Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies ***NLM ID:*** *101716117*

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr Index Copernicus value = 85.10

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

Comparative Efficacy of Topical Versus Systemic Treatments in Early-Stage Melanoma: A Multicenter Study

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ABSTRACT:

Background: Early-stage melanoma is a critical point for intervention, where treatment decisions can significantly impact patient outcomes. Both topical and systemic treatments are employed, but their comparative efficacy in early-stage melanoma remains uncertain. This multicenter study aims to evaluate the effectiveness of topical versus systemic treatments in achieving long-term remission and preventing progression in patients with early-stage melanoma. **Methods**: A prospective, multicenter study was conducted across five hospitals in India. A total of 200 patients diagnosed with early-stage melanoma were enrolled and randomly assigned to receive either topical treatment (Group A) or systemic treatment (Group B). Outcomes were measured based on tumor regression rates, recurrence rates, and overall survival at 1-year and 2-year follow-ups. Data were analyzed using survival analysis and logistic regression models. **Results**: The study found that 1-year tumor regression rates were significantly higher in Group B (systemic treatment) at 85% compared to 70% in Group A (topical treatment) ($p = 0.02$). However, recurrence rates at 2 years were lower in the topical treatment group (Group A) at 15% compared to 25% in Group B ($p = 0.05$). Overall survival rates did not differ significantly between the two groups. **Conclusions**: Systemic treatments demonstrate a higher initial efficacy in tumor regression for early-stage melanoma, while topical treatments show a better long-term profile with lower recurrence rates. These findings suggest that the choice of treatment may need to be tailored based on patient-specific factors and long-term management goals.

Keywords: Early-stage melanoma; Topical treatment; Systemic treatment; Tumor regression; Recurrence rates; Multicenter study

Received: 19 March, 2020 Accepted: 09 May, 2020

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This article may be cited as: N Radhika V, C Megha, Kumar RCK. Comparative Efficacy of Topical Versus Systemic Treatments in Early-Stage Melanoma: A Multicenter Study. J Adv Med Dent Scie Res 2020;8(5): 184-187.

INTRODUCTION

Melanoma is a malignant tumor originating from melanocytes, and its incidence has been steadily increasing worldwide. Early detection and treatment are crucial for improving patient outcomes, as early-stage melanoma has a significantly better prognosis compared to advanced stages [1]. The treatment of early-stage melanoma typically involves surgical excision, but adjunctive therapies, including topical and systemic treatments, are often employed to reduce the risk of recurrence and improve long-term outcomes [2].

Topical treatments, such as imiquimod, offer localized action with fewer systemic side effects, making them an attractive option for early-stage melanoma. These treatments target the tumor site directly, enhancing local immune responses and potentially reducing tumor size. On the other hand, systemic treatments, including interferon and targeted therapies, provide a broader scope of action, potentially addressing micrometastatic disease and reducing the risk of progression [3].

However, the comparative efficacy of these two approaches in early-stage melanoma remains under debate. While systemic treatments are generally associated with higher initial tumor regression rates, they also carry a higher risk of systemic side effects. Conversely, topical treatments are less invasive but may have limited efficacy in controlling the disease beyond the primary tumor site [4].

This multicenter study aims to provide a comprehensive comparison of the efficacy of topical versus systemic treatments in patients with early-stage melanoma. By analyzing tumor regression, recurrence rates, and overall survival, this study seeks to inform

clinical decision-making and optimize treatment strategies for this critical patient population.

METHODOLOGY

This multicenter, prospective study was conducted across five hospitals in India, each specializing in oncology and dermatology. Ethical approval was obtained from the institutional review boards of all participating centers, and informed consent was secured from all patients.

Study Design and Setting

The study employed a randomized controlled design, with patients assigned to either topical or systemic treatment groups. The study was conducted over two years, with regular follow-ups to assess outcomes.

Participants

Inclusion Criteria

- Patients aged 18 and above diagnosed with early-stage melanoma (stage 0-II).
- Tumors suitable for either topical or systemic treatment.
- No prior history of melanoma or other skin cancers.

Exclusion Criteria:

- Patients with advanced melanoma (stage III-IV).
- Patients with significant comorbidities or contraindications to either treatment modality.
- Pregnancy or breastfeeding.

Randomization and Treatment Protocols

Patients were randomly assigned to one of two groups:

- **Group A (Topical Treatment)**: Patients received imiquimod 5% cream applied to the tumor site once daily, five times per week, for 12 weeks.
- **Group B (Systemic Treatment)**: Patients received interferon-alpha subcutaneously at a dose of 3 million IU three times per week for 12 weeks.

Follow-Up and Outcome Measures

Patients were followed up at 3, 6, 12, and 24 months post-treatment. The primary outcomes measured were:

- **Tumor Regression**: Assessed by clinical examination and imaging, defined as complete or partial response.
- **Recurrence Rates**: Defined as the reappearance of melanoma at the primary site or at distant sites.
- **Overall Survival**: Defined as the time from treatment initiation to death from any cause.

Statistical Analysis

Survival analysis was conducted using Kaplan-Meier curves, with differences between groups assessed by the log-rank test. Logistic regression was used to identify factors associated with tumor regression and recurrence. A p-value of <0.05 was considered statistically significant. Data analysis was performed using SPSS software.

RESULTS

Table 1: Baseline Characteristics of Participants

Characteristic	Group A (n=100)	Group B (n=100)
Mean Age (years)	52.4 ± 10.7	53.1 ± 11.2
Gender (M/F)	60/40	58/42
Tumor Location (Head/Trunk/Extremities)	25/50/25	28/48/24
Mean Tumor Size (cm)	1.2 ± 0.5	1.3 ± 0.6
Breslow Thickness (mm)	0.8 ± 0.3	0.9 ± 0.4

This table summarizes the baseline characteristics of the participants, showing comparable demographic and clinical features between the two groups.

Table 2: Tumor Regression Rates at 1-Year Follow-Up

Tumor Response	Group A (Topical)	Group B (Systemic)	p-value
Complete Response (%)	50	65	0.04
Partial Response (%)	20	20	0.89
Stable Disease (%)	20	10	0.07
Progressive Disease (%)	10	5	0.18

This table compares the tumor regression rates between the two groups at the 1-year follow-up.

Table 3: Recurrence Rates at 2-Year Follow-Up

Recurrence Type	Group A (Topical)	Group B (Systemic)	p-value
Local Recurrence (%)	10	15	0.30
Regional Recurrence (%)	5	10	0.18
Distant Metastasis (%)	0	5	0.05
Total Recurrence (%)	15	25	0.05

This table presents the recurrence rates at the 2-year follow-up, highlighting the differences between topical and systemic treatments.

Table 4: Overall Survival Rates at 2-Year Follow-Up

Survival Rate (%)	Group A (Topical)	Group B (Systemic)	p-value
1-Year Overall Survival	95	97	0.50
2-Year Overall Survival	90	92	0.65

This table compares the overall survival rates between the two groups at 1-year and 2-year follow-ups.

Table 5: Adverse Events

Adverse Event	Group A (Topical)	Group B (Systemic)	p-value
Local Skin Irritation (%)	30	10	0.001
Flu-like Symptoms (%)	5	50	0.001
Fatigue (%)	15	40	0.002
Systemic Toxicity (%)	0	20	0.001

This table summarizes the adverse events experienced by patients in each group.

DISCUSSION

The results of this multicenter study provide valuable insights into the comparative efficacy of topical versus systemic treatments for early-stage melanoma. The study found that systemic treatments were more effective in achieving higher tumor regression rates at 1-year follow-up, with 85% of patients in Group B showing complete or partial responses compared to 70% in Group A. However, the recurrence rates at 2 years were significantly lower in the topical treatment group, suggesting that topical therapies may provide better long-term control of the disease [5].

Efficacy of Topical vs. Systemic Treatments

Systemic treatments, particularly interferon, are known for their robust immune-modulating effects, which likely contributed to the higher initial tumor regression observed in this study. However, these treatments also come with a higher burden of systemic side effects, including flu-like symptoms, fatigue, and systemic toxicity, which were significantly more common in the systemic treatment group (Group B). These adverse effects may limit the tolerability and long-term use of systemic therapies, particularly in older or frailer patients [6-8].

On the other hand, topical treatments like imiquimod offer a more localized approach, directly targeting the tumor with minimal systemic involvement. The lower recurrence rates observed in the topical treatment group at 2 years suggest that, while initial tumor regression may be slower, the localized immune response induced by topical agents may provide more durable control over the disease. The lower incidence of adverse events in the topical group further supports its use, particularly in patients who are less suited for systemic therapies due to comorbid conditions or poor tolerance to systemic side effects [8-11].

Clinical Implications

The findings of this study have significant implications for the management of early-stage melanoma. The choice between topical and systemic treatments should be guided by a thorough assessment of patient-specific factors, including the extent of disease, patient age, comorbidities, and the ability to tolerate potential side effects. For patients who can tolerate systemic therapy and require rapid tumor regression, systemic treatments may be the preferred option. Conversely, for patients who are at higher risk for systemic toxicity or who require long-term disease control, topical treatments may offer a safer and more sustainable alternative [12,13].

Patient Selection and Treatment Tailoring

The study underscores the importance of individualized treatment planning in early-stage melanoma. Given the varying efficacy and side effect profiles of topical versus systemic treatments, clinicians must weigh the benefits and risks of each approach in the context of the patient's overall health status and treatment goals. For example, younger patients with fewer comorbidities might benefit from the aggressive tumor regression associated with systemic therapy, while older patients or those with significant comorbidities may achieve better outcomes with the less invasive topical treatments [1,5,13].

Limitations of the Study

While this study provides valuable insights, it is important to acknowledge its limitations. The study was conducted in a specific geographic region (India), which may limit the generalizability of the findings to other populations with different genetic backgrounds, environmental exposures, and healthcare systems. Additionally, the follow-up period of 2 years, while sufficient to assess initial outcomes, may not fully capture the long-term efficacy and safety of the treatments. Further studies with longer follow-up and broader patient populations are needed to validate these findings.

Future Research Directions

Future research should focus on exploring the combination of topical and systemic treatments to determine whether a multimodal approach could enhance outcomes for early-stage melanoma patients. Additionally, studies investigating the molecular mechanisms underlying the differential responses to these treatments could provide deeper insights into optimizing therapeutic strategies. Further research into patient-reported outcomes and quality of life measures could also help in understanding the broader

impact of these treatments on patients' lives, beyond clinical efficacy alone.

CONCLUSION

This multicenter study highlights the differing strengths of topical and systemic treatments for early-stage melanoma. While systemic treatments offer superior initial tumor regression, topical treatments demonstrate better long-term control with fewer adverse effects. These findings suggest that the choice of treatment should be carefully tailored to the individual patient's needs, balancing the urgency of tumor control with the potential for side effects. As the understanding of melanoma biology and treatment continues to evolve, personalized treatment strategies that optimize both efficacy and safety will be key to improving patient outcomes in early-stage melanoma. Further research is warranted to explore the potential for combined therapies and to validate these findings across diverse patient populations.

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