thromboembolism was noted in 7 (6.7%) subjects, nausea in 14 (13.3%), diarrhea in 9 (8.6%), and mood changes in 6
(5.7%). Statistically significant associations were found with thromboembolism ($p = 0.041$), edema ($p = 0.050$), and nausea ($p = 0.030$). This distribution suggests that while most toxicities were of Grade 1–2 severity, a few cases experienced Grade 3–4 toxicity.

5. Discussion

In this study, majority of the study subjects 26.7%, belonged to the age group of 50–59 years, followed by 19.0% in the 40–49 years age group. The mean age of the study participants was 52.34 ±13.9. Study done by **Fatima et al. (2021)** showed that the mean age of the study participants was 54.47±14.

In our study, 54.3% of the study subjects were female and 45.7% were male. Our study also showed that majority of the study participants, 52.4% had an ECOG Grade 1 performance status, followed by 44.8% participants with Grade 2 status. Study done by **Fatima et al. (2021)** showed that 71% of the study subjects were male and 29% were female. As for ECOG status, 48% had an ECOG Grade 3 performance status, followed by 30% participants with Grade 1 status.

The present study showed that 45.7% of the study participants were in Stage 3 of the disease, followed by 29.5% of the study participants were in Stage 2. Study done by **Cheng X et al. (2025)** showed that 82% of the study participants were in Stage 4 of the disease, followed by 10% of the study participants were in Stage 3.

In this study, 66.7% of the study participants received palliative chemotherapy and 33.3% were not receiving it. This was similar to study done by **Fatima et al. (2021)** where 67% of the study participants received palliative chemotherapy and 33% of the study participants were not receiving it.

In the present study, a statistically significant improvement was observed in all measured parameters following treatment. The mean body weight increased from 44.08 ± 9.80 kg to 45.09 ± 9.84 kg ($p < 0.00001$). Appetite scores improved from 2.1 ± 0.6 to 4.0 ± 0.8 ($p < 0.001$). Similarly, the quality of life as assessed by the EORTC QLQ-C30 questionnaire improved from a mean score of 52.6 ± 11.8 to 67.4 ± 12.3 ($p < 0.001$). Meta-analysis done by **Cheng X et al. (2025) and Zhan P et al. (2013)** showed that Cancer patients who received MA had increased weight gain and increased appetite improvement ($p < 0.001$).

In this study, the most common toxicities observed were fatigue in 25.7% subjects, followed by oedema in 20.0% subjects and hyperglycemia 20.0%. Thromboembolism was noted in 6.7% subjects, nausea in 13.3%, diarrhea in 8.6% and mood changes in 5.7%. Study done by **Cheng X et al. (2025)** showed that the overall incidence of AEs was 66.0% in the MA tablet group. The incidence of grade ≥3 AEs was 20.0% in the MA tablet group. In the MA tablet group, AEs with an incidence exceeding 5% included rash, pain, diarrhea, constipation, fatigue, nausea, vomiting, abdominal distension, and muscular weakness.

6. Conclusion

This prospective observational study highlights the clinical utility of Megestrol Acetate in managing cancer cachexia among patients at a tertiary care center. Megestrol Acetate led to notable improvements in appetite, weight gain, and overall quality of life in a subset of patients, suggesting its potential benefit in the palliative management of cancer-related cachexia.

However, risk of adverse effects, including thromboembolism, edema, and hyperglycemia, underscores the need for careful patient selection and close monitoring during therapy. Further large-scale, controlled studies and long term follow ups are warranted to confirm these findings and to optimize dosing strategies for maximum benefit with minimal risk.

Conflict of Interest
The authors declare no conflict of interest

Funding
No funding was undertaken for this study

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