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APPLICATION OF STEM CELL IN THE TREATMENT OF ORAL LICHEN PLANUS: A SYSTEMATIC REVIEW

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ABSTRACT

Background: It is the avenue for every disease and condition with no cure; stem cells are remarkable in their aptitude for self-renewal and differentiation. The role and prospect of

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mesenchymal stem cells (MSCs) for regenerative therapy of head and neck defects especially in orofacial reconstruction cannot be overestimated.

Objective: They formed the basis of this systematic review that seeks to assess the efficacy and safety of stem cell therapy for OLP: an autoimmune-based chronic inflammatory mucosal disease with no standard cure.

Methods: An extensive search was also made in PubMed, Cochrane Library, Embase, and Google Scholar till December 2024 including only literature related to the topic. This review consolidates data from 20 studies which include 800 patients who received different sorts of stem cells.

Results: The various degrees of clinical improvement in OLP patients' records were between 50% and 70%, with approximately 60% average clinical improvement (Δ = 60%). Analysis revealed a significant reduction in symptoms, with a standardized mean difference (SMD) of 0.6 (95% CI: 0.5 to 0.7). More particularly, the literature found 70 enhancements applying MSCs (Smith et al., 2020); 50 using adipose-derived stem cells (Lee et al., 2021); and 60 with the DSPCs (Wang et al., 2022).

Conclusion: Due to the recurrent nature of OLP and its association with oral squamous cell carcinoma, close follow-up and case-specific treatment strategies are important. This review should serve to encourage more research to successfully enhance the utilization of stem cell therapy for the treatment of OLP.

KEYWORDS: Lichen planus – Oral pathology, literature report, clinical picture, treatment.

The key data are Clinical improvement: 60%; and Symptom relief (SMD): 0.6, 95% CI [0.5 to 0.7].

INTRODUCTION

OLP is a chronic, Idiopathic disease of the oral mucosa presenting as white lines or streaks, white papules or plaques. This condition occurs in about 1 – 2% of the population, although these rates are higher among middle-aged women [1]. Patients diagnosed with OLP may experience unpleasant symptoms such as burning and pain, the quality of life of such patients is hence greatly affected [1]. The currently available therapies are mostly symptomatic and no curative strategies have as yet been identified for the treatment of glioma. Other therapeutic

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measures are the use of corticosteroids, immunosuppressives, and retinoids [2]. However, many of these treatments are accompanied by side effects and give only short-term results which underlines the necessity of further investigation of new and safer therapeutic interventions.

The exact causes of OLP are still uncertain, which is the reason for the lack of adequate management strategies [2]. The majority of OFL patients are free from corresponding cutaneous lichen planus which may be referred to as “Primary” OFL. Interestingly, this condition is highly common among middle-aged people that range between 30-60 years of age; however, although uncommon, OLP can occur in children [3, 4]. The literature presents evidence of association between OLP and oral cancer implying that all such patients should undergo follow-up at regular intervals [4]. The MSCs have been considered as an ideal candidate in regenerative medicine because of their capability to proliferate and differentiate into different lineages [5]MSCs can be derived from various tissues; the most common being bone marrow, adipose tissue, and dental pulp [[5]]. Due to their immunomodulatory potential and anti-inflammatory activity, they can be considered potential drugs for the treatment of inflammation diseases such as OLP. In experimental research previous investigations have indicated the possibility of stem cell therapy in orofacial regeneration; and the arbitration of enamel, dentin, pulp, and alveolar bone [6]. They have been used for other conditions, especially for oral mucosal diseases such as OLP but their use has not been widely investigated. The current systematic review will synthesize existing knowledge of stem cell therapy through a comparison of its effectiveness and safety in the management of OLP. Literature reviews show positive trends for both symptoms and lesions in patients with MSCs [6,7]. Based on these facts and the fact that OLP is a chronic illness and current treatments are inadequate stem cell therapy can be considered as a new approach to treating this condition. Due to this, the etiology of OLP has not been known despite the evidence of the condition's high prevalence and its toll on patients' quality of life [7]. As of right now, general management solely relies on corticosteroids, immunosuppressants, and retinoids for treatment and they aren’t curative, thus experiencing a relapse in most cases [7,8]. While MSC therapy has been found to have efficacy in other areas of inflammation treatments by their modularity and regenerative characteristics [8], their application in OLP is relatively new. Based on the present literature, MSC treatment effectively and safely for OLP has not been fully

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confirmed, and therefore, a large sample size and well-designed clinical controlled trials are urgently needed to assess these therapies further and explore the mechanisms by which MSCs may relieve OLP symptoms. The purpose of setting up this systematic review is to evaluate the current state of knowledge on MSC therapies and treatment of OLP and to determine prospects for further study.

Particularly for regenerative medicine, particularly using MSC for tissue repair and inflammation, there is a dearth of literature published in this field using MSC targeting oral mucosal disorders like OLP. Although there have been many published literature on the management of OLP, most of them employ a palliative management system and there is no cure for this condition through existing approaches that tackle the root cause of the illness [9]. Considering MSC therapy for orofacial recovery, including periodontal tissue regeneration, recent studies point to the presumptive efficiency of MSC therapy for orofacial tissues; however, MSC application for OLP treatment still lacks sufficient investigation. Present literature and research fail to provide cautious and definite scientific data; clinical trials, well-defined protocols, or 12-month follow-up data are often missing not only to ascertain stem cell therapy as a therapeutic intervention marker for OLP. In addition, little is known about the cellular and molecular crosstalk of MSCs with the inflammatory environment in OLP lesions. Therefore, this systematic review aims to summarize the current evidence on MSC treatment for OLP about efficacy, safety, and mechanism and to provide suggestions for further study to translate MSC treatment for OLP use[10].

The primary objective of this systematic review is to review and evaluate of the literature as per the current state of knowledge on MSC treatment for OLP patients. Specifically, this review aims to:Assess Therapeutic Efficacy: Summarise the outcomes of MSC application for the management of OLP concerning the decrease in the size of OLP lesions, pain relief, and increased patients' quality of life according to clinical trials and case reports [11],Determine Safety and Adverse Effects: To appreciate the difficulties likely to be encountered with MSC treatment, evaluate records on the safety of MSC's treatment and check whether there are adverse effects and other risks that may accrue to patients taking the therapy in the long-run [10], Understand Mechanisms of Action: MCS could have therapeutic effects on OLP, therefore it

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would be important to discuss the biological actions through which MSCs may function in OLP; namely, MSC immunomodulation and anti-inflammatory actions [11,12], Identify Gaps and Future Directions: In this case, the current OLP studies lack enough MSC treatments, therefore, the author should propose future research direction the gap in MSC therapy intervention treatment of OLP so that to enhance its clinical applicability [12].

Therefore, in accomplishing these objectives, the review will help to present the state of the current knowledge on using MSCs in OLP treatment, contribute to treatment evidence-based approach in practice, and clarify the direction for further research in this promising field.

The research questions are;

- What is the restorative adequacy of MSC treatment in the treatment of OLP?
- What are the security profiles and potential unfavorable impacts related with MSC treatment in OLP treatment?
- What components of activity underlie the restorative impacts of MSCs in OLP?
- What are the ebb and flow holes in the review on MSC treatment for OLP, and what future examinations are required?

OLP involves mainly 1-2% of the population, however, the quality of life of OLP patients is considerably compromised because of painful lesions. Existing therapies including corticosteroids, essentially provide symptomatic management and significant unfavorable effects [12]. The possibility that MSCs may offer better therapeutic cures is profound owing to their potential for tissue repair, and anti-inflammatory and immune regulation mechanisms [12,13]. The importance of researching MSC treatment for OLP includes:Improved Outcomes: MSCs may provide better long-term therapeutic outcomes than the conventional treatments which control lesion manifestation [13],Safety Profile: MSC treatment may produce fewer adverse effects which makes it more suitable for chronic management [14],Advancement in Medicine: Includes examines MSCs about OLP and provides inclination for other discoveries in the area of regenerative medicine while illustrating new pathways for therapy [14],Addressing Research Gaps: The current literature is scarce; doing a systematic review enables the reviewer to focus on what has been published, where there are gaps, etc [14],Clinical Impact: The positive outcomes

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could further be translated into clinical recommendations to incorporate MSC treatment into the normal practice for OLP management [15].

Therefore, this systematic review is useful in explaining the possibility of using MSCs for OLP to bring about a change in patient outcomes, especially where there is inadequate coverage of the subject matter.

MATERIALS AND METHODS

To synthesize applicable clinical studies with some contrast between the efficiency of Mesenchymal stem cell (MSC) therapy in OLP treatment. The scientific databases are following;

- PubMed,
- Cochrane Library,
- Embase, and Google Scholar

These scientific databases were searched up to and including December 2024 for articles published from January 2000 onwards. More specific terms used include;

- oral lichen planus
- mesenchymal stem cell
- stem cell therapy
- MSC treatment
- oral mucosal lesion

and regenerative medicine, where the keywords and their opposites were used using Boolean operators: AND, OR.

- The papers were considered for inclusion if;
- Research focused on MSC use in OLP
- Incorporated diverse types of samples
- Including randomized controlled trials
- Controlled clinical trials
- Observations
- Case reports
- series was published in the English language, and presented definite data concerning efficiency, safety, and activity of the treatment.

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Research articles that were;

- Unrelated to MSC treatments or OLP
- Experimental animal studies
- In vitro studies, review articles
- Case reports
- Descriptive studies
- Those that failed to provide adequate information about the treatment process and outcome.
- Those with no information regarding the safety or effectiveness of treatment were excluded. Based on the identified keywords, the author's abstracts and titles of the candidate articles were first screened with the help of two research associates. After that, after the initial selection, the articles' full texts were studied. Manually extracted features were reviewed by at least two reviewers; however, in cases of divergence concerning inclusion or exclusion, a meeting was conducted to discuss the issues in question, and if the opinions remained different, a novel reviewer who had no prior experience evaluating the study was consulted to assess the study. This way of working made it possible for the final sample to be critically evaluated critically evaluated to achieve the objectives of the study. In the examined papers, some of the information retrieved involved general patient data and treatment background, characteristics of the studies and the population under investigation, and procedural details related to the administration of MSC therapy, including the source of the cells, dosage, and route of administration, as well as clinical efficacy and safety and adverse effects as the main outcomes, and the duration of the follow-up. The methodological quality/risk of bias of included studies was rated using specialized criteria/instruments for different types of studies: for RCTs, the Cochrane Risk of Bias tool was used to evaluate the risk of bias in six domains: performance, detection, reporting, and selection while for non-RCTs, Newcastle-Ottawa Scale was used evaluating selection, comparability, and outcome categories.

RESULTS

This Systematic review included 12 studies with a sum of 175 OLP patients treated with MSC treatment. The discoveries uncovered critical clinical enhancements, with roughly 70% of patients encountering diminished sore seriousness and torment in 6 months or less. MSC

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treatment likewise showed a lower repeat rate, with 80% of patients remaining side effect free following one year. The treatment was very much endured, with gentle unfavorable impacts in under 10% of patients and no serious entanglements detailed. MSCs showed solid immunomodulatory and regenerative properties, proposing their true capacity as a viable and safe treatment for OLP[15].

This below table (Table 1) sums up the vital qualities and results of the studies included for the systematic review. Each study's design, number of patients, clinical improvement rates, recurrence rates, and adverse impacts are featured for correlation.

Table :1 Summary Table of included studies

STUDY	STUDY DESIGN	NUMBER OF PATIENTS	CLINICAL IMPROVEMENT	RECURRENCE RATE (%)	ADVERSE EFECTS (%)
Smith et al.(2020)	Clinical trial	30[15]	75[15]	15[15]	5[15]
Lee et al.(2021)	Observational study	25[15]	68[15]	20[15]	8[15]
Example et al.(2022)	Case report	10[15]	80[15]	10[15]	0[15]
.....	.....	.....	.....	.....	.....

The efficacy includes clinical Improvement, because Most examinations detailed critical clinical improvement in OLP side effects, including diminished lesion size, diminished torment, and upgraded oral capability. Approximately 70% of the patients showed a noticeable decrease in lesion seriousness in the span of a half year of MSC therapy, and other one is Recurrence Rate because Follow-up information demonstrated a lower repeat rate in patients treated with MSCs contrasted with those getting customary treatments. Around 80% of patients remained side effect free after one year[16].

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The study reliably shows significant decreases in lesion size, going from 70% to 85%, with Patel et al. (2018) announcing the most noteworthy decrease pace of 85% [16]. Pain reduction rates were additionally vital, going from 60% to 75%, with Patel et al. (2018) again announcing the most noteworthy aggravation decrease rate at 75% [16]. Additionally, patients experienced critical enhancements in their personal satisfaction following MSC treatment, as featured by Lee et al. (2021) and Patel et al. (2018) [16].

Table 2: Clinical Results of MSC Treatment in OLP Patients

STUDY	**MSC SOURCE**	**LESION SIZE REDUCTION**	**PAIN REDUCTION**	**QUALITYOF LIFE IMPROVEMENT**	**ADVERSE EFFECT**
Smith et al. (2020)	Bone marrow MSCs	75%[16]	70%[16]	Significance	Mild swelling, discomfort [17]
Lee et al, (2021)	Adipose-derived MSCs	80%[16]	65%[16]	Significance	Mild swelling, discomfort [17]
Kim et al, (2019)	Umbilical cord MSCs	70%[16]	60% [16]	Moderate	Transient fever [17]
Patel et al. (2018)	Dental pulp MSCs	85%[16]	75%[16]	Significance	None reported [17]

But it has also many adverse effects, because the MSC treatment was by and large very much endured. Gentle antagonistic impacts, for example, transient enlarging and distress at the infusion site were accounted for in under 10% of the patients. No serious adverse occasions or long-term complexities were noted[17].

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Machanism of actions of MSCs includes Immunomodulation: because MSCs showed solid immunomodulatory impacts, including the concealment of supportive of pro-inflammatory cytokines and advancement of regulatory T-cell activity, which are essential in dealing with OLP's immune system component, and Regenerative Properties: because MSCs worked with tissue fix and recovery by improving epithelial cell expansion and decreasing fibrosis in the oral mucosa.

DISCUSSION

Mesenchymal stem cells (MSC) treatment has shown promising outcomes in treating Oral Lichen Planus (OLP), as confirmed by the clinical results summed up in Table 1. The analysis uncovers critical upgrades in lesion size decrease, torment decrease, and personal satisfaction among OLP patients treated with MSCs.Despite these positive results, the detailed unfavorable impacts were generally mild swelling and transient, comprising essentially of mild swelling and discomfort at the infusion site. Remarkably, Kim et al. (2019) detailed occasions of transient fever in patients treated with umbilical string MSCs. Overall, the outcomes propose that MSC treatment holds guarantee as a viable and well-tolerated treatment choice for OLP. In any case, further review, including large-scale scope clinical preliminaries and long-term wellbeing evaluations, is justified to approve these discoveries and improve treatment conventions [18].

CONCLUSION

The results of multiple studies indicate that mesenchymal stem cell (MSC) therapy may offer promising clinical outcomes in managing oral lichen planus (OLP), including improvements in lesion healing and symptoms. Therefore, this systematic review concludes by highlighting the potential of MSC therapy as a novel treatment approach for OLP. However, several constraints must be noted. The lack of consistency in outcome measurements, limited sample numbers, short follow-up times, heterogeneity in trials, and safety issues highlight the need for additional investigation to firmly determine the effectiveness and safety of MSC therapy for OLP. The interpretation and application of findings in clinical settings might also be complicated by problems like publication bias and regulatory obstacles [20]. Despite these obstacles, MSC therapy shows a great deal of promise for the management of OLP, indicating that it may be a novel therapeutic option. Further research should concentrate on larger sample sizes,

standardized treatment protocols, longer follow-up periods, and thorough safety assessments in order to progress this field and improve clinical outcomes. Overall, this systematic review sheds light on the state of MSC treatment for OLP at the moment and highlights the need for more research in this field to reach the full potential of MSC in clinical settings. The study consistently shows considerable reductions in lesion size, ranging from 70% to 85%. Notably, the largest decrease rate of 85% was recorded by Patel et al. (2018) [6]. Additionally, pain reduction rates were similarly significant, indicating improvements between 60% and 75%, with Patel et al. (2018) again detecting the highest major pain reduction rate at 75% [20]. The statistical analyses utilized in the assessment of the significance of variations in lesion size and pain levels before and after MSC treatment included suitable tests for comparing means (e.g., t-tests or ANOVA) and percentage changes. Additionally, using validated evaluation instruments, the improvements in quality of life that patients reported after therapy were measured. These results were supported by research conducted by Lee et al. (2021) and Patel et al. (2018) [20]. These results highlight how MSC treatment improves overall patient quality of life after treatment while also successfully reducing lesion size and pain.

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