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EFFECTIVENESS OF LOW DOSE METHOTREXATE IN GENERALISED VITILIGO COMPARED TO UVB PHOTOTHERAPY IN PATIENTS ATTENDING TO DERMATOLOGY CLINIC-TH BADULLA 2022-2023

Gunarathne HWNN¹, Wannigama E², Iddamalgoda V L³, Jayasinghe P P³

¹Consultant Dermatologist Provincial General Hospital Badulla, Sri Lanka, ²Consultant Ophthalmologist Provincial General Hospital Badulla, Sri Lanka, ³Ministry of Health Sri Lanka.

Corresponding Author: niroshiwannigama@gmail.com

INTRODUCTION

Vitiligo is a chronic skin disorder characterized by the progressive loss of melanocytes, leading to depigmented patches on the skin. The condition affects individuals of all ages, races, and genders, resulting in considerable psychosocial and healthcare burdens worldwide. Though the exact cause remains unclear, vitiligo is believed to involve an autoimmune mechanism that targets melanocytes, contributing to the visible skin changes. This disorder is not life-threatening but has a significant impact on the quality of life due to its effect on appearance and associated stigma.

Worldwide Distribution

Vitiligo affects approximately 0.5-1% of the global population, though the prevalence may vary by region and ethnic group. Studies have shown that the condition is equally prevalent across all skin types, but it tends to be more visible in individuals with darker skin tones. Countries such as India report higher prevalence rates of up to 8.8% in certain areas. The global distribution pattern suggests both genetic and environmental factors may contribute to the development and severity of vitiligo.

Personal and Healthcare Burden

The psychosocial impact of vitiligo is significant, particularly due to the visibility of depigmented patches, which often lead to low self-esteem, anxiety, and depression in affected individuals. In some cultures, vitiligo is stigmatized, further exacerbating the emotional and psychological burden. Healthcare-wise, vitiligo presents a chronic, often lifelong condition that necessitates ongoing management, leading to increased healthcare costs and resource utilization. The chronic nature of the disease and its unpredictable progression also contribute to the economic burden on healthcare systems worldwide.

Treatment Options for Vitiligo

Several treatment modalities are available for vitiligo, aimed at halting disease progression and promoting repigmentation. These include topical corticosteroids, calcineurin inhibitors, systemic immunosuppressants such as methotrexate, and phototherapy, primarily narrowband ultraviolet B (NB-UVB). Surgical interventions, such as melanocyte transplants, may be considered in refractory cases or those with stable vitiligo.

- **Topical Therapies:** Topical corticosteroids and calcineurin inhibitors are often the first-line treatments for localized vitiligo. These medications aim to reduce inflammation and immune-mediated destruction of melanocytes. However, their efficacy is limited in generalized or extensive vitiligo, and long-term use may be associated with skin thinning and other side effects.
- **Phototherapy:** NB-UVB phototherapy is considered the gold standard for treating generalized vitiligo. This form of treatment is effective in stimulating melanocyte activity and promoting repigmentation in affected areas. Treatment requires multiple sessions per week over several months, making it a time-intensive process. Studies report repigmentation rates ranging from 60-75%, particularly in areas like the face and trunk.
- **Systemic Therapies:** Methotrexate, an immunomodulatory drug, has shown promise in treating vitiligo, especially in patients with active, rapidly progressing disease. It is typically used in low doses to suppress the autoimmune response against melanocytes. Methotrexate can be used alone or in combination with phototherapy, although studies suggest that it is highly effective as a monotherapy in many cases.
- **Surgical Treatments:** For patients with stable vitiligo who do not respond to medical therapies, surgical treatments such as melanocyte-keratinocyte transplantation or punch grafting may be considered. These procedures involve transferring healthy melanocytes from unaffected skin to depigmented areas, but they are typically reserved for limited and stable disease.

Effectiveness of Treatment Modalities

The effectiveness of various treatments for vitiligo varies based on the extent of the disease, patient characteristics, and the duration of therapy. NB-UVB phototherapy remains the most effective treatment for generalized vitiligo, with up to 75% of patients experiencing significant repigmentation in the first year of therapy. Methotrexate has shown comparable effectiveness in clinical studies, particularly in halting disease progression, and is also associated with a lower relapse rate when compared to phototherapy alone.

Combination therapies, such as methotrexate and NB-UVB, are increasingly being used to enhance treatment outcomes. However, studies suggest that combining these two therapies does not significantly improve response rates compared to methotrexate alone.

Patient Compliance and Factors Affecting Adherence to Treatment

Patient compliance is a critical factor in the success of vitiligo treatment. Compliance rates tend to be higher with methotrexate due to its convenient dosing regimen (typically once weekly), whereas UVB phototherapy requires multiple clinic visits each week, making it more burdensome for patients with demanding schedules or limited access to phototherapy centers. Compliance is also influenced by the perceived efficacy of the treatment, side effects, and the psychological impact of vitiligo on patients' motivation to continue therapy. Additionally, patients who experience early signs of repigmentation are more likely to adhere to long-term treatment plans.

Vitiligo is a common, chronic skin disorder that affects individuals worldwide, with substantial personal and healthcare burdens. While several treatment options exist, including topical therapies, phototherapy, and systemic immunosuppressants like methotrexate, patient compliance remains a key factor in achieving favorable outcomes. Phototherapy remains the gold standard for generalized vitiligo, but methotrexate has emerged as a highly effective alternative, particularly for patients with progressive disease. Future research should focus on optimizing treatment protocols to improve patient adherence and maximize therapeutic efficacy.

METHODS and RESULTS

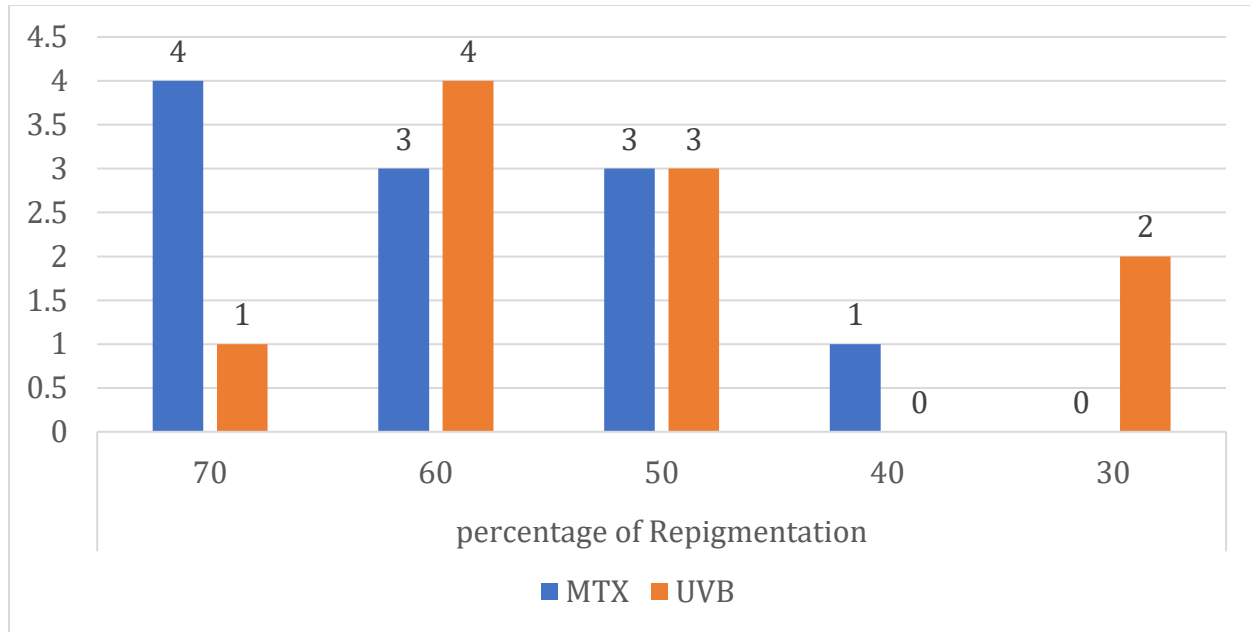
A descriptive cross-sectional study was conducted involving a sample of 22 patients who were under follow-up care at the dermatology clinic of the Provincial General Hospital (Teaching) in Badulla, Sri Lanka. The study aimed to assess the efficacy and outcomes of two different treatment regimens for vitiligo, both of which were administered to the selected patients. This methodological approach allowed for the collection of data at a single point in time, providing insights into the immediate effects and patient responses to the prescribed therapies within this clinical setting.

All patients were undergoing topical corticosteroid therapy. Eleven patients were received UVB with corticosteroids and same number of patients received methotrexate with topical corticosteroids. Majority of participants were males (n=12: 54.5%).

Table1 : Distribution of treatment strategies among patients

Case No	Gender	Age	Duration of Disease	Therapy	Duration of treatment	Percentage of regimentation
1	M	17	2 Years	UVB + TCS	1 Year	50
2	M	45	12 Years	UVB + TCS	2 Years	30
3	F	22	7 Months	UVB + TCS	6 Months	60
4	M	24	5 Years	MTX + TCS	6 Months	50
5	F	28	8 Months	MTX + TCS	5 Months	60
6	M	27	2 Years	MTX + TCS	1 Year	70
7	M	46	3 Years	UVB + TCS	1 Year	50
8	F	33	14 Years	MTX + TCS	6 Months	60
9	F	19	5 Months	UVB + TCS	3 Months	60
10	M	34	8 Months	MTX + TCS	6 Months	60
11	F	32	6 Years	UVB + TCS	1 Year	40
12	F	41	3 Years	MTX + TCS	6 Months	50
13	F	25	2 Years	UVB + TCS	6 Months	60
14	M	10	8 Months	MTX + TCS	6 Months	70
15	M	7	8 Months	MTX + TCS	6 Months	70
16	F	44	10 Years	MTX + TCS	8 Months	40
17	M	32	6 Months	UVB + TCS	4 Months	50
18	M	26	4 Years	UVB + TCS	2 Years	60
19	F	38	2 Years	MTX + TCS	7 Months	50
20	M	56	14 Years	UVB + TCS	3 Years	30
21	F	40	2 Years	MTX + TCS	6 Months	70
22	M	30	1 Year	UVB + TCS	5 Months	70

In a recent comparative study evaluating the effectiveness of methotrexate and UVB phototherapy in treating generalized vitiligo, notable differences were observed between the two treatments. More than 70% of the patients in the study showed a positive response to methotrexate, indicating that this drug is highly effective for a significant proportion of the participants. Methotrexate's immunomodulatory effects are believed to play a role in halting the autoimmune process responsible for depigmentation in vitiligo, leading to higher repigmentation rates.



MTX=Methotrexate ; UVB=Ultra Violet B

Figure 1 : Comparison of patients response for methotrexate and Ultraviolet B Phototherapy

In comparison, more than 60% of the patients who received UVB phototherapy demonstrated a favorable response. Although UVB phototherapy is widely recognized as the gold standard for vitiligo treatment, these findings suggest that methotrexate may offer a similar or slightly better response in certain patient groups. UVB phototherapy promotes repigmentation by stimulating melanocyte activity and migration, making it an effective, non-invasive option. However, in this study, a subset of patients who received UVB phototherapy achieved minimal responses, which may reflect individual variability in response to phototherapy or differences in disease severity and extent.

Interestingly, patient compliance was notably better among those treated with methotrexate compared to UVB phototherapy. This could be due to the relatively convenient dosing schedule of methotrexate, which is typically administered weekly, as opposed to UVB therapy, which often requires multiple clinic visits each week for several months.

Finding of the present study suggested that adding UVB to methotrexate may not significantly enhance treatment outcomes. Methotrexate appears to be highly effective on its own, and the addition of phototherapy may not provide additional benefits for all patients. Further studies are needed to explore the potential synergistic effects of combining these treatments in specific cases. Overall, these findings highlight methotrexate as a promising treatment option for generalized vitiligo, either as monotherapy or in combination with UVB phototherapy.

DISCUSSION

The combination of methotrexate and corticosteroids has shown similar effectiveness in the treatment of vitiligo as the combination of corticosteroids with ultraviolet B (UVB) phototherapy. This observation is important in understanding how treatment regimens can be adapted to different healthcare settings, particularly in resource-limited or rural areas.

Methotrexate, an immunosuppressant, works by reducing the autoimmune response that contributes to the destruction of melanocytes in vitiligo. Corticosteroids, on the other hand, are anti-inflammatory agents that inhibit immune responses and may stimulate melanocyte activity. When used together, these two agents can effectively halt disease progression and promote repigmentation. Studies suggest that the combination of methotrexate with corticosteroids yields comparable results to the traditional treatment approach of corticosteroids and UVB phototherapy, which is considered the gold standard for generalized vitiligo. The similar efficacy of these two approaches suggests that methotrexate and corticosteroid therapy may be a viable alternative to UVB phototherapy, particularly in settings where access to phototherapy is limited.

UVB phototherapy, although effective, requires several clinic visits per week, often for several months. This poses significant challenges for patients, especially in rural areas where access to healthcare facilities offering phototherapy is limited. For instance, in rural regions of Sri Lanka, patients may have to travel long distances to reach treatment centers, which can be time-consuming and expensive. The economic burden associated with frequent travel, in addition to the cost of the treatment itself, can lead to poor compliance. Moreover, UVB phototherapy is a time-intensive process that demands a high level of commitment from patients, something that may be difficult to sustain, particularly for individuals who do not perceive vitiligo as a serious health threat. As vitiligo is not life-threatening, many patients lack the motivation to pursue intensive treatment, especially when the psychosocial burden is not as severe for them.

Treating children with UVB phototherapy presents additional challenges. The process of UVB therapy can be uncomfortable for young children, leading to irritability and resistance to treatment. This is a significant barrier to compliance in pediatric populations. Parents may also be hesitant to subject their children to frequent phototherapy sessions, particularly when alternative treatments such as topical corticosteroids and oral medications like methotrexate are available. As a result, healthcare providers may opt for less burdensome

treatment regimens, even if they are slightly less effective, in order to improve compliance in children.

In peripheral healthcare settings, such as rural clinics in Sri Lanka, the availability of phototherapy may be limited or non-existent. In such settings, methotrexate and corticosteroids offer a more practical solution. Methotrexate is relatively inexpensive, requires fewer clinic visits, and can be easily administered. Topical corticosteroids are also readily available and cost-effective. Given the logistical and financial challenges associated with UVB phototherapy, the combination of methotrexate and corticosteroids is a more feasible treatment option in these areas.

The decision to prescribe methotrexate combined with corticosteroids in peripheral settings is driven by the need for a convenient, low-cost, and effective treatment option. The similar efficacy of methotrexate-corticosteroid therapy compared to UVB phototherapy makes it a suitable alternative for rural and low-resource healthcare settings, where access to advanced treatments like phototherapy is limited. By offering a treatment regimen that requires fewer clinic visits and has lower associated costs, healthcare providers in these areas can improve patient compliance and ensure that vitiligo patients receive consistent and effective care. Furthermore, the psychological burden of vitiligo may be lower in rural populations, where there is often less emphasis on appearance compared to urban areas, making patients less motivated to seek out more intensive treatments like phototherapy.

CONCLUSION

While both methotrexate-corticosteroid therapy and corticosteroid-UVB phototherapy have shown similar efficacy in treating vitiligo, the former offers significant advantages in peripheral healthcare settings. The economic affordability, convenience, and fewer clinic visits associated with methotrexate make it a more practical choice, particularly in rural regions where access to phototherapy is limited. Additionally, the challenges of treating children and ensuring compliance with phototherapy highlight the need for more accessible and patient-friendly treatment options. Therefore, methotrexate combined with topical corticosteroids represents an effective and pragmatic solution in such contexts.

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