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Comparative Study of Netarsudil /Latanoprost (0.02% + 0.005% Sun Pharma) vs. Latanoprost (0.005% FDA) in Reducing Intraocular Pressure.

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ABSTRACT

This study aimed to compare the efficacy and safety of a once-daily, fixed-dose combination of Netarsudil and Latanoprost (Sun Pharma) with Latanoprost (FDA) in patients with Open Angle Glaucoma or Ocular Hypertension, focusing on the reduction of elevated Intraocular Pressure (IOP). A randomized, active-controlled parallel-group study was conducted with two groups of 50 patients each, totaling 100 participants. Group A received once-daily Netarsudil 0.02% / Latanoprost 0.005% (Sun Pharma). Group B received Latanoprost 0.005% (FDA). Patients administered the study drug into one eye at 9.00 PM daily. Main Outcome Measures: IOP measurements were obtained at 9.00 AM and 5.00 PM on day 1 (baseline), at weeks 2, 6, and months 3, 6, 9, and 12. Ocular and systemic safety were evaluated throughout the 12-month study period. Netarsudil/Latanoprost (Sun Pharma) demonstrated statistically superior IOP reduction compared to Latanoprost (FDA) at all assessment points over 12 months. The mean diurnal IOP (± standard error) at 12 months was 16.2 ± 0.23 mmHg for Netarsudil/Latanoprost (Sun Pharma) and 17.6 ± 0.18 mmHg for Latanoprost ($p < 0.05$). One adverse event, conjunctival hyperemia, was observed, with mild severity in 8 out of 50 patients (16%) in the Netarsudil/Latanoprost group and in 2 out of 50 patients (4%) in the Latanoprost group. The 12-month study results indicated superior efficacy for Netarsudil/Latanoprost (Sun Pharma) compared with the individual component Latanoprost (FDA). This combination therapy offers a promising approach for managing elevated IOP in patients with Open Angle Glaucoma or Ocular Hypertension.

Keywords: Intraocular Pressure, Netarsudil, Latanoprost, Glaucoma, Fixed-Dose Combination, Ocular Hypertension, Efficacy, Safety.

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INTRODUCTION

The management of elevated intraocular pressure (IOP) is a critical aspect of the treatment of Open Angle Glaucoma and Ocular Hypertension, with the primary objective of preventing vision loss. In this context, the present study conducted a rigorous comparative assessment of the efficacy and safety of a fixed-dose combination of Netarsudil and Latanoprost (0.02% + 0.005%, Sun Pharma) in comparison to Latanoprost (0.005%, FDA). The primary motivation behind this investigation is to determine whether the combination therapy provides superior IOP reduction compared to the individual component, Latanoprost, which is a well-established IOP-lowering medication.

IOP fluctuations throughout the day are a key concern, and a once-daily dosing regimen can enhance patient adherence. Over the course of 12 months, the study meticulously monitored IOP at multiple time points and evaluated ocular and systemic safety, focusing on the incidence of adverse events. The results of this research are expected to provide valuable insights into the optimal treatment strategy for managing elevated IOP in patients with glaucoma or ocular hypertension, potentially contributing to improved vision preservation [1-11].

METHODOLOGY

This prospective, randomized, active-controlled study aimed to assess the efficacy and safety of a once-daily fixed-dose combination of Netarsudil 0.02% and Latanoprost 0.005% (Sun Pharma) compared to Latanoprost 0.005% (FDA) in patients with Open Angle Glaucoma (OAG) and Ocular Hypertension (OHT). The study was conducted from March 2021 to February 2022 and was conducted with ethical approval from the Institutional Ethical Committee of B.J. Government Medical College in Pune. All enrolled patients provided written informed consent.

Inclusion and Exclusion Criteria

Patients aged 18 years or older with unmedicated Intraocular Pressure (IOP) levels ranging from ≥ 21 mmHg to ≤ 36 mmHg in one eye at 9.00 AM and with best-corrected visual acuity (BCVA) of 20/200 or better on the ETDRS chart were included in the study. Patients using ocular hypotensive medications were required to undergo specific washout periods based on the class of medication before study entry. Exclusion criteria included unmedicated IOP ≥ 36 mmHg in the study eye, the presence of OHT with certain conditions, previous ocular surgeries or laser procedures within 3 months of screening, clinically significant ocular diseases, ocular trauma within 6 months of screening, and pregnancy or lactation. Eligible patients were randomized in a 1:1 ratio to receive either Netarsudil 0.02%/Latanoprost 0.005% or Latanoprost 0.005% once daily for 12 months, with the study eye selected based on higher IOP at 9.00 AM on day 1 or the right eye if IOP was the same in both eyes.

Endpoints and Statistical Analysis

The primary efficacy endpoint was the mean IOP in the study eye at various study visits, including weeks 2, 6, and months 3, 6, 9, and 12. The IOP measurements were obtained using a calibrated Goldman Applanation Tonometer at 9 AM and 5 PM. Ocular safety assessments included a range of parameters such as BCVA, pachymetry, visual field assessments, cup/disc ratio, and ocular examinations. Heart rate and blood pressure were also recorded at each visit, and adverse events were assessed over the 12-month study duration.

Statistical analysis was conducted using a linear model to compare the mean IOP in the study eye between the two treatment groups at different time points. The analysis aimed to determine if there was a true mean difference of 1.5 mmHg between Netarsudil/Latanoprost (Sun Pharma) and Latanoprost.

RESULTS

A total of 100 patients were included in the study, with a 1:1 randomization, to assess the primary efficacy endpoint and safety parameters.

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Table 1: Patients distribution

	Netarsudil/Latanoprost (Sun Pharma)	Latanoprost (FDC)
Total Patients	100	100
Completed 12 Months	Yes	Yes
Mean Diurnal IOP (mmHg)	Baseline: 23.7	Baseline: 23.5
	12 Months: 16.2	12 Months: 17.6
IOP Reduction at 12 Months	30% or greater	27%

Table 2: Demographic and Prior Hypotensive Therapy Information

	Netarsudil / Latanoprost (Sun Pharma)	Latanoprost (FDC)
Gender	Male/Female	Male/Female
Age (Years)	<65 years/>65 years	<65 years/>65 years
Prior Therapy	Combination Therapy	Prostaglandin (Monotherapy)
	Prostaglandin (Monotherapy)	Beta Blockers (Monotherapy)
	Beta Blockers (Monotherapy)	Other Monotherapy
	Other Monotherapy	No Prior Therapy

DISCUSSION

In this 12-month study, the primary efficacy endpoint was successfully met, demonstrating that Netarsudil / Latanoprost (Sun Pharma) provided statistically superior IOP lowering compared to the active component, Latanoprost (FDC). The study rigorously assessed IOP at various time points, including 9.00 AM and 5.00 PM, at weeks 2, 6, and months 3, 6, 9, and 12. The results clearly indicate that the fixed-dose combination of Netarsudil and Latanoprost offers a more effective approach to reducing intraocular pressure. The primary efficacy endpoint in glaucoma management is IOP control, and achieving a statistically significant reduction in IOP is of paramount importance in preventing disease progression and preserving vision.

One potential mechanism contributing to the superior IOP reduction observed in the Netarsudil / Latanoprost group is Netarsudil's ability to induce structural changes in the trabecular meshwork (TM) and block the profibrotic effects of transforming growth factor beta (TGF-β) on TM cells. The trabecular meshwork is a critical component of the eye's drainage system, and improving its function can enhance aqueous humor outflow, reducing IOP. The specific action of Netarsudil on TGF-β and its vasodilatory effects on TM cells may explain its superior performance in combination with Latanoprost.

Conjunctival hyperemia was the most frequent ocular adverse event observed during treatment. This side effect is an expected consequence of the vasodilatory effect of RHO-Kinase inhibition. Importantly, it appears to be self-resolving within several days, which is consistent with previous research. There was no evidence of treatment-related systemic effects in patients receiving Netarsudil / Latanoprost (Sun Pharma), and no systemic serious treatment-related adverse events were reported. This is reassuring for the safety profile of this fixed-dose combination.

The study also provided a comparative analysis of Netarsudil / Latanoprost with Latanoprost (FDC) as a monotherapy, demonstrating that the combination therapy achieved a 30% or greater reduction in IOP at 12 months, compared to a 27% reduction in IOP in patients treated with Latanoprost monotherapy. This highlights the potential benefits of combination therapy over monotherapy in managing elevated IOP in patients with Open Angle Glaucoma or Ocular Hypertension.

The charts presented illustrate the distribution of patients with baseline IOP levels, further supporting the efficacy of Netarsudil / Latanoprost in reducing IOP.

In conclusion, while this study provides valuable insights into the efficacy and safety of Netarsudil / Latanoprost (Sun Pharma) in the management of elevated IOP, it is essential to acknowledge certain limitations. The 12-month duration of the study, while substantial, falls short of capturing the long-term management of chronic conditions like Open Angle Glaucoma and Ocular Hypertension. Long-term follow-up data for a full year showed consistent IOP-lowering efficacy, which is a positive indicator

of the treatment's ongoing effectiveness. However, additional long-term studies may further strengthen the evidence for the sustained benefits of this combination therapy [12-22].

CONCLUSION

Despite these limitations, the results from this study strongly support the use of Netarsudil / Latanoprost (Sun Pharma) as a safe and effective treatment for Open Angle Glaucoma and Ocular Hypertension. The combination therapy not only demonstrated superior IOP reduction compared to PGA monotherapy but also maintained a good tolerability profile. This is promising news for both clinicians and patients seeking improved strategies for IOP management, which is critical for preventing vision loss in these chronic eye conditions. Further research and long-term follow-up studies are warranted to confirm and expand upon these findings.

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