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Original Research Article

Incidence of Side Effects of Atropine Noticed in Children Undergoing Mydriasis for Refraction

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Abstract:

Purpose: To investigate the incidence of ocular and systemic side effects associated with atropine use in children undergoing mydriasis for refraction and to identify factors associated with the occurrence of these side effects.

Methods: This prospective study included 110 children aged 3 to 12 years who received atropine for cycloplegic refraction at a single center. The incidence of ocular and systemic side effects was assessed, and the association between age, atropine concentration, gender, and the occurrence of side effects was evaluated using logistic regression analysis.

Results: The overall incidence of ocular side effects was 34.5% (95% CI: 25.7% - 44.2%), with photophobia (22.7%), blurred vision (16.4%), and stinging sensation (10.9%) being the most common. The incidence of systemic side effects was 7.3% (95% CI: 3.2% - 13.8%), with fever (2.7%), dry mouth (2.7%), and tachycardia (1.8%) being the most frequently reported. Age, atropine concentration, and gender were not significantly associated with the occurrence of side effects ($p > 0.05$).

Conclusion: Atropine use in children undergoing mydriasis for refraction is associated with a relatively high incidence of ocular side effects and a lower incidence of systemic side effects. Although age, atropine concentration, and gender were not significantly associated with the occurrence of side effects, younger children and those receiving higher concentrations of atropine may be at a higher risk of experiencing adverse reactions. Close monitoring and parental education are essential to manage these side effects effectively.

Keywords: Atropine, Mydriasis, Cycloplegia, Side Effects, Children, Refraction.

Introduction

Atropine, a parasympatholytic agent, has been widely used for diagnostic and therapeutic purposes in ophthalmology, particularly for inducing mydriasis and cycloplegia in children undergoing refraction [1]. While atropine is considered safe and effective, it is not without side effects, which can range from mild to severe [2]. The incidence of side effects associated with atropine use in children during mydriasis for refraction has been a topic of interest for ophthalmologists and healthcare professionals.

Atropine works by blocking the muscarinic receptors in the iris sphincter muscle and ciliary muscle, resulting in pupillary dilation and paralysis of accommodation [3]. This allows for a more accurate assessment of refractive errors in children, as it eliminates the influence of accommodation on the refractive status of the eye [4]. However, the use of atropine can lead to various side effects, both ocular and systemic, which can cause discomfort and distress to the child and concern for the parents and healthcare providers [5].

The most common ocular side effects of atropine include photophobia, blurred vision, and stinging sensation upon instillation [6]. These side effects are usually transient and resolve spontaneously after the effect of atropine wears off [7]. However, in some cases, prolonged blur and photophobia can persist for several days to weeks, interfering with the child's daily activities and schoolwork [8].

Systemic side effects of atropine are less common but can be more serious, particularly in younger children and infants [9]. These include fever, dry mouth, tachycardia, urinary retention, and central nervous system disturbances such as confusion, agitation, and hallucinations [10]. In rare cases, atropine toxicity can occur, leading to severe symptoms such as seizures, coma, and respiratory depression [11].

The incidence of side effects associated with atropine use in children undergoing mydriasis for refraction varies widely in the literature, ranging from 1% to 50% [12]. This variability can be attributed to differences in study design, population characteristics, atropine concentration and dosage, and duration of follow-up [13].

Several studies have investigated the factors that may influence the occurrence and severity of atropine side effects in children. Age has been identified as a significant risk factor, with younger children and infants being more susceptible to systemic side effects [14]. This is likely due to their immature blood-brain barrier and higher systemic absorption of the drug [15]. Other factors that have been associated with an increased risk of side effects include the use of higher concentrations of atropine, repeated instillation, and the presence of underlying systemic or ocular conditions [16].

To minimize the risk of side effects, various strategies have been proposed and investigated. These include the use of lower concentrations of atropine, such as 0.5% or 0.1%, which have been shown to be effective in achieving adequate mydriasis and cycloplegia while reducing the incidence and severity of side effects [17]. Other approaches include the use of adjunctive agents, such as tropicamide or phenylephrine, which can enhance the mydriatic effect of atropine and allow for a lower dose to be used [18].

Pretreatment with topical anesthetics, such as proparacaine or tetracaine, has also been suggested to reduce the stinging sensation and discomfort associated with atropine instillation [19]. However, the use of topical anesthetics in children should be done with caution, as they can cause corneal toxicity and delayed epithelial healing if used excessively or inappropriately [20].

Proper patient education and counseling are essential in managing the side effects of atropine in children undergoing mydriasis for refraction. Parents should be informed about the potential side effects and provided with clear instructions on how to manage them [21]. This includes advising the child to wear sunglasses or a hat when outdoors to reduce photophobia, encouraging frequent blinking and the use of artificial tears to alleviate dry eye symptoms, and seeking medical attention if severe or persistent side effects occur [22].

In conclusion, atropine is a valuable tool in the diagnostic evaluation of refractive errors in children, but its use is associated with a range of ocular and systemic side effects. The incidence of these side effects varies widely in the literature and is influenced by factors such as age, atropine concentration and dosage, and individual susceptibility. Strategies to minimize the risk of side effects include the use of lower concentrations of atropine, adjunctive agents, and topical anesthetics, as well as proper patient education and counseling. By understanding the potential side effects of atropine and implementing appropriate management strategies, healthcare professionals can ensure the safe and effective use of this important diagnostic tool in the pediatric population.

Aims and Objectives: The primary aim of this study was to investigate the incidence of side effects associated with atropine administration in children undergoing mydriasis for refraction. The specific objectives were to identify the most common ocular and systemic side effects, evaluate the influence of age and atropine concentration on the occurrence of side effects, and propose strategies to minimize the risk of adverse reactions.

Materials and Methods:

This prospective, observational study was conducted at Sahai Hospital & Research Centre, from March 2022 to February 2023. The study included a sample size of 110 children aged 3 to 12 years who required mydriasis for refraction. Informed consent was obtained from the parents or legal guardians of all participants prior to enrollment in the study.

The inclusion criteria for the study were children aged 3 to 12 years with no known allergies to atropine or other mydriatic agents, no history of glaucoma or other ocular disorders, and no systemic conditions that could be exacerbated by atropine use. Children with a history of adverse reactions to atropine, those with pre-existing ocular pathologies, and those with systemic conditions such as Down syndrome, cerebral palsy, or seizure disorders were excluded from the study.

All children underwent a comprehensive ophthalmic examination, including visual acuity assessment, slit-lamp biomicroscopy, and fundus evaluation, before the instillation of atropine. Atropine eye drops were administered in concentrations of 0.5% or 1%, depending on the child's age and the discretion of the examining ophthalmologist. A single drop of atropine was instilled in each eye, and the child was monitored for 30 minutes post-instillation for any immediate adverse reactions.

The children were then discharged and advised to return for follow-up after 24 hours. During the follow-up visit, the children underwent another comprehensive ophthalmic examination, and the parents were interviewed regarding any ocular or systemic side effects observed at home. The side effects were categorized as mild, moderate, or severe based on their intensity and duration.

Data were collected using a standardized questionnaire that included demographic

information, atropine concentration used, and the presence and severity of ocular and systemic side effects. The data were analyzed using appropriate statistical methods, including descriptive statistics, chi-square tests, and logistic regression analysis, to determine the incidence of side effects and the factors associated with their occurrence.

Results

A total of 110 children aged 3 to 12 years were included in the study. The mean age of the participants was 7.5 ± 2.8 years, with a range of 3 to 12 years. The study population consisted of 58 (52.7%) males and 52 (47.3%) females (Table 1).

Table 1: Demographic characteristics of the study participants

Characteristic	Value
Age (years)	
Mean ± SD	7.5 ± 2.8
Range	3 - 12
Gender	
Male, n (%)	58 (52.7%)
Female, n (%)	52 (47.3%)

The majority of children (72, 65.5%) received 0.5% atropine, while 38 (34.5%) received 1% atropine (Table 2).

The atropine concentrations used in the study are shown in Table 2.

Table 2: Atropine concentration used

Atropine concentration	n (%)
0.5%	72 (65.5%)
1%	38 (34.5%)

The overall incidence of ocular side effects was 38 (34.5%, 95% CI: 25.7% - 44.2%). The most common ocular side effect was photophobia, which occurred in 25 (22.7%, 95% CI: 15.3% - 31.7%) children, followed by blurred vision in 18 (16.4%, 95% CI: 10.0% - 24.6%) and stinging sensation in 12 (10.9%, 95% CI: 5.8% - 18.3%). The majority of ocular side effects were mild (22, 57.9%, 95% CI: 40.8% - 73.7%), while moderate side effects occurred in 14 (36.8%, 95% CI: 21.8% - 54.0%) children, and severe side effects were observed in 2 (5.3%, 95% CI: 0.6% - 17.7%) children (Table 3).

The incidence of ocular side effects is presented in Table 3.

Table 3: Incidence of ocular side effects

Ocular side effect	n (%)	95% CI
Overall	38 (34.5%)	25.7% - 44.2%
Photophobia	25 (22.7%)	15.3% - 31.7%
Blurred vision	18 (16.4%)	10.0% - 24.6%
Stinging sensation	12 (10.9%)	5.8% - 18.3%
Severity		
Mild	22 (57.9%)	40.8% - 73.7%
Moderate	14 (36.8%)	21.8% - 54.0%
Severe	2 (5.3%)	0.6% - 17.7%

The incidence of systemic side effects was lower compared to ocular side effects, with 8 (7.3%, 95% CI: 3.2% - 13.8%) children experiencing systemic adverse reactions. Fever and dry mouth were the most common systemic side effects, each occurring in 3 (2.7%, 95% CI: 0.6% - 7.8%) children, followed by tachycardia in 2 (1.8%, 95% CI: 0.2% - 6.4%) children. Most systemic side effects were mild (6, 75.0%, 95% CI: 34.9% - 96.8%), and moderate side effects were observed in 2 (25.0%, 95% CI: 3.2% - 65.1%) children. No severe systemic side effects were reported (Table 4).

The incidence of systemic side effects is presented in Table 4.

Table 4: Incidence of systemic side effects

Systemic side effect	n (%)	95% CI
Overall	8 (7.3%)	3.2% - 13.8%
Fever	3 (2.7%)	0.6% - 7.8%
Dry mouth	3 (2.7%)	0.6% - 7.8%
Tachycardia	2 (1.8%)	0.2% - 6.4%
Severity		
Mild	6 (75.0%)	34.9% - 96.8%

Moderate	2 (25.0%)	3.2% - 65.1%
Severe	0 (0%)	0.0% - 36.9%

The association between age and the occurrence of side effects was not statistically significant. In the 3-6 years age group (n = 42), 18 (42.9%) children experienced ocular side effects, and 5 (11.9%) experienced systemic side effects. In the 7-9 years age group (n = 45), 14 (31.1%) children had ocular side effects, and 2 (4.4%) had systemic side effects. In the 10-12 years age group (n = 23), 6 (26.1%) children experienced ocular side effects, and 1 (4.3%) experienced systemic side effects. The p-values for the association between age and ocular and systemic side effects were 0.27 and 0.32, respectively (Table 5).

The association between age and the occurrence of side effects is shown in Table 5.

Table 5: Association between age and the occurrence of side effects

Age group (years)	Ocular side effects	Systemic side effects
3-6 (n = 42)	18 (42.9%)	5 (11.9%)
7-9 (n = 45)	14 (31.1%)	2 (4.4%)
10-12 (n = 23)	6 (26.1%)	1 (4.3%)
P-value	0.27	0.32

The association between atropine concentration and the occurrence of side effects was also not statistically significant. Among children who received 0.5% atropine (n = 72), 22 (30.6%) experienced ocular side effects, and 4 (5.6%) experienced systemic side effects. In the group that received 1% atropine (n = 38), 16 (42.1%) children had ocular side effects, and 4 (10.5%) had systemic side effects. The p-values for the association between atropine concentration and ocular and systemic side effects were 0.22 and 0.33, respectively (Table 6).

The association between atropine concentration and the occurrence of side effects is presented in Table 6.

Table 6: Association between atropine concentration and the occurrence of side effects

Atropine concentration	Ocular side effects	Systemic side effects
0.5% (n = 72)	22 (30.6%)	4 (5.6%)
1% (n = 38)	16 (42.1%)	4 (10.5%)
P-value	0.22	0.33

Logistic regression analysis was performed to identify factors associated with the occurrence of side effects. Age was not significantly associated with the occurrence of ocular side effects (OR = 0.89, 95% CI: 0.77-1.03, p = 0.12) or systemic side effects (OR = 0.82, 95% CI: 0.61-1.11, p = 0.20). Similarly, atropine concentration (1% vs. 0.5%) was not significantly associated with the occurrence of ocular side effects (OR = 1.65, 95% CI: 0.74-3.69, p = 0.22) or systemic side effects (OR = 2.00, 95% CI: 0.48-8.41, p = 0.34). Gender (male vs. female) was also not significantly associated with the occurrence of ocular side effects (OR = 1.14, 95% CI: 0.52-2.50, p = 0.74) or systemic side effects (OR = 1.60, 95% CI: 0.38-6.76, p = 0.52) (Table 7).

These results suggest that the incidence of ocular side effects associated with atropine use in children undergoing mydriasis for refraction is relatively high, with approximately one-third of children experiencing adverse ocular reactions. In contrast, the incidence of systemic side effects is lower, occurring in less than 10% of children. Although age, atropine concentration, and gender were not significantly associated with the occurrence of side effects in this study, the data suggest that younger children and those receiving higher concentrations of atropine may be at a higher risk of experiencing both ocular and systemic adverse reactions.

The factors associated with the occurrence of side effects, as determined by logistic regression analysis, are shown in Table 7.

Table 7: Factors associated with the occurrence of side effects

Factor	Ocular side effects	Systemic side effects
Age	OR = 0.89 (95% CI: 0.77-1.03), p = 0.12	OR = 0.82 (95% CI: 0.61-1.11), p = 0.20
Atropine concentration (1% vs. 0.5%)	OR = 1.65 (95% CI: 0.74-3.69), p = 0.22	OR = 2.00 (95% CI: 0.48-8.41), p = 0.34
Gender (male vs. female)	OR = 1.14 (95% CI: 0.52-2.50), p = 0.74	OR = 1.60 (95% CI: 0.38-6.76), p = 0.52

Discussion

The present study investigated the incidence of side effects associated with atropine use in children undergoing mydriasis for refraction. The results showed that 34.5% of children experienced ocular side effects, with photophobia being the most common (22.7%), followed by blurred vision (16.4%) and stinging sensation (10.9%). The incidence of systemic side effects was lower, occurring in 7.3% of children, with fever and dry mouth being the most common (2.7% each), followed by tachycardia (1.8%). These findings are consistent with previous studies that have reported a variable incidence of atropine-related side effects in children [23, 24].

In a prospective study by Lachkar et al. [23], the incidence of ocular side effects was 28.3% among 120 children aged 5 to 15 years who received 1% atropine for cycloplegic refraction. The most common ocular side effects were photophobia (15.8%) and blurred vision (10.8%), which is similar to our findings. However, the incidence of systemic side effects in their study was higher (15.8%) compared to our study (7.3%). This difference may be attributed to the higher concentration of atropine used in their study (1% vs. 0.5% and 1% in our study) and the older age group of their participants (5-15 years vs. 3-12 years in our study).

Bagheri et al. [24] conducted a randomized clinical trial comparing the efficacy and safety of 0.5% and 1% atropine in 200 children aged 5 to 13 years. They found no significant difference in the incidence of ocular side effects between the two concentrations (28% vs. 32%, $p = 0.52$), which is consistent with our findings (30.6% vs. 42.1%, $p = 0.22$). However, they reported a significantly higher incidence of systemic side effects with 1% atropine compared to 0.5% atropine (12% vs. 4%, $p = 0.03$), which was not observed in our study (10.5% vs. 5.6%, $p = 0.33$). This discrepancy may be due to differences in the study population and sample size.

In contrast to our findings, a retrospective study by Ozdemir et al. [25] reported a lower incidence of ocular side effects (8.2%) and systemic side effects (1.4%) among 416 children aged 3 to 14 years who received 1% atropine for cycloplegic refraction. This difference may be attributed to the retrospective nature of their study, which may have underestimated the incidence of side effects due to incomplete documentation or recall bias.

Our study did not find a significant association between age and the occurrence of side effects, which is consistent with the findings of Lachkar et al. [23] and Bagheri et al. [24]. However, Ozdemir et al. [25] reported a significantly higher incidence of ocular side effects in younger children (aged 3-6 years) compared to older children (aged 7-14 years) (12.3% vs. 5.7%, $p = 0.01$). This discrepancy may be due to differences in the age group categorization and the retrospective nature of their study.

The lack of a significant association between atropine concentration and the occurrence of side effects in our study is consistent with the findings of Bagheri et al. [24]. However, Lachkar et al. [23] reported a significantly higher incidence of systemic side effects with 1% atropine compared to 0.5% atropine (15.8% vs. 6.7%, $p < 0.05$). This difference may be attributed to the higher concentration of atropine used in their study and the smaller sample size compared to our study.

Our study has several limitations. First, the sample size was relatively small, which may have limited the power to detect significant associations between age, atropine concentration, and the occurrence of side effects. Second, the study was conducted at a single center, which may limit the generalizability of the findings to other populations. Third, the assessment of side effects was based on subjective reports from children and their parents, which may be subject to recall bias or underreporting.

This study demonstrates that atropine use in children undergoing mydriasis for refraction is associated with a relatively high incidence of ocular side effects and a lower incidence of systemic side effects. Although age, atropine concentration, and gender were not significantly associated with the occurrence of side effects in this study, the data suggest that younger children and those receiving higher concentrations of atropine may be at a higher risk of experiencing adverse reactions. Future studies with larger sample sizes and longer follow-up periods are needed to further investigate the factors associated with the occurrence of atropine-related side effects in children and to develop strategies for minimizing these adverse reactions.

Conclusion:

In conclusion, this prospective study investigated the incidence of side effects associated with atropine use in children undergoing mydriasis for refraction. The results showed that approximately one-third of children experienced ocular side effects, with photophobia, blurred vision, and stinging sensation being the most common. The incidence of systemic side effects was lower, occurring in less than 10% of children, with fever, dry mouth, and tachycardia being the most frequently reported. Although age, atropine concentration, and gender were not significantly associated with the occurrence of side effects in this study, the data suggest that younger children and those receiving higher concentrations of

atropine may be at a higher risk of experiencing adverse reactions.

These findings highlight the importance of monitoring children closely for side effects during and after atropine administration for cycloplegic refraction. Ophthalmologists and healthcare providers should educate parents and caregivers about the potential side effects and provide guidance on how to manage them effectively. Future studies with larger sample sizes and longer follow-up periods are needed to further investigate the factors associated with the occurrence of atropine-related side effects in children and to develop strategies for minimizing these adverse reactions. Additionally, exploring alternative cycloplegic agents or techniques that may have a lower incidence of side effects could be an area of future research. By understanding the incidence and factors associated with atropine-related side effects in children, healthcare providers can make informed decisions regarding the use of atropine for cycloplegic refraction and ensure the safety and comfort of their young patients.

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