ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

ATROPINE FOR MYOPIA CONTROL: EFFICACY, CHALLENGES AND FUTURE DIRECTIONS

Dr. Namrata Srivastava[1], Dr. Nitesh Srivastava[2]
[1]*Department of Optometry ERA University of Allied Health Science, Lucknow, Uttar Pradesh, India*
[2]*Department of Optometry personal line Command Hospital Lucknow, Uttar Pradesh, India*

**Correspondence: Dr. Namrata Srivastava*

Article DOI: https://doi.org/10.36713/epra18682
DOI No: 10.36713/epra18682

ABSTRACT

Myopia, or near-sightedness, is rapidly emerging as a major global health issue, with projections indicating that by 2050, it will affect nearly 50% of the world's population. This condition arises from excessive elongation of the eyeball, leading to blurred vision at a distance and increasing the risk of severe ocular complications, such as retinal detachment and glaucoma. Effective management strategies are critical to mitigating the public health impact of this growing epidemic.

Atropine, a muscarinic antagonist, has gained attention for its potential in myopia control. By inhibiting muscarinic acetylcholine receptors (mAChRs) in the eye, atropine slows down axial elongation, the anatomical hallmark of myopia. Low-dose atropine (0.01%) has demonstrated efficacy in clinical trials, such as the ATOM2 study, which showed a 50% reduction in myopia progression with minimal side effects, including photophobia and blurred vision. Meanwhile, the LAMP study indicates that slightly higher concentrations (0.05%) may further balance efficacy and tolerability, especially in children at high risk of severe myopia.

Despite these promising results, critical knowledge gaps persist, particularly concerning atropine's long-term safety, optimal dosing, and the rebound effect, where myopia progression may accelerate after stopping treatment. Ethnic and genetic variability also calls for a more diverse research focus. Future studies should explore combining atropine with other interventions, such as orthokeratology or multifocal lenses, to optimize outcomes. As leading pharmacological option for myopia management, atropine holds potential for integration into multifaceted treatment strategies to address this pressing public health concern.

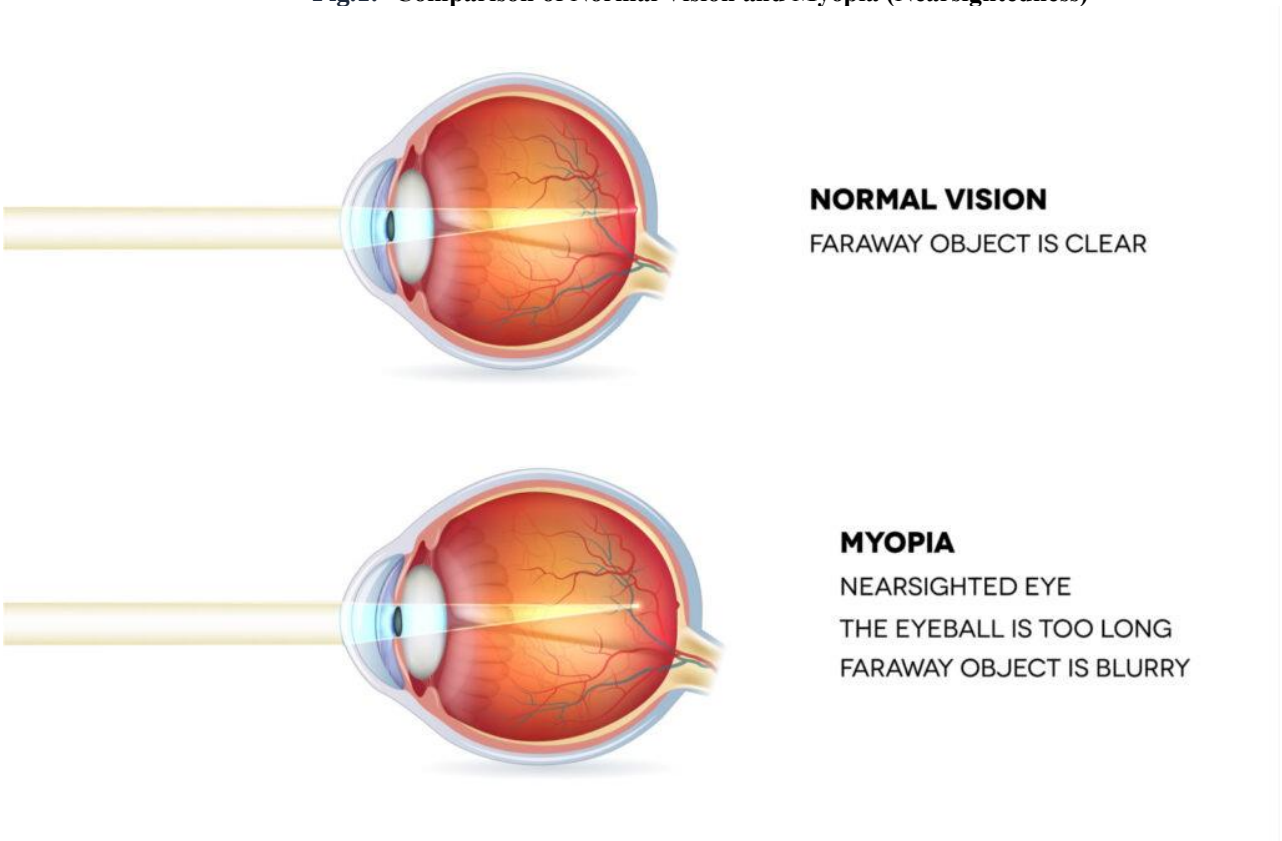
KEYWORDS: *Atropine, Myopia, Pediatric Populations, Muscarinic Acetylcholine Receptors, LAMP.*

INTRODUCTION

Myopia or near-sightedness has become a significant global public health concern, particularly among children and adolescents [1]. Recent estimates suggest that approximately 5 billion people (approximately 50% of the world's population) will be affected by myopia by 2050[2]. As its prevalence continues to rise, effective interventions for its control are urgently needed The impact that myopia possesses is not just limited to ocular health but has a long-term burden on the health-care system, impact on the global economy, and quality of life [1, 3-6] .Among the various treatment modalities, atropine, a muscarinic antagonist, has garnered attention for its potential in myopia management [7]. Many strategies have been implemented to achieve this goal, including the use of beautiful bifocal lenses [8-12], peripheral defocus lenses [13-15], protective lenses [16], orthokeratology [17-20], multifocal contact lenses [21], ophthalmic, outdoor activities [22-25] and drug interactions [26-30] .The evidence from good research is changing the way myopia is managed, especially in children, where myopia is a common eye care problem. This review delves into the mechanisms underlying atropine's effects in myopia control, assessing its efficacy, safety, and the implications for future research and clinical practice.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

Fig.1:- Comparison of Normal Vision and Myopia (Nearsightedness)



Atropine

Atropine's primary mechanism involves its action on the muscarinic acetylcholine receptors (mAChRs) found within the eye. Research indicates that the modulation of these receptors influences the elongation of the eyeball, a hallmark of myopia progression [31]. Atropine functions as a competitive antagonist to muscarinic receptors, inhibiting their activation by the neurotransmitter acetylcholine [32]. One notable characteristic of atropine is that it is non-selective, meaning it blocks multiple types of muscarinic receptors (M1, M2, and M3), rather than targeting any specific one. After absorption, primarily in the gastrointestinal tract, it is distributed widely throughout the body, metabolized in the liver, and excreted in the urine. Atropine has various physiological effects, including the inhibition of secretions, relaxation of smooth muscles, an increase in heart rate, and heightened respiratory depth and rate.

Ocular Applications

In ophthalmology, atropine is commonly used to induce mydriasis (pupil dilation) and Cycloplegia (paralysis of the ciliary muscles). Atropine achieves mydriasis by blocking the contraction of the circular pupillary sphincter muscle, which is usually triggered by acetylcholine. This inhibition allows the radial iris dilator muscle to contract, leading to pupil dilation [39]. Cycloplegia occurs as atropine paralyzes the ciliary muscles, preventing accommodation, which is the eye's ability to focus on near objects. This is particularly helpful in refracting young children and treating conditions like Iridocyclitis and ciliary block glaucoma. However, for the purposes of myopia control, both pupil dilation and Cycloplegia are considered undesirable side effects with no therapeutic benefit.

Mechanisms of Action

Atropine's primary mechanism involves its action on the muscarinic acetylcholine receptors (mAChRs) found within the eye [39]. Research indicates that the modulation of these receptors influences the elongation of the eyeball, a hallmark of myopia progression. The precise pathways remain an area of active investigation, but several hypotheses offer insights into how atropine may exert its protective effects against myopia:

1. **Ciliary Muscle Relaxation**: Atropine's ability to paralyze the ciliary muscle may reduce the eye's effort during accommodation, thereby decreasing the stimulus for axial elongation. By inhibiting the reflex associated with prolonged near work, atropine mitigates a significant risk factor for myopia progression.
2. **Choroidal Thickening**: Studies suggest that atropine may promote choroidal thickening, which can, in turn, lead to a reduced rate of elongation of the eyeball. This effect appears to be dose-dependent, with lower concentrations demonstrating a more pronounced benefit in controlling the progression of myopia compared to higher concentrations.
3. **Influence on Retinal Dopamine Release**: Recent findings propose a potential role for retinal dopamine in the pathogenesis of myopia. By modulating dopaminergic activity through muscarinic receptor interactions, atropine may help regulate the biochemical processes that govern eye growth and development.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

TABLE:-1. SIDE EFFECTS OF ATROPINE

CATEGORY	SIDE EFFECT
OCULAR SIDE EFFECTS	
1. Blurred near vision	Difficulty focusing on close objects (temporary).
2. Photophobia	Increased sensitivity to light due to pupil dilation.
3. Pupil dilation (mydriasis)	Prolonged dilation of pupils, causing vision issues
4. Eye irritation	Redness, discomfort, or itching of the eyes.
5. Allergic conjunctivitis	Rare occurrence of eye inflammation or irritation.
6. Decreased accommodation	Difficulty adjusting focuses between near and far objects.
SYSTEMIC SIDE EFFECTS	
1. Dry mouth (xerostomia)	Reduced salivary secretion due to anticholinergic effects.
2. Urinary retention	Difficulty in urination, especially in predisposed individuals.
3. Headache	Mild to moderate headaches.
4. Increased body temperature	Elevated temperature, particularly in young children (rare).
5. Drowsiness/fatigue	Feeling tired or sleepy, though rare at low doses.

Efficacy and Safety

Clinical trials have established that topical atropine, particularly at low concentrations (e.g., 0.01%), is effective in slowing myopia progression with a favourable safety profile. Common side effects, such as photophobia and blurred vision, tend to be mild and manageable. The long-term implications of atropine use, particularly on visual acuity and potential rebound effects upon cessation, require further scrutiny. Nevertheless, current evidence supports its use as a first-line therapy for managing myopia in children.

Atropine in Myopia Control

The use of atropine as a pharmacological intervention for myopia control has gained significant attention over the past several decades. Unlike traditional optical and surgical approaches, which primarily aim to correct visual acuity without addressing the underlying progression of myopia, atropine has emerged as a promising agent that directly targets the mechanisms involved in the development and worsening of myopia. Research into the use of atropine for myopia management has spanned over half a century, with varying levels of success and refinement in understanding its role and effectiveness.

Early Research and Limitations

The exploration of atropine for myopia control began in the mid-20th century, with early studies led by researchers like Bedrossian in the 1960s and 1970s [34, 35]. Bedrossian's work suggested that atropine could reduce the progression of myopia, but his research was limited by an inability to clearly differentiate between the effects of long-term.

Cycloplegia (the paralysis of the ciliary muscle, which prevents the eye from focusing on near objects) and reductions in axial elongation (the lengthening of the eyeball, which is a key factor in the progression of myopia). Although some reductions in myopia progression were observed, the studies lacked the precision necessary to draw definitive conclusions about atropine's long-term efficacy in preventing the pathological consequences of high myopia, such as retinal detachment, maculopathy, and glaucoma.

Subsequent studies, such as those conducted by Kelly et al., [36] sought to improve upon this early research. Kelly's retrospective study compared different groups of individuals treated with atropine, but the study design was not randomized, and treatment regimens varied widely between the groups. This lack of consistency made it difficult to generalize the findings or establish atropine as a reliable treatment for myopia control.

Gimbel was the first to suggest that atropine's effectiveness in controlling myopia might be time-limited, [37] indicating that its beneficial effects could diminish over time. However, like previous studies, Gimbel's research was flawed by the lack of control groups and the combination of atropine treatment with other interventions, such as spectacle use. These limitations hindered the practical utility of his findings.

The First Randomized Controlled Trials

The breakthrough in atropine research for myopia control came in 1989 when Yen et al. [33] conducted the first randomized, placebo-controlled trial using 1% atropine. This study was a significant step forward, as it introduced a more rigorous scientific approach to evaluating atropine's efficacy. By randomly assigning participants to either an atropine treatment group or a placebo group, Yen et al. were able to control for variables that had plagued earlier studies, such as differing treatment regimens and unblinded study designs.

Their findings demonstrated that atropine significantly slowed the progression of myopia compared to the placebo group [38]. This pivotal study marked the beginning of a new era in myopia research, firmly establishing atropine as a potential therapeutic agent for myopia control. It also opened the door to further research aimed at optimizing atropine's dosage, minimizing its side effects, and understanding its long-term implications.

Mechanism of Action in Myopia Control

The exact mechanism by which atropine controls myopia is still not fully understood, but several theories have been proposed. One prevailing hypothesis is that atropine's antimuscarinic properties interfere with the signaling pathways involved in eye growth. Specifically, atropine blocks muscarinic receptors in the retina and sclera, the outer layer of the eye, which are thought to play a role in regulating axial elongation [40, 41]. By inhibiting these receptors, atropine may slow or halt the elongation of the eye, thereby preventing myopia from worsening.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

Additionally, atropine's ability to induce Cycloplegia might also contribute to its effectiveness in myopia control. Cycloplegia reduces the eye's ability to focus on near objects, which could alleviate the visual stress that has been linked to myopia progression [42], particularly in children who engage in prolonged near-work activities such as reading and using digital devices.

Evolving Research and Dosage Optimization

While 1% atropine was initially used in early studies, this concentration was associated with significant side effects, such as pupil dilation (mydriasis) and difficulty focusing on near objects (Cycloplegia). These side effects, although not dangerous, were inconvenient and could discourage long-term adherence to treatment, especially among children. As a result, researchers began exploring the use of lower concentrations of atropine to strike a balance between efficacy and tolerability.

The landmark *Atropine for the Treatment of Myopia (ATOM)* studies, conducted in Singapore, was among the first to systematically evaluate different concentrations of atropine. The ATOM1 study, which used 1% atropine, confirmed its effectiveness but also highlighted its side effects.6This led to the ATOM2 study, which investigated lower concentrations (0.5%, 0.1%, and 0.01%) of atropine.5The results of ATOM2 were ground-breaking, showing that even very low doses of atropine, particularly 0.01%, could significantly slow myopia progression with minimal side effects [43], This low-dose atropine did not cause significant pupil dilation or affect near vision, making it a much more practical option for long-term use in children.

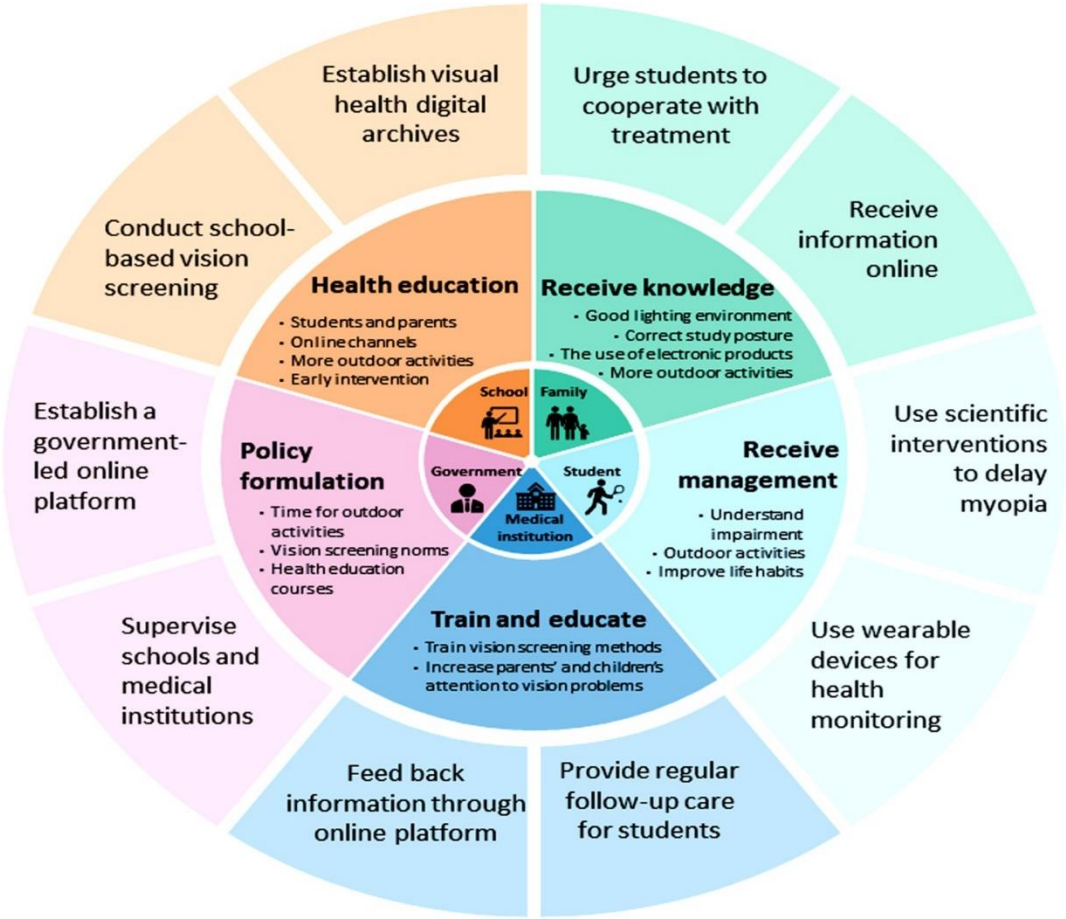
Long-Term Efficacy and Rebound Effects

Another critical area of research has been the long-term efficacy of atropine and the potential for rebound effects, where myopia progression accelerates once treatment is stopped. Studies have shown that while higher concentrations of atropine (1%) are effective in the short term, they are also more likely to lead to rebound myopia when treatment is discontinued [44].In contrast, low-dose atropine (0.01%) not only slows myopia progression effectively but also minimizes rebound effects, making it a more sustainable option for prolonged use.

Atropine in Routine Clinical Practice

Today, atropine, particularly in low doses, has become an integral part of routine clinical practice for myopia management. It is widely used in many countries, particularly in Asia, where the prevalence of myopia is highest. Ophthalmologists and optometrists are increasingly incorporating atropine into their treatment plans for children who are at high risk of developing high myopia. Ongoing research continues to refine our understanding of atropine's long-term safety and effectiveness, as well as its potential to be combined with other myopia control strategies, such as multifocal contact lenses or increased outdoor activity.

Fig.2:-A comprehensive myopia strategy requires cooperation across schools, families, and health sectors to integrate vision care into education.



ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

Dose of Atropine for Myopia Control

The exploration of atropine as a treatment for myopia control has evolved significantly over the years, especially regarding the optimal dosing that balances efficacy and minimal side effects. The concentration of atropine administered plays a crucial role in both its effectiveness and the likelihood of side effects such as pupil dilation, light sensitivity, and difficulty with near vision. As a result, the choice of dosage has been a primary focus in both clinical research and real-world application of atropine for myopia management.

High-Dose Atropine (1%)

Initially, studies on atropine for myopia control focused on using a high concentration of 1%, as this was the standard dosage used for other ocular applications, such as inducing pupil dilation (mydriasis) and cycloplegia for diagnostic purposes.[45] Early studies, including those by Bedrossian and Yen et al., confirmed the efficacy of 1% atropine in significantly slowing myopia progression.

In these early trials, 1% atropine was found to be highly effective in reducing the axial elongation of the eye, which is the primary cause of myopia progression. For example, the ATOM1 (*Atropine for the Treatment of Myopia*) study conducted in Singapore in the early 2000s showed that 1% atropine could reduce myopia progression by as much as 77%. However, despite its efficacy, this high concentration was associated with notable side effects, such as blurred near vision due to cycloplegia (the paralysis of the eye's focusing ability), severe light sensitivity due to pupil dilation, and dry eyes. These side effects were significant enough to limit the practical use of 1% atropine, especially in children, who are the primary candidates for myopia control. [46]

Medium-Dose Atropine (0.5% - 0.1%)

As concerns about the side effects of high-dose atropine grew, researchers began exploring lower concentrations to find a balance between effectiveness and tolerability. Studies investigating medium-dose atropine (concentrations ranging from 0.5% to 0.1%) found that these doses still provided considerable myopia control, though the effectiveness was somewhat reduced compared to the 1% concentration.

The ATOM2 study, which followed the ATOM1 trial, evaluated the use of 0.5%, 0.1%, and 0.01% atropine.[47] The results showed that both 0.5% and 0.1% concentrations continued to provide strong control over myopia progression, with reductions of 65-70% in myopia progression compared to placebo. However, while the side effects of medium-dose atropine were less severe than those seen with 1% atropine, issues such as pupil dilation, light sensitivity, and near vision difficulties persisted to some degree. This raised questions about whether even lower doses might offer a better therapeutic balance, especially for long-term use in children.

Low-Dose Atropine (0.01%)

The most significant breakthrough in atropine dosing came with the investigation of ultra-low-dose atropine (0.01%). The ATOM2 study revealed that 0.01% atropine, although less effective in absolute terms than the higher concentrations, still slowed myopia progression by around 50% compared to placebo. Importantly, this low concentration was associated with minimal side effects, making it much more tolerable for children over long periods.

Low-dose atropine (0.01%) does not induce significant pupil dilation or cycloplegia, meaning children retain their ability to focus on near objects, and they experience little to no light sensitivity. This dramatically improves patient comfort and compliance, which is crucial in long-term myopia management. In fact, 0.01% atropine has become the preferred dose in many clinical settings due to its strong balance between reducing myopia progression and minimizing side effects. Moreover, studies have shown that low-dose atropine significantly reduces the risk of a "rebound effect" after treatment cessation, a common issue with higher doses where myopia progression accelerates after stopping treatment.[50]

Rebound Effects and Long-Term Efficacy

An important consideration in atropine treatment is the rebound effect, where myopia progression worsens once the treatment is stopped. High concentrations of atropine (1%) are more likely to result in a pronounced rebound effect, meaning that while the treatment is initially effective; its discontinuation often leads to a rapid increase in myopia. In contrast, studies have shown that 0.01% atropine is much less likely to cause this rebound effect, making it a safer option for long-term use. Children treated with low-dose atropine are less likely to experience a rapid worsening of myopia once the medication is stopped, which is an essential factor in developing sustainable treatment plans.

Personalization of Atropine Dosing

Recent trends in myopia management emphasize personalized treatment approaches, including the dosing of atropine. Not every patient responds the same way to atropine, and while 0.01% is the standard recommendation for many children, some cases may benefit from slightly higher concentrations, such as 0.05% or 0.025%, depending on the severity of their myopia and their tolerance to the drug.[57] Some studies suggest that a personalized dosing approach, in which treatment begins with a low concentration and is adjusted as needed, could optimize both the effectiveness and comfort of atropine therapy.

Ongoing Research and Future Directions

The success of low-dose atropine has sparked continued research into further optimizing the concentration and application of atropine for myopia control. Trials are underway to determine whether concentrations between 0.01% and 0.05% could offer an even better balance between efficacy and minimal side effects.[52] Moreover, combination therapies that include atropine alongside other myopia control interventions, such as orthokeratology (Ortho- k) lenses or outdoor activity recommendations, are being explored to enhance overall treatment outcomes.

Clinical Myopia Control Studies

Over the past several decades, numerous clinical studies have explored the effectiveness of various interventions for controlling myopia progression[53,54].These studies have provided critical insights into both pharmacological and non-pharmacological strategies for managing myopia, with a particular focus on reducing axial elongation, which is the key driver of myopia progression. Among these interventions,

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

atropine and other optical devices have emerged as central components of myopia management. This section elaborates on key clinical trials and studies, with a particular focus on the use of atropine, lenses, and lifestyle modifications.[55]

Here is a table-2:- summarizing key studies on clinical myopia control. This covers various treatment strategies such as orthokeratology, atropine eye drops, multifocal contact lenses, and specialized spectacle lenses.

Study	Treatment	Participants	Duration	Key Results	Reference
ATOM Study (2006)	Atropine 1% eye drops	400 children	2 years	77% reduction in myopia progression in the atropine group compared to placebo	Chia et al., 2006
ATOM2 Study (2012	Atropine 0.5%, 0.1%, 0.01% drops	400 children	5 years	Atropine 0.01% most effective with fewer side effects, reduced	Chia et al., 2012
LAMP Study (2019)	Atropine 0.05%, 0.025%, 0.01%	438 children	2 years	Atropine 0.05% most effective, showing a 67% reduction in progression	Yam et al., 2019
COMET Study (2003)	Progressive addition lenses (PAL)	469 children	3 years	PAL slowed myopia progression by 0.20D compared to single-vision lenses	Gwiazda et al., 2003
BLINK Study (2019)	Multifocal contact lenses	287 children	3 years	High add power lenses reduced myopia progression by 43%	Walline et al., 2019
CHAMP Study (2020)	Hoya MiYOSMART spectacle lenses	160 children	2 years	59% reduction in myopia progression compared to single-vision lenses	Lam et al., 2020
SMART Study (2014)	Orthokeratology (Ortho-K)	50 children	2 years	43% reduction in axial length growth in the Ortho-K group	Cho et al., 2014

This table provides a concise overview of different myopia control strategies and their clinical outcomes.

The ATOM Studies (Atropine for the Treatment of Myopia)
The most significant studies on atropine for myopia control are the *Atropine for the Treatment of Myopia* (ATOM) studies, which took place in Singapore and were conducted in two major phases: ATOM1 and ATOM2.

ATOM1 Study
The *ATOM1* study, conducted in the early 2000s, was a randomized, placebo-controlled trial that evaluated the efficacy of 1% atropine in reducing myopia progression among children aged 6-12 years. The trial included 400 children who were randomly assigned to receive either 1% atropine eye drops or a placebo, administered nightly in one eye. The primary outcome measure was the progression of myopia, assessed by changes in spherical equivalent refraction and axial length.[56]

The results of the ATOM1 study were ground-breaking. After two years, children in the atropine group had a mean myopia progression of only 0.28 dioptres (D), compared to 1.20 D in the placebo group. Additionally, axial elongation was significantly less in the atropine group, with an average increase of 0.02 mm compared to 0.38 mm in the placebo group. These findings demonstrated that 1% atropine was highly effective in slowing both the refractive error and axial elongation associated with myopia progression.

However, the study also highlighted the drawbacks of 1% atropine, most notably significant side effects such as pupil dilation (mydriasis), light sensitivity, and blurred near vision due to cyclopaedia. These side effects limited the practicality of long-term use, particularly in children, and led researchers to investigate lower doses of atropine.

ATOM2 Study
In response to the side effects observed in ATOM1, the ATOM2 study, conducted between 2006 and 2010, evaluated the efficacy of lower doses of atropine: 0.5%, 0.1%, and 0.01%. Like ATOM1, the study included children aged 6-12 years and followed them for two years to measure changes in myopia progression and axial elongation. The primary aim was to

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

determine whether lower concentrations of atropine could provide comparable myopia control with fewer side effects.

The findings of ATOM2 were pivotal. After two years, myopia progression in the 0.5% group was 0.30 D, in the 0.1% group was 0.38 D, and in the 0.01% group was 0.49 D, all significantly less than the untreated rates typically observed in myopia progression. Axial elongation was also reduced in all three groups, though to a lesser degree at the 0.01% concentration. Most importantly, the 0.01% atropine group experienced minimal side effects, with little to no impact on pupil size or near vision.

The ATOM2 study established 0.01% atropine as a viable, low-risk option for long-term myopia management. While it was slightly less effective than higher concentrations, its minimal side effect profile made it a preferable option for many patients, particularly children requiring long-term treatment.

LAMP Study (Low-Concentration Atropine for Myopia Progression)

Building on the findings of the ATOM studies, the *LAMP* (Low-concentration Atropine for Myopia Progression) study, initiated in Hong Kong, explored even more precise dosing regimens of low-concentration atropine. The LAMP study evaluated three concentrations: 0.05%, 0.025%, and 0.01%, in a large cohort of children aged 4-12 years, aiming to determine the optimal concentration for long-term use in myopia control.[57, 58]

Over the course of one year, the LAMP study demonstrated that all three concentrations of atropine slowed myopia progression significantly compared to baseline rates. However, the 0.05% concentration showed the greatest effect, reducing myopia progression by 0.27 D per year and axial elongation by 0.20 mm per year. The 0.025% and 0.01% concentrations were also effective, but to a lesser extent, with myopia progression reductions of 0.34 D and 0.59 D, respectively. Importantly, even at the 0.05% concentration, side effects were minimal, with most children tolerating the treatment well without experiencing significant pupil dilation or loss of near vision.

The LAMP study findings suggest that 0.05% atropine may provide an ideal balance between efficacy and tolerability, particularly for children at higher risk of severe myopia progression.

Optical Interventions: Multifocal Lenses and Orthokeratology

While atropine remains one of the most effective pharmacological interventions for myopia control, several optical approaches have also shown promise in clinical studies. These include multifocal soft contact lenses, peripheral defocus spectacle lenses, and orthokeratology (Ortho-k).

Multifocal Contact Lenses

Multifocal contact lenses are designed to reduce the hyperopic defocus that occurs on the peripheral retina, which is thought to contribute to myopia progression. Clinical trials have shown that these lenses can slow myopia progression by 25-50%. One of the landmark studies in this area is the *BLINK* (Bifocal Lenses in Near-sighted Kids) study, which found that children wearing high-addition multifocal lenses experienced 43% less myopia progression over three years compared to those wearing single-vision lenses.

Orthokeratology (Ortho-K)

Ortho-k is another non-pharmacological method that has gained popularity for myopia control. It involves wearing specially designed rigid gas-permeable contact lenses overnight, which temporarily reshape the cornea to reduce refractive error. Studies have shown that Ortho-k can slow axial elongation by up to 45% compared to single-vision lenses. However, Ortho-k is not without risks, including the potential for corneal infections, making proper hygiene and follow-up essential.

Outdoor Activity and Myopia Progression

Increasing outdoor activity is another non-pharmacological intervention that has been extensively studied in the context of myopia control. Several large-scale studies have demonstrated that increased time spent outdoors can significantly reduce the risk of developing myopia in children and may also slow the progression of existing myopia. The exact mechanism behind this protective effect is not fully understood, but it is thought that exposure to natural light and reduced near work may play important roles.

The *Sydney Myopia Study* and other population-based studies have found that children who spend at least two hours per day outdoors are significantly less likely to develop myopia than those who spend less time outside. As a result, many eye health professionals now recommend increased outdoor activity as part of a comprehensive myopia management strategy.

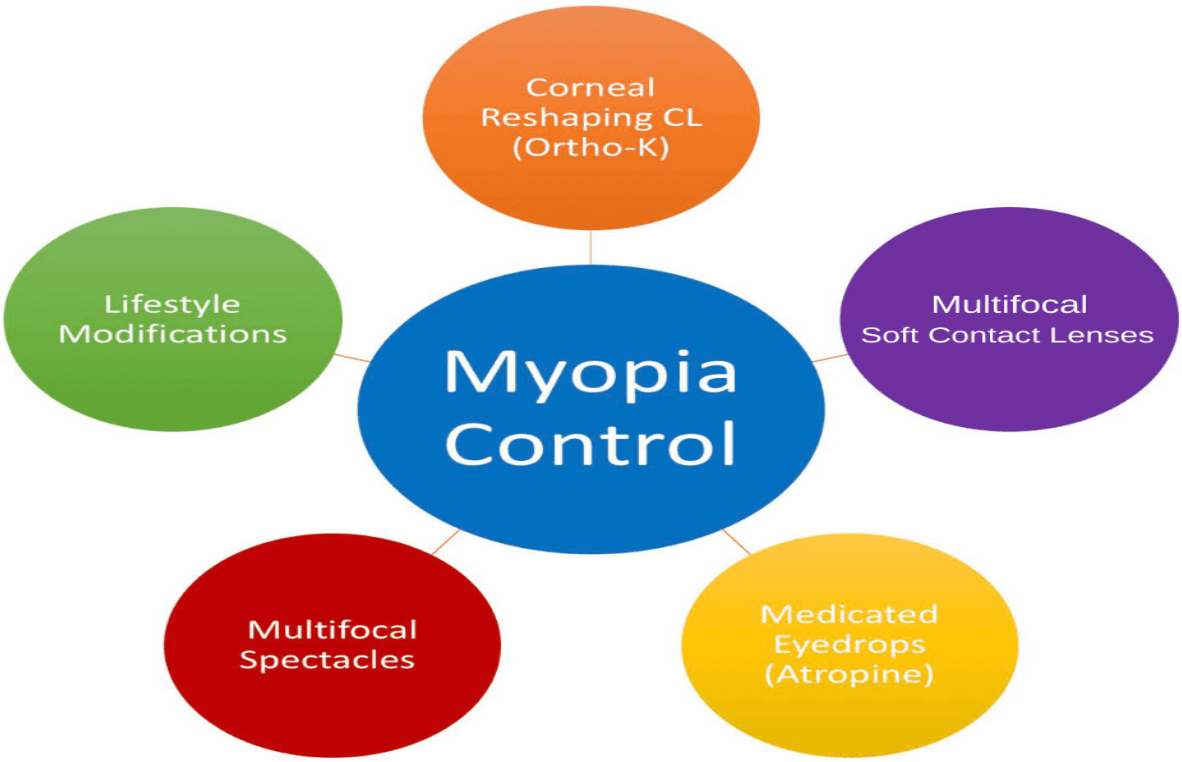
Clinical studies on myopia control have greatly advanced our understanding of effective interventions, from pharmacological treatments like atropine to optical devices and lifestyle modifications. The ATOM and LAMP studies have been instrumental in establishing low-dose atropine as a mainstay of myopia control, while trials on multifocal lenses, Ortho-k, and outdoor activity have broadened the range of options available for managing this increasingly prevalent condition. Ongoing research continues to refine these strategies, with the goal of improving outcomes and minimizing long-term complications associated with progressive myopia.

Research Gap

Myopia, or near-sightedness, is an increasingly prevalent condition globally, particularly among children. Uncontrolled progression of myopia can lead to severe vision problems later in life, including retinal detachment, macular degeneration, and glaucoma. Over the years, atropine eye drops have emerged as one of the most studied pharmacological interventions for controlling the progression of myopia in children. However, several research gaps exist that need to be addressed for a more comprehensive understanding of atropine's role, mechanisms, and long-term efficacy in controlling myopia progression.

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

Fig.3:- Methods for Myopia Control



Understanding the Existing Research

1. **Mechanism of Action Uncertainty**: Atropine, primarily used to dilate pupils and inhibit accommodation, has been found effective in slowing down the elongation of the eye (axial length growth), a key factor in myopia progression. However, the exact molecular or biochemical mechanism by which atropine exerts this effect on myopia control is not fully understood. Although it has been hypothesized that atropine may act on muscarinic receptors in the retina or sclera, direct evidence is lacking.
2. **Dose-Response Relationship**: Studies have demonstrated that low-dose atropine (0.01%) is effective in controlling myopia with fewer side effects compared to higher doses (0.5% or 1%). However, the optimal dosage that provides a balance between efficacy and side effects remains debatable. Some studies suggest that even lower doses (e.g., 0.005%) may be sufficient, but long-term data on their efficacy and safety is still sparse.
3. **Long-Term Effects and Rebound Phenomenon**: One of the major challenges in atropine therapy is the so-called "rebound effect" that occurs when the treatment is stopped. Studies have shown that myopia progression may accelerate once atropine therapy is discontinued, particularly in higher concentrations. Research gaps exist in understanding how to mitigate this rebound effect, whether through gradual dose reduction, intermittent use, or combination therapy.
4. **Ethnic and Genetic Variations**: Most of the research on atropine for myopia control has been conducted in East Asian populations, where the prevalence of myopia is exceptionally high. Less is known about the efficacy of atropine in other ethnic groups, and whether genetic factors may influence the treatment outcomes. Studies investigating these variations are limited, creating a gap in generalizing the results across diverse populations.
5. **Combination Therapies and Synergistic Effects**: While atropine monotherapy has been widely researched, its potential in combination with other interventions, such as orthokeratology (Ortho-K) lenses, bifocal or multifocal glasses, and outdoor activity regimens, is not well understood. There is a need for more studies exploring how atropine may be integrated into multi-faceted myopia control strategies, and whether such combinations can provide superior outcomes with fewer side effects.
6. **Age-Related Effectiveness**: Research is primarily focused on children aged 6–12, but there is a gap in understanding the role of atropine in myopia control for younger children (under 6 years) or older adolescents. It remains unclear whether starting atropine therapy earlier or continuing it into the later teen years can result in more significant long-term benefits in slowing myopia progression.
7. **Safety and Side Effects**: While low-dose atropine is considered safe, there are still some concerns about potential long-term effects on ocular health, particularly in terms of retinal health, photophobia, and the impact on accommodation. More comprehensive studies on the safety profile over extended treatment periods are needed, particularly in

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

younger patients who may require treatment for several years.

CONCLUSION

In conclusion, myopia represents a growing global health concern, particularly among younger populations, with projections suggesting that half of the world's population may be affected by 2050. This alarming trend underscores the urgency of developing effective management strategies to slow myopia progression and mitigate the associated risks of long-term vision problems, such as retinal detachment and glaucoma. Atropine eye drops, particularly in low concentrations, have emerged as a leading pharmacological intervention, demonstrating efficacy in slowing myopia progression by inhibiting muscarinic acetylcholine receptors, which play a role in controlling axial elongation of the eye. The success of clinical trials like the ATOM and LAMP studies in confirming the safety and effectiveness of low-dose atropine (0.01%) has positioned it as a first-line treatment for children at risk of high myopia.

However, despite its promising benefits, there remain important gaps in the research that need to be addressed. The precise mechanism of action by which atropine slows myopia progression is still not fully understood, and this limits the ability to optimize treatment further. In addition, long-term safety data, particularly regarding potential side effects on ocular health after prolonged use, remains incomplete, necessitating ongoing monitoring. Another key challenge is the rebound effect observed in some patients after discontinuing atropine treatment, where myopia progression accelerates. Research exploring how to mitigate this rebound effect, whether through gradual tapering of dosage or alternative treatment strategies, is still needed.

Ethnic and genetic variations in treatment response also represent a critical area for further exploration, as most studies have been conducted in East Asian populations, where myopia prevalence is particularly high. Understanding how atropine performs in different ethnic groups could lead to more personalized and effective treatment protocols. Additionally, combining atropine with other therapies, such as orthokeratology or multifocal lenses, and incorporating lifestyle changes like increased outdoor activities, may offer synergistic effects that enhance treatment outcomes.

Finally, while most research has focused on children between the ages of 6 and 12, it remains unclear how effective atropine may be in younger children or older adolescents. Determining the optimal age range for treatment initiation and duration is crucial for maximizing long-term benefits. Addressing these knowledge gaps through further research will be essential to refining atropine's role in myopia management, ensuring that it is not only effective but also safe for widespread, long-term use in children across diverse populations. In sum, atropine holds significant potential as a cornerstone in the global effort to control myopia, but continued research is imperative to unlocking its full therapeutic potential.

REFERENCES

1. *Dolgin, E. (2015). The myopia boom. Nature, 519(7543), 276.*
2. *Holden, B. A., Fricke, T. R., Wilson, D. A., Jong, M., Naidoo, K. S., Sankaridurg, P., ... & Resnikoff, S. (2016). Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology, 123(5), 1036-1042.*
3. *Vitale, S., Cotch, M. F., & Sperduto, R. D. (2006). Prevalence of visual impairment in the United States. Jama, 295(18), 2158-2163.*
4. *Zheng, Y. F., Pan, C. W., Chay, J., Wong, T. Y., Finkelstein, E., & Saw, S. M. (2013). The economic cost of myopia in adults aged over 40 years in Singapore. Investigative ophthalmology & visual science, 54(12), 7532-7537.*
5. *Liang, Yuan Bo, et al. "Refractive errors in a rural Chinese adult population: the Handan eye study." Ophthalmology 116.11 (2009): 2119-2127.*
6. *Morgan, I. G., Ohno-Matsui, K., & Saw, S. M. (2012). Myopia. The Lancet, 379(9827), 1739-1748.*
7. *Gwiazda, J., Hyman, L., Hussein, M., Everett, D., Norton, T. T., Kurtz, D., ... & COMET Group. (2003). A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. Investigative ophthalmology & visual science, 44(4), 1492-1500.*
8. *Hasebe, S., Ohtsuki, H., Nonaka, T., Nakatsuka, C., Miyata, M., Hamasaki, I., & Kimura, S. (2008). Effect of progressive addition lenses on myopia progression in Japanese children: a prospective, randomized, double-masked, crossover trial. Investigative ophthalmology & visual science, 49(7), 2781-2789.*
9. *Leung, J. T., & Brown, B. (1999). Progression of myopia in Hong Kong Chinese schoolchildren is slowed by wearing progressive lenses. Optometry and Vision Science, 76(6), 346-354.*
10. *Lee, D. (2009). CURRENT METHODS OF MYOPIA CONTROL A LITERATURE REVIEW & UPDATE. Journal of Behavioral Optometry, 20(4).*
11. *Fulk, G. W., Cyert, L. A., & Parker, D. E. (2000). A randomized trial of the effect of single-vision vs. bifocal lenses on myopia progression in children with esophoria. Optometry and Vision Science, 77(8), 395-401.*
12. *Berntsen, D. A., Sinnott, L. T., Mutti, D. O., & Zadnik, K. (2012). A randomized trial using progressive addition lenses to evaluate theories of myopia progression in children with a high lag of accommodation. Investigative ophthalmology & visual science, 53(2), 640-649.*
13. *Walline, J. J., Lindsley, K. B., Vedula, S. S., Cotter, S. A., Mutti, D. O., Ng, S. M., & Twelker, J. D. (2020). Interventions to slow progression of myopia in children. Cochrane Database of Systematic Reviews, (1).*
14. *Kanda, H., Oshika, T., Hiraoka, T., Hasebe, S., Ohno-Matsui, K., Ishiko, S., ... & Fujikado, T. (2018). Effect of spectacle lenses designed to reduce relative peripheral hyperopia on myopia progression in Japanese children: a 2-year multicenter randomized controlled trial. Japanese journal of ophthalmology, 62, 537-543.*
15. *Lam, C. S. Y., Tang, W. C., Tse, D. Y. Y., Lee, R. P. K., Chun, R. K. M., Hasegawa, K., ... & To, C. H. (2020). Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. British Journal of Ophthalmology, 104(3), 363-368.*

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

16. *GROSVENOR, T., PERRIGIN, J., PERRIGIN, D., & QUINTERO, S. (1989). Use of silicone-acrylate contact lenses for the control of myopia: results after two years of lens wear. Optometry and Vision Science, 66(1), 41-47.*
17. *Cho, P., & Cheung, S. W. (2012). Retardation of myopia in Orthokeratology (ROMIO) study: a 2-year randomized clinical trial. Investigative ophthalmology & visual science, 53(11), 7077-7085.*
18. *Hiraoka, T., Kakita, T., Okamoto, F., Takahashi, H., & Oshika, T. (2012). Long-term effect of overnight orthokeratology on axial length elongation in childhood myopia: a 5-year follow-up study. Investigative ophthalmology & visual science, 53(7), 3913-3919.*
19. *Sun, Y., Xu, F., Zhang, T., Liu, M., Wang, D., Chen, Y., & Liu, Q. (2015). Orthokeratology to control myopia progression: a meta-analysis. PloS one, 10(4), e0124535.*
20. *Chan, D. K. C., Fung, Y. K., Xing, S., & Hagger, M. S. (2014). Myopia prevention, near work, and visual acuity of college students: integrating the theory of planned behavior and self-determination theory. Journal of Behavioral Medicine, 37, 369-380.*
21. *Kang, P., McAlinden, C., & Wildsoet, C. F. (2017). Effects of multifocal soft contact lenses used to slow myopia progression on quality of vision in young adults. Acta ophthalmologica, 95(1), e43-e53.*
22. *Xiong, S., Sankaridurg, P., Naduvilath, T., Zang, J., Zou, H., Zhu, J., ... & Xu, X. (2017). Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review. Acta ophthalmologica, 95(6), 551-566.*
23. *He, M., Xiang, F., Zeng, Y., Mai, J., Chen, Q., Zhang, J., ... & Morgan, I. G. (2015). Effect of time spent outdoors at school on the development of myopia among children in China: a randomized clinical trial. Jama, 314(11), 1142-1148.*
24. *Rose, K. A., Morgan, I. G., Ip, J., Kifley, A., Huynh, S., Smith, W., & Mitchell, P. (2008). Outdoor activity reduces the prevalence of myopia in children. Ophthalmology, 115(8), 1279-1285.*
25. *Wu, P. C., Chen, C. T., Lin, K. K., Sun, C. C., Kuo, C. N., Huang, H. M., ... & Yang, Y. H. (2018). Myopia prevention and outdoor light intensity in a school-based cluster randomized trial. Ophthalmology, 125(8), 1239-1250.*
26. *Gwiazda, J. (2009). Treatment options for myopia. Optometry and Vision Science, 86(6), 624-628.*
27. *Fan, D. S., Lam, D. S., Chan, C. K., Fan, A. H., Cheung, E. Y., & Rao, S. K. (2007). Topical atropine in retarding myopic progression and axial length growth in children with moderate to severe myopia: a pilot study. Japanese journal of ophthalmology, 51, 27-33.*
28. *Chua, W. H., Balakrishnan, V., Chan, Y. H., Tong, L., Ling, Y., Quah, B. L., & Tan, D. (2006). Atropine for the treatment of childhood myopia. Ophthalmology, 113(12), 2285-2291.*
29. *Chia, A., Chua, W. H., Cheung, Y. B., Wong, W. L., Lingham, A., Fong, A., & Tan, D. (2012). Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). Ophthalmology, 119(2), 347-354.*
30. *Yam, J. C., Jiang, Y., Tang, S. M., Law, A. K., Chan, J. J., Wong, E., ... & Pang, C. P. (2019). Low-concentration atropine for myopia progression (LAMP) study: a randomized, double-blinded, placebo-controlled trial of 0.05%, 0.025%, and 0.01% atropine eye drops in myopia control. Ophthalmology, 126(1), 113-124.*
31. *Huang, J., Wen, D., Wang, Q., McAlinden, C., Flitcroft, I., Chen, H., ... & Qu, J. (2016). Efficacy comparison of 16 interventions for myopia control in children: a network meta-analysis. Ophthalmology, 123(4), 697-708.*
32. *AMBACHE N. The use and limitations of atropine for pharmacological studies on autonomic effectors. Pharmacol Rev 1955;7:467–94*
33. *Yen, M. Y., Liu, J. H., Kao, S. C., & Shiao, C. H. (1989). Comparison of the effect of atropine and cyclopentolate on myopia. Annals of ophthalmology, 21(5), 180-2.*
34. *Bedrossian, R. H. (1966, August). Treatment of progressive myopia with atropine. In XX International Congress of Ophthalmology. Munich, Germany (pp. 14-19).*
35. *Bedrossian, R. H. (1979). The effect of atropine on myopia. Ophthalmology, 86(5), 713-717.*
36. *Kelly, T. S., Chatfield, C., & Tustin, G. (1975). Clinical assessment of the arrest of myopia. The British journal of ophthalmology, 59(10), 529.*
37. *Gimbel, H. V. (1973). The control of myopia with atropine. Can J Ophthalmol, 8, 527-532.*
38. *McBrien, N. A., Moghaddam, H. O., & Reeder, A. P. (1993). Atropine reduces experimental myopia and eye enlargement via a nonaccommodative mechanism. Investigative ophthalmology & visual science, 34(1), 205-215.*
39. *McBrien, N. A., Stell, W. K., & Carr, B. (2013). How does atropine exert its anti-myopia effects?. Ophthalmic and Physiological Optics, 33(3), 373-378.*
40. *Barathi, V. A., & Beuerman, R. W. (2011). Molecular mechanisms of muscarinic receptors in mouse scleral fibroblasts: Prior to and after induction of experimental myopia with atropine treatment. Molecular vision, 17, 680.*
41. *Lind, G. J., Chew, S. J., Marzani, D., & Wallman, J. (1998). Muscarinic acetylcholine receptor antagonists inhibit chick scleral chondrocytes. Investigative ophthalmology & visual science, 39(12), 2217-2231.*
42. *Larkin, G. L., Tahir, A., Epley, K. D., Beauchamp, C. L., Tong, J. T., & Clark, R. A. (2019). Atropine 0.01% eye drops for myopia control in American children: a multiethnic sample across three US sites. Ophthalmology and therapy, 8, 589-598.*
43. *Gong, Q., Janowski, M., Luo, M., Wei, H., Chen, B., Yang, G., & Liu, L. (2017). Efficacy and adverse effects of atropine in childhood myopia: a meta-analysis. JAMA ophthalmology, 135(6), 624-630.*
44. *Du, L., Chen, J., Ding, L., Wang, J., Yang, J., Xie, H., ... & Zhu, M. (2023). Add-On Effect of 0.01% Atropine in Orthokeratology Wearers for Myopia Control in Children: A 2-Year Retrospective Study. Ophthalmology and Therapy, 12(5), 2557-2568.*
45. *Sander, B. P. (2017). The influence of the autonomic nervous system on the human choroid (Doctoral dissertation, Queensland University of Technology).*
46. *Seward, C. W., Barrowman, J. A., Corner, R. W., Turner, R. W. D., Legge, R. I., McLaren, D. S., ... & Chalmers, A. D. (1961). Res Medica, May 1961, Volume II, Number 4. Res Medica, 2(4).*
47. *Lee, S. S., Mackey, D. A., Lingham, G., Crewe, J. M., Richards, M. D., Chen, F. K., ... & Clark, A. (2020). Western Australia Atropine for the Treatment of Myopia (WA-ATOM) study: Rationale, methodology and participant baseline characteristics. Clinical & Experimental Ophthalmology, 48(5), 569-579.*

ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 10| October 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

48. *Eppenberger, L. S., Grzybowski, A., Schmetterer, L., & Ang, M. (2024). Myopia Control: Are We Ready for an Evidence Based Approach?. Ophthalmology and Therapy, 1-25.*
49. *Berton, B., Chennell, P., Yessaad, M., Bouattour, Y., Jouannet, M., Wasiak, M., & Sautou, V. (2020). Stability of ophthalmic atropine solutions for child myopia control. Pharmaceutics, 12(8), 781.*
50. *Berton, B., Chennell, P., Yessaad, M., Bouattour, Y., Jouannet, M., Wasiak, M., & Sautou, V. (2020). Stability of ophthalmic atropine solutions for child myopia control. Pharmaceutics, 12(8), 781.*
51. *Jacobs, D. S., Afshari, N. A., Bishop, R. J., Keenan, J. D., Lee, J., Shen, T. T., & Vitale, S. (2023). Refractive Errors Preferred Practice Pattern®. Ophthalmology, 130(3), P1-P60.*
52. *Lyman, G. H., Carrier, M., Ay, C., Di Nisio, M., Hicks, L. K., Khorana, A. A., ... & Alonso-Coello, P. (2021). American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer. Blood advances, 5(4), 927-974.*
53. *Shan, M., Dong, Y., Chen, J., Su, Q., & Wang, Y. (2022). Global tendency and frontiers of research on myopia from 1900 to 2020: a bibliometrics analysis. Frontiers in Public Health, 10, 846601.*
54. *Gomes, J. A. P., Azar, D. T., Baudouin, C., Bitton, E., Chen, W., Hafezi, F., ... & Willcox, M. D. (2023). TFOS Lifestyle: Impact of elective medications and procedures on the ocular surface. The Ocular Surface, 29, 331-385.*
55. *Tarutta, E., Chua, W. H., Young, T., Goldschmidt, E., Saw, S. M., Rose, K. A., ... & Wallman, J. (2011). Myopia: why study the mechanisms of myopia? Novel approaches to risk factors Signaling eye growth-how could basic biology be translated into clinical insights? Where are genetic and proteomic approaches leading? How does visual function contribute to and interact with ametropia? Does eye shape matter? Why ametropia at all?. Optometry and vision science, 88(3), 404-447.*
56. *Jacobs, D. S., Afshari, N. A., Bishop, R. J., Keenan, J. D., Lee, J., Shen, T. T., & Vitale, S. (2023). Refractive Errors Preferred Practice Pattern®. Ophthalmology, 130(3), P1-P60.*
57. *Lee, S. S., Mackey, D. A., Lingham, G., Crewe, J. M., Richards, M. D., Chen, F. K., ... & Clark, A. (2020). Western Australia Atropine for the Treatment of Myopia (WA-ATOM) study: Rationale, methodology and participant baseline characteristics. Clinical & Experimental Ophthalmology, 48(5), 569-579.*
58. *Lee, S. H., Tseng, B. Y., Wang, J. H., & Chiu, C. J. (2024). Efficacy and Safety of Low-Dose Atropine on Myopia Prevention in Premyopic Children: Systematic Review and Meta-Analysis. Journal of Clinical Medicine, 13(5), 1506.*