



E-ISSN: 2663-8274
P-ISSN: 2663-8266
www.opthalmoljournal.com
IJMO 2024; 6(1): 05-10
Received: 06-10-2023
Accepted: 11-11-2023

Dr. Manjula S
Sr. Vice President,
Department of Medical
Services, Micro Labs Limited,
Bangalore, Karnataka, India

Krishna Kumar M
Department of Medical
Services, Micro Labs Limited,
Bangalore, Karnataka, India

Corresponding Author:
Dr. Manjula S
Sr. Vice President,
Department of Medical
Services, Micro Labs Limited,
Bangalore, Karnataka, India

Expert opinion on netarsudil for the management of glaucoma in Indian settings

Dr. Manjula S and Krishna Kumar M

DOI: <https://doi.org/10.33545/26638266.2024.v6.i1a.168>

Abstract

Background: Despite topical treatments for glaucoma are generally successful and well tolerated, there is a need for newer drugs to manage patients who are unable to tolerate previous topical treatments due to adverse effects or those who experience side effects or insufficient reduction in IOP with current medical treatments.

Objective: The study was intended to gather diverse perspectives of experts on the use of netarsudil for the management of glaucoma.

Methodology: This cross-sectional study examined the opinions of specialists from different parts of India about the usage of netarsudil for patients with glaucoma. Twenty-one questions in the survey aimed to elicit thoughts from specialists on whether they would advise netarsudil for glaucoma management.

Results: The survey assessed the preferences of experts on prescribing netarsudil for glaucoma management. Out of 42 respondents, 57.14% indicated that glaucoma frequently affects individuals beyond the age of 50. The most commonly used method of diagnosing glaucoma was using a slit lamp examination and tonometer. The results demonstrate that 33.33% of respondents used travoprost and bimatoprost equally among prostaglandin analogues. Netarsudil was usually recommended for patients who were unable to control their symptoms with combination therapy, according to 47.61% of study participants. It was also suggested for individuals whose illnesses cannot be treated with prostaglandin analogues, according to about 14.28% of survey participants. Adding netarsudil can lower intraocular pressure (IOP) and delay the need for glaucoma laser or incisional surgery. According to a significant portion of respondents (30.95%), netarsudil can be prescribed for all patient with uncontrolled prostaglandin analogues, uncontrolled combination therapy, add-on therapy, or who needs surgery.

Conclusion: The findings contribute to the knowledge base surrounding the use of netarsudil in clinical practice, providing insights into its potential role as a valuable therapeutic option for glaucoma patients.

Keywords: Netarsudil, glaucoma, primary open-angle glaucoma, angle-closure glaucoma, intraocular pressure

Introduction

A progressive degenerative optic neuropathy, also known as glaucoma, results in typical vision field loss and abnormalities of the eyes' mechanics and function (such as loss of retinal ganglion cells and the ensuing damage to the optic nerve ^[1]). Glaucoma affects more than 64 million individuals aged 40 to 80 and was the main cause of irreversible blindness in the world. By 2040, the cases are projected to rise to 112 million globally with an additional 27.8 million cases of glaucoma in Asia. India and China will account for the majority of the burden ^[2]. Glaucoma was one of the main causes of permanent blindness in India, causing blindness in 1.2 million individuals and 5.5% of all cases of blindness ^[3]. Hence, there was a growing need to address the difficulty of managing glaucoma as a public health issue at several levels, with a focus on the general public, service providers, and the eye healthcare system.

Based on the type of angle produced between the iris and cornea (wide and open angle or closed/narrow-angle), primary glaucoma was commonly divided into two main categories namely primary open-angle glaucoma (POAG) and primary angle-closure glaucoma. The POAG was further categorized based on the intraocular pressure (IOP) as POAG with high IOP and POAG with IOP within the normal range (normal-tension glaucoma). Elevated IOP was a significant risk factor for glaucomatous visual field loss ^[4].

In the literature, there have been several comparisons of various types, combinations, or modalities of medicinal therapies for open-angle glaucoma [5, 7]. Some evidence suggested that surgical intervention more effectively reduces IOP, but it was also linked to higher complications [8]. Therefore, it was important to explore more effective ways to lower IOP and potentially avoid the surgery.

Although topical treatments for glaucoma are generally successful and well tolerated, there is a need for newer drugs to manage patients who are unable to tolerate previous topical treatments due to adverse effects or those who experience side effects or insufficient reduction in IOP with current medical treatments. Netarsudil, belonging to the class of Rho kinase inhibitor, was extensively used for the management of open-angle glaucoma and ocular hypertension. The drug acts by reducing the pressure within the eye by enhancing the outflow of aqueous humor, thereby preventing or reducing the progression of optic nerve damage. The Rho Kinase Elevated IOP Treatment (ROCKET) studies showed that netarsudil was a safe topical drug that significantly decreases IOP, and the efficacy was comparable to timolol and latanoprost [9, 11]. However, there is a lack of sufficient evidence on the efficacy of netarsudil in specific patient groups such as those with angle closure or secondary open-angle glaucoma, individuals who have undergone previous laser treatment or surgery for glaucoma, or patients who are currently on multiple IOP-lowering drugs [12, 14]. It was commonly used in clinical practice as an adjunctive therapy for patients who were already on topical drugs and for individuals whose IOP was inadequately managed, despite prior glaucoma laser or surgery. There was no consensus based on pivotal studies regarding the management of such clinical situations. Therefore, the primary objective of the present study was to provide clinicians with expert opinions on the efficacy of using netarsudil in various clinical settings.

Methodology

A cross sectional, multiple-response questionnaire based survey was carried out among ophthalmologists specialized in treating glaucoma patients in the major Indian cities from June 2022 to December 2022.

Questionnaire

The questionnaire booklet titled MIGS (Micro vision's Initiative for Glaucoma Survey) study was sent to the ophthalmologists who were interested to participate. The MIGS study questionnaire consisted of 21 questions seeking the perspectives of the specialists regarding their recommendation of netarsudil to patients with glaucoma. The study was conducted after getting approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

Participants

An invitation was sent to leading ophthalmologists in managing glaucoma in the month of March 2022 for participation in this Indian survey. About 42 ophthalmologists from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Ophthalmologists were requested to complete the questionnaire without discussing with peers. A written informed consent was obtained from each clinicians before initiation of the study.

Statistical Analysis

Descriptive statistics were carried out for the data analysis. Categorical variables were presented as percentages, which allowed the representation of the distribution of each variable. Pie charts and bar charts were created using Excel 2013 (16.0.13901.20400).

Results

Based on the given response rate of 42 ophthalmologists, the majority of respondents (57.14%) reported the diagnosis of glaucoma in patients >50 years of age. Around 40% of respondents reported glaucoma in patients within the 40-50 age group. The 35-40 age group was represented by only one respondent, making up approximately 2.38% of the total sample size. No respondents reported patients from the 30-35 age group according to the given data.

Nearly 28% of the subjects reported slit lamp examination and tonometer as the most commonly reported methods for diagnosing glaucoma, followed by optical coherence tomography (OCT, 14.28%). Gonioscopy and perimetry were less commonly mentioned by 7.14% and 4.76% of the respondents respectively. Approximately 17% of the respondents reported using all of the above methods for diagnosing glaucoma in clinical practice. About 79% of the respondents stated that the applanation tonometer was the most common type of tonometer used for measuring IOP in glaucoma patients, followed by Goldmann's tonometer (14.28%). A smaller percentage of respondents (7.14%) reported using the air puff tonometer. However, it was worth noting that the Schiottz tonometer was not mentioned by any of the respondents.

According to the data, angle closure glaucoma was the most common type of glaucoma noted in patients with provisional diagnosis. The majority of respondents (64.28%) reported 10-25% incidence of angle closure glaucoma in glaucoma patients. Nearly 45% of the respondents stated that primary open-angle glaucoma occurs in 50-75% of patients. Figure 1 summarizes the percentage of glaucoma individuals diagnosed with primary open-angle and angle closure glaucoma.

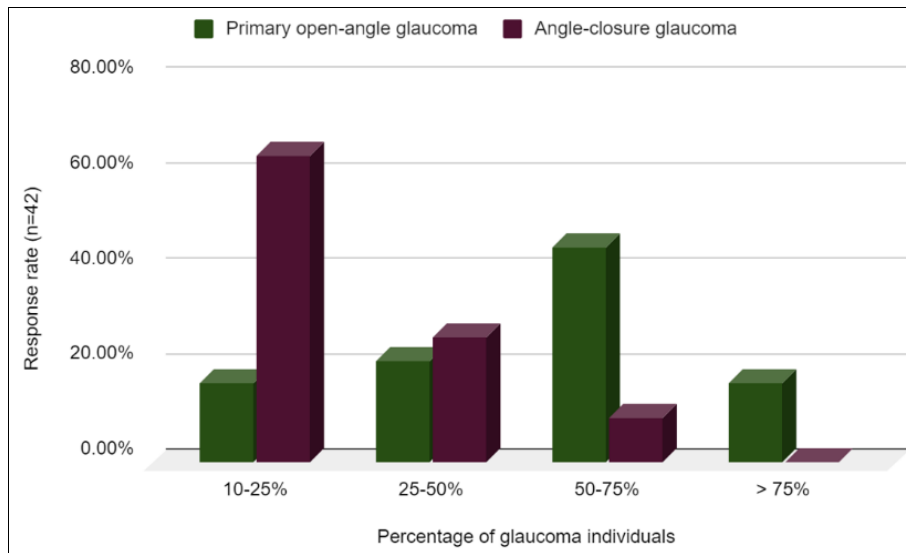


Fig 1: Percentage of glaucoma individuals diagnosed with primary open-angle and angle-closure glaucoma

Prostaglandin analogues were cited by 54.76% of the respondents as the commonly used first-line therapy for glaucoma. The use of beta-blockers was also common, according to 38.10% of the respondents whereas alpha agonists were cited by a lesser percentage of participants (4.76%). Combination therapy was not mentioned as a first-line management strategy for glaucoma patients by any of the responders. The financial situation of the patient and their dependability were also mentioned by one responder as factors influencing therapeutic management. Around 33% of the respondents reported using travoprost and bimatoprost equally among prostaglandin analogues, followed by latanoprost by nearly 29% of the respondents. Tafluprost was the least commonly reported prostaglandin analogue (4.76%) (Table 1).

Table 1: Experts' preference on prescribing prostaglandin analogues

Prostaglandin analogues	Response rate (n=42)
Travoprost	14 (33.33%)
Latanoprost	12 (28.57%)
Bimatoprost	14 (33.33%)
Tafluprost	2 (4.76%)

Prostaglandin analogues were recommended by 50% of the respondents to manage all types of patients including newly diagnosed POAG, optical hypertension patients, and patient's refractory to beta-blockers. Among the specific patient types, patient's refractory to beta blockers were most commonly recommended with prostaglandin analogues, as indicated by 33.33% of the respondents. However, none of the respondents recommended prostaglandin analogues specifically for optical hypertension patients (Figure 2).

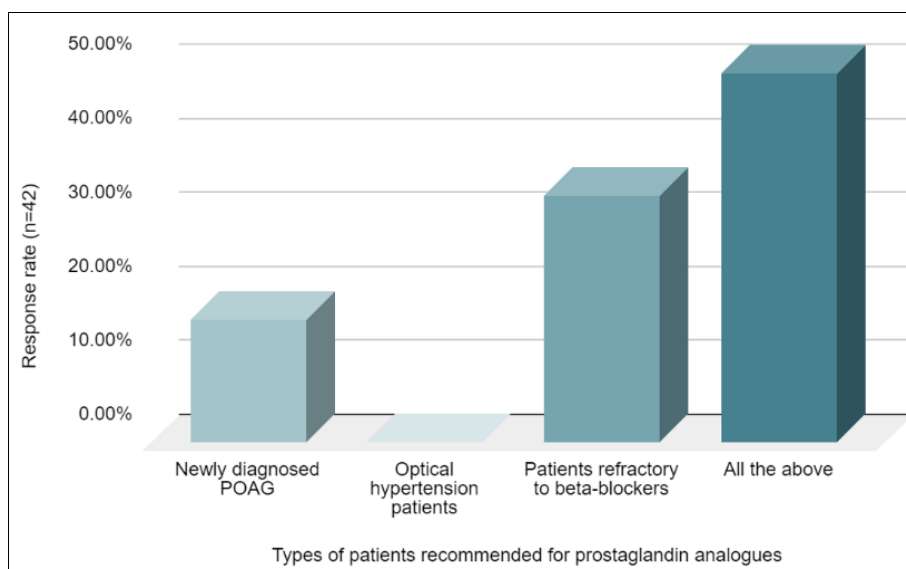


Fig 2: Data on the recommendation of prostaglandin analogues

The majority of respondents (59.52%) reported surgical intervention as the preferred treatment for managing glaucoma patients. Additionally, 38% of the respondents preferred using combination therapy. None of the respondents who took the survey cited laser therapy as a preferred treatment option. Only one respondent (2.38%)

mentioned considering surgery if the patient's compliance with other therapies was subpar. The majority (66.66%) preferred surgical intervention as a treatment choice for managing glaucoma patients who do not respond to anti-glaucoma therapy and add-on therapy was also preferred by a significant portion of respondents (21.43%). A smaller

percentage of respondents (11.90%) considered switching over to other anti-glaucoma medications, while none of the respondents mentioned laser therapy as a preferred treatment option. More than 50% of the respondents (52.38%) stated that 25

to 50% of patients need a combination of two medications to treat IOP and a sizable portion of participants (28.57%) reported the need for a two-drug combination in 50 and 75% of patients (Table 2).

Table 2: Data on the requirement of two drugs combination for managing IOP in glaucoma patients

Patients requiring two drugs combination to manage IOP	Response rate (n=42)
<25%	6 (14.28%)
25-50%	22 (52.38%)
50-75%	12 (28.57%)
>75%	2 (4.76%)

Out of 42 responses, around 43% of the participants expressed their interest in conducting patient educator sessions once every three months, followed by 21.43% who preferred conducting them monthly. Moreover, 19.04% and 9.52% of the respondents suggested organizing such sessions every six months and every two months, respectively. However, only 2.38% of the respondents stated that these sessions should involve the presence of relatives for patient education and examination purposes. In terms of usage, approximately 48% of the respondents

recommended the use of netarsudil in patients who do not respond to combination therapy. Furthermore, 14.28% of the respondents suggested netarsudil for patients who do not respond to prostaglandin analogues. A significant portion of the participants (30.95%) recommended the use of netarsudil to manage the mentioned patient categories. Additionally, a small percentage of respondents (2.38%) reported using netarsudil as an additional medication (Figure 3).

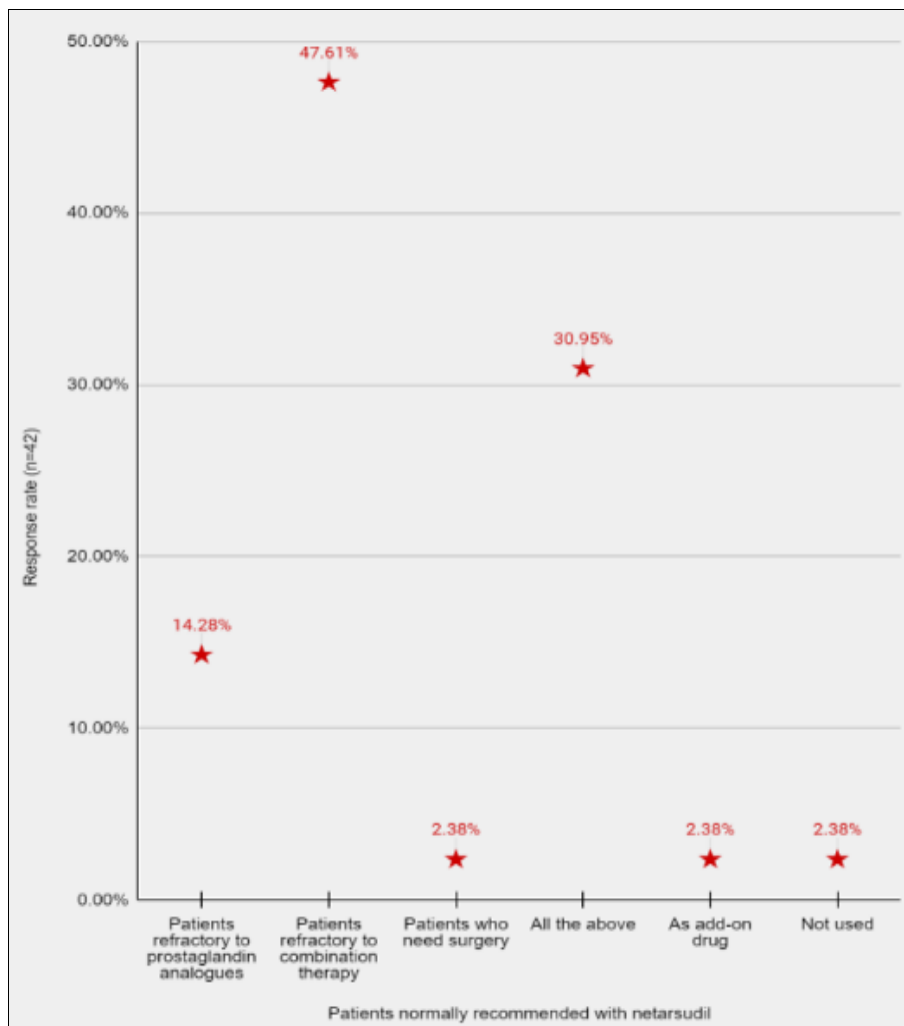


Fig 3: Recommendation of netarsudil to glaucoma patients

Discussion

The survey was intended to capture diverse perspectives of clinicians experienced in glaucoma management. Their opinions were considered crucial in evaluating the practical application of netarsudil and determining its place among existing treatment options. Furthermore, by conducting this

survey, the study aimed to bridge the gap between research evidence and clinical decision-making. While previous studies have demonstrated the efficacy of netarsudil in lowering IOP, understanding how clinicians incorporate this medication into their treatment strategies provides valuable insights for optimizing glaucoma management in real-world

settings.

In the current study, out of 42 respondents, 57.14% indicated that glaucoma frequently affects individuals beyond the age of 50. Prostaglandin F2 α analogues have been extensively used as the first line of treatment due to their effectiveness in reducing IOP and glaucoma management over antihypertensive drugs, β -blockers, carbonic anhydrase inhibitors, sympathomimetics, and α -2 adrenergic agonists^[15, 7]. However, prior research did not uncover significant differences in the effectiveness of prostaglandin analogues^[16].

The current study findings showed that among prostaglandin analogues, 33.33% of respondents used travoprost and bimatoprost equally. Latanoprost, the second most often mentioned prostaglandin analogue, was mentioned by 28.57% of the respondents. Tafluprost was the least often stated prostaglandin analogue, being named by just 4.76% of the respondents. The crossover study by Gandolfi *et al.* in the two studies examining the responsiveness of bimatoprost in latanoprost non-responders, revealed that of the 15 patients who had not responded to latanoprost after 6-8 weeks of treatment, none of them showed a response when latanoprost treatment was continued for one month^[17]. However, 13 patients showed a response after switching to bimatoprost treatment for one month. It was clear that the majority of respondents (50.00%) recommended prostaglandin analogues for all the described patients, including those with newly diagnosed POAG, those with OHT, and those who were unable to control their symptoms with beta-blockers. According to 33.33% of the respondents, prostaglandin analogues were most frequently prescribed for individual's refractory to beta-blockers.

All four prostaglandin analogues, bimatoprost, latanoprost, travoprost, and tafluprost were found to be equally significant in reducing IOP among patients with POAG as reported in a single-center open-label trial. Besides, based on OSDI scores, latanoprost was reported to be the least tolerated^[18]. There are limited choices available when a patient who has received topical prostaglandin analogue therapy still requires additional IOP lowering: (1) including a single additional agent, (2) including a combination of agents, or (3) switching to a fixed combination of a prostaglandin analogue and a beta-blocker^[19]. In this current survey, a significant proportion of responders (21.43%) also listed add-on therapy as a possible therapeutic option. According to 52.38% of respondents, approximately 25 to 50% of patients require a combination of two medications to treat their IOP.

In the present study, around 60% of the respondents preferred surgical intervention as a form of treatment for glaucoma sufferers who do not respond to anti-glaucoma therapy. It was important to note that the only effective treatment for all stages and types of glaucoma was IOP lowering by pharmaceutical medications or surgical intervention^[20]. In a previous retrospective study involving 6 patients who underwent glaucoma surgery despite initial treatment success, surgery was performed due to treatment failures in 3 patients^[21].

According to a phase II randomized clinical study conducted by Araie *et al.*, patients in the netarsudil groups (0.01%, 0.02%, and 0.04% concentration) had lower mean diurnal IOP values than those in the placebo group^[22]. According to 47.61% of the respondents in the present study, netarsudil was frequently advised for patients who were unable to control their symptoms with combination therapy. About 14.28% of the respondents indicated that it was also advised for patients whose conditions cannot be

treated with prostaglandin analogues. When glaucoma patients were receiving normally highly effective medicinal treatment, adding netarsudil 0.02% once daily can significantly reduce IOP, postponing the need for glaucoma laser or incisional surgery^[21]. Netarsudil can be suggested for each of the patient categories with uncontrolled prostaglandin analogues, combination therapy, add-on therapy, or who needs surgery, according to a sizable portion of responders (30.95%). These data imply that while prescribing netarsudil to glaucoma patients, doctors should be realistic about the results.

The current study offered a comprehensive and well-rounded perspective on the usage of netarsudil, enhancing the reliability and validity of its findings. It places a strong emphasis on evidence-based decision-making by incorporating the best available evidence regarding the usage of netarsudil. Furthermore, the study acknowledged the significance of tailoring treatment decisions to individual patient characteristics in order to achieve the most favorable treatment outcomes. However, it was important to acknowledge certain limitations of the current study. Firstly, the small sample size may have limited the generalizability of the results. Additionally, as the study relied on professional judgments, there was a possibility of bias influencing the findings. Therefore, it was necessary to validate the results of the current study through future research using larger sample sizes and randomized controlled methodologies.

Conclusion

The study findings underscore the significance of netarsudil as a therapeutic option for patients with uncontrolled prostaglandin analogues, uncontrolled combination therapy, or those requiring additional intervention. Overall, the survey contributes to the knowledge base surrounding the use of netarsudil in clinical practice and provides valuable insights for healthcare professionals in making informed treatment decisions for glaucoma patients.

Acknowledgement

We would like to thank all the ophthalmologists participated in this study.

Conflict of Interest

Nothing to disclose.

Funding Support

Nil.

References

1. Rewri P. Towards better management of glaucoma in India. *Indian Journal of Ophthalmology*. 2023 Mar 1;71(3):686-688.
2. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY, *et al.* Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta-analysis. *Ophthalmology*. 2014 Nov 1;121(11):2081-2090.
3. Rewri P. Towards better management of glaucoma in India. *Indian Journal of Ophthalmology*. 2023 Mar 1;71(3):686-8.
4. Agis Investigators. The Advanced Glaucoma Intervention Study (AGIS) 7: The relationship between control of intraocular pressure and visual field deterioration. *Am J Ophthalmol*. 2000;130:429-40.
5. Li X, Wang W, Zhang X. Meta-analysis of selective laser trabeculoplasty versus topical medication in the

- treatment of open-angle glaucoma. *BMC ophthalmology*. 2015 Dec;15(1):1-9.
6. Rolim-de-Moura CR, Paranhos Jr A, Loutfi M, Burton D, Wormald R, Evans JR, *et al*. Laser trabeculoplasty for open-angle glaucoma and ocular hypertension. *Cochrane Database Syst. Rev.* 2022 Aug 9;8(8):CD003919.
 7. Li T, Lindsley K, Rouse B, Hong H, Shi Q, Friedman DS, *et al*. Comparative effectiveness of first-line medications for primary open-angle glaucoma: a systematic review and network meta-analysis. *Ophthalmology*. 2016 Jan 1;123(1):129-40.
 8. Burr J, Azuara-Blanco A, Avenell A, Tuulonen A. Medical versus surgical interventions for open angle glaucoma. *Cochrane Database of Systematic Reviews*. 2012 Sep 12;(9):CD004399.
 9. Serle JB, Katz LJ, McLaurin E, Heah T, Ramirez-Davis N, Usner DW, *et al*. Two phase 3 clinical trials comparing the safety and efficacy of netarsudil to timolol in patients with elevated intraocular pressure: Rho kinase elevated IOP treatment trial 1 and 2 (ROCKET-1 and ROCKET-2). *American journal of ophthalmology*. 2018 Feb 1;186:116-27.
 10. Khouri AS, Serle JB, Bacharach J, Usner DW, Lewis RA, Braswell P, *et al*. Once-daily netarsudil versus twice-daily timolol in patients with elevated intraocular pressure: the randomized phase 3 ROCKET-4 study. *American journal of ophthalmology*. 2019 Aug 1;204:97-104.
 11. Bacharach J, Dubiner HB, Levy B, Kopczynski CC, Novack GD. AR-13324-CS202 Study Group. Double-masked, randomized, dose - response study of AR-13324 versus latanoprost in patients with elevated intraocular pressure. *Ophthalmology*. 2015 Feb 1;122(2):302-7.
 12. Prager AJ, Tang M, Pleet AL, Petito LC, Tanna AP. Effectiveness and tolerability of netarsudil in combination with other ocular hypotensive agents. *Ophthalmology Glaucoma*. 2021 Nov 1;4(6):597-603.
 13. Mehta P, Kaplowitz K, Lenoci J, Nemesure B, Regina-Gigliotti M, Honkanen R, *et al*. IOP lowering efficacy of adjunctive netarsudil (Rhopressa): A retrospective chart review. *Investigative Ophthalmology & Visual Science*. 2020 Jun 10;61(7):1237.
 14. Ustaoglu M, Shiuey E, Sanvicente C, Razeghinejad R, Katz LJ, Myers JS, *et al*. The efficacy and safety profile of netarsudil 0.02% in glaucoma treatment: real-world outcomes. *Investigative Ophthalmology & Visual Science*. 2019 Jul 22;60(9):2393.
 15. Boland MV, Ervin AM, Friedman DS, Jampel HD, Hawkins BS, Vollenweider D, *et al*. Comparative effectiveness of treatments for open-angle glaucoma: A systematic review for the US Preventive Services Task Force. *Annals of internal medicine*. 2013 Feb 19;158(4):271-279.
 16. Noecker RJ, Earl ML, Mundorf TK, Silverstein SM, Phillips MP. Comparing bimatoprost and travoprost in black Americans. *Current medical research and opinion*. 2006 Nov 1;22(11):2175-80.
 17. Gandolfi SA, Cimino L. Effect of bimatoprost on patients with primary open-angle glaucoma or ocular hypertension who are nonresponders to latanoprost. *Ophthalmology*. 2003 Mar 1;110(3):609-614.
 18. El Hajj Moussa WG, Farhat RG, Nehme JC, Sahyoun MA, Schakal AR, Jalkh AE, *et al*. Comparison of efficacy and ocular surface disease index score between bimatoprost, latanoprost, travoprost, and tafluprost in glaucoma patients. *Journal of Ophthalmology*. 2018 Mar 7;2018:1319628.
 19. Harasymowycz P, Birt C, Gooi P, Heckler L, Hutnik C, Jinapriya D, *et al*. Medical management of glaucoma in the 21st century from a Canadian perspective. *Journal of ophthalmology*. 2016 Nov 8;2016:6509809.
 20. Lusthaus J, Goldberg I. Current management of glaucoma. *Medical Journal of Australia*. 2019 Mar;210(4):180-187.
 21. Villegas NC, Lee WS. Effectiveness of netarsudil as an additional therapy for glaucoma in patients already on maximally tolerated medical therapy. *Clinical Ophthalmology*. 2021 Nov 2;4367-4372.
 22. Araie M, Sugiyama K, Aso K, Kanemoto K, Kothapalli K, Kopczynski C, *et al*. Phase 2 randomized clinical study of netarsudil ophthalmic solution in Japanese patients with primary open-angle glaucoma or ocular hypertension. *Advances in Therapy*. 2021 Apr;38:1757-1775.

How to Cite This Article

Manjula S, Kumar KM. Expert opinion on netarsudil for the management of glaucoma in Indian settings. *International Journal of Medical Ophthalmology* 2024; 6(1): 05-10.

Creative Commons (CC) License

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0) License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.