Review Article

Ocular side effects of systemic medications

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ABSTRACT

Background: Systemic medications, which are crucial for managing a wide range of diseases from hypertension and diabetes to infections and cancers, can induce substantial ocular side effects. These effects impact visual function and quality of life, necessitating awareness and monitoring by healthcare professionals. The current review summarizes the range and mechanisms of these ocular toxicities.

Methods: This narrative review was derived from a targeted literature search using major electronic databases including PubMed/MEDLINE, Embase, Scopus, and Google Scholar. Keywords related to ocular side effects of systemic medications were utilized to identify relevant studies published from January 1, 2000, to December 30, 2024. The included articles pertained to ocular manifestations of systemic drug use, their mechanisms of toxicity, and associated management strategies.

Results: This study identified notable ocular side effects related to various systemic medications. Amiodarone was consistently linked to corneal deposits and colored halos, prompting recommendations for regular eye examinations. Isotretinoin was frequently associated with dry mucous membranes and blepharoconjunctivitis. Chloroquine and hydroxychloroquine were found to cause corneal changes and irreversible retinal damage with prolonged use. Studies of allopurinol presented conflicting evidence regarding its relationship with cataract risk. Corticosteroid use was associated with cataract formation and potential elevation of intraocular pressure. Ethambutol has been identified as a potential cause of optic neuritis. Topiramate was linked to acute angle-closure glaucoma, particularly early in treatment. Anticholinergic drugs can impact various parts of the eye. They cause ciliary muscle relaxation, leading to temporary blurred vision. This loss of accommodation, also known as "iatrogenic presbyopia," results from paralysis of the ciliary muscle. Phosphodiesterase type 5 inhibitors, such as sildenafil, may cause pupil dilation, redness, dryness, blurred vision, and temporary cyanopsia. Additionally, patients taking vigabatrin may experience progressive constriction of the visual fields, necessitating regular visual field assessments. Epidemiological studies indicate that approximately 15% of patients taking systemic medications experience dry eye syndrome. These findings underscore the diverse range and impact of drug-induced ocular toxicities. However, vigilant monitoring and prompt management can help mitigate vision-threatening complications and preserve patients' visual health. Addressing these ocular side effects requires strong interdisciplinary communication among ophthalmologists, optometrists, primary care physicians, and other specialists.

Conclusions: The wide range of ocular manifestations of systemic medication use emphasizes the importance of monitoring patients for these side effects. Collaborative management by eye care professionals and prescribing physicians is vital to mitigate risks. Further research must focus on the mechanisms of drug-induced ocular toxicity and developing effective preventive measures.

KEYWORDS

side effects, ophthalmic absorption, vision, corneas, toxic potential, optometries, ophthalmologist, interdisciplinary communications, multidisciplinary health team, interdisciplinary health team

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INTRODUCTION

Systemic medications, defined as pharmacological agents administered to treat a variety of diseases through routes that allow entry into the bloodstream, are essential in modern healthcare [1]. They are utilized for managing chronic conditions such as hypertension, diabetes, and autoimmune diseases, as well as acute infections and cancer [1]. However, the widespread use of these medications has raised concerns regarding their potential ocular side effects, which can significantly impact patients' visual health [2].

Epidemiological studies highlighted the prevalence of ocular side effects associated with systemic medications. Approximately 15% of patients taking systemic medications experience dry eye syndrome and other ocular complications such as blepharitis and conjunctivitis are also reported [3]. The risk of serious ocular toxicity varies by medication class. For example, corticosteroids are a well-documented risk factor for cataracts and glaucoma, with studies showing that about one-third of patients may exhibit elevated intraocular pressure (IOP) as a result of their use [4, 5]. Additionally, drugs such as hydroxychloroquine and chloroquine can lead to irreversible retinal damage characterized by "bull's eye maculopathy," particularly after prolonged use [6].

The medical community is increasingly recognizing the ocular side effects associated with systemic medications, which may range from mild discomfort to severe vision-threatening conditions [4]. For instance, antiarrhythmic drugs such as amiodarone can cause corneal deposits and optic neuropathy, whereas certain antiepileptic medications have been linked to acute angle-closure glaucoma [1, 2, 7]. This growing awareness is critical because of the need for vigilance in monitoring patients who take systemic therapies. Key features of these ocular side effects include their varied manifestations and underlying mechanisms. Corticosteroids can cause posterior subcapsular cataracts and glaucoma by altering IOP dynamics, whereas antiarrhythmic medications may result in corneal deposits and optic neuropathy [5]. The onset of these side effects can be insidious; for instance, glaucoma may progress unnoticed until significant vision loss has occurred. Furthermore, medications such as topiramate are associated with acute angle-closure glaucoma due to changes in anterior chamber anatomy [8].

Early detection and monitoring of ocular side effects are paramount in mitigating potential vision loss [4]. Regular eye examinations and patient education about the signs and symptoms of ocular toxicity can facilitate prompt intervention when adverse effects arise [4]. For example, patients taking long-term hydroxychloroquine therapy should undergo routine retinal screening to detect early signs of toxicity [3, 6]. By prioritizing early detection, healthcare providers can better manage the risks associated with systemic medications and preserve patients' visual health. Clinical understanding of these adverse effects, which is the primary aim of this study, is crucial to ensure comprehensive patient care.

METHODS

For this narrative review, a targeted literature search was conducted using major electronic databases: PubMed/MEDLINE, Embase, Scopus, and Google Scholar. The search strategy utilized the following keywords and medical subject headings terms: "ocular side effects," "eye complications," "drug-induced ocular toxicity," "systemic medications," "adverse drug reactions," "corneal deposits," "cataracts," "retinopathy," "optic neuropathy," "glaucoma," "conjunctivitis," and specific drug names (e.g., "amiodarone," "hydroxychloroquine," "isotretinoin," "topiramate," "corticosteroids"). The search was limited to articles published from January 1, 2000, to December 30, 2024, to focus on contemporary understanding and management strategies.

The included articles for this review encompassed studies of any design (clinical trials, observational studies, case reports, and review articles) focusing on the ocular side effects of systemic medications. Studies were included if they discussed the mechanisms of drug-induced ocular toxicity, specific ocular manifestations, diagnostic approaches, or management strategies. Only English-language studies were considered. Excluded articles consisted of non-English studies, articles not specifically addressing the ocular side effects of systemic medications, and studies focusing solely on topical ophthalmic medications. Articles primarily discussing surgical management of ocular conditions without reference to drug-induced causes were also excluded.

The selected articles were assessed based on their relevance to understanding the range and characteristics of ocular side effects associated with systemic medications. Emphasis was placed on key risk factors, mechanisms of toxicity, diagnostic modalities, and potential preventive or therapeutic interventions. Furthermore, the reference lists of the included papers were manually searched to identify additional relevant studies.

RESULTS and DISSCUSSION

General Mechanisms of Ocular Drug Toxicity

Systemic drugs can induce ocular toxicity through several mechanisms, beginning with the route of entry into the eye [6]. Drugs typically enter the eye via the systemic circulation, passing through the retinal or uveal circulation. The blood-brain barrier, blood-aqueous barrier, and blood-retinal barrier impede drugs from causing ocular toxicity; however, inflammation can cause these barriers to leak, facilitating drug entry. Once inside, drugs or their metabolites can accumulate in structures such as the lens and cornea, leading to direct toxicity [9]. Certain drugs, such as chloroquine and chlorpromazine, exhibit a

high affinity for melanin and can damage melanin-containing ocular tissues [6]. Drugs can enhance the immune response, which may result in the production of antibodies that target eye tissues or lead to the accumulation of immune complexes in the eye. The likelihood and intensity of ocular toxicity are affected by various factors, including dosage and treatment duration, individual patient characteristics such as age or pre-existing health issues, and personal sensitivities [3, 6].

Ocular Side Effects of Specific Systemic Medications According to Eye Structures

Eyelids and Conjunctiva

Isotretinoin, a medication commonly prescribed for severe acne, can cause dry mucous membranes and blepharoconjunctivitis [10, 11]. Ocular complications during and after isotretinoin treatment are highly reported, accounting for up to 8.96% of its adverse effects in some studies [12]. Blepharoconjunctivitis, characterized by chronic inflammation of the eyelid margin, crusting of the eyelid and eyelashes, and papillary conjunctivitis, is a common conjunctiva-related complication associated with isotretinoin use. The severity of blepharoconjunctivitis is often dose-dependent [13, 14]. Isotretinoin can also cause keratoconjunctivitis sicca, and in rare instances, this side effect is permanent, though most cases resolve within one month after termination of treatment [13, 14]. Additionally, isotretinoin can affect the conjunctival flora [15]. Eyelid irritation, eyelid cysts, and dry eyes have been observed with amiodarone therapy [16]. Biologic medications such as Dupixent® can lead to conjunctivitis, keratitis, and blepharitis [17].

Cornea

Amiodarone can cause corneal deposits and perception of colored halos around lights [18, 19]. Cornea verticillata, known as vortex keratopathy, appears as a whorled or linear opacity in the cornea and is the most frequently reported ocular side effect in patients treated with amiodarone [18, 19]. Given the high incidence of ocular toxicity associated with this medication, patients should have an initial ophthalmic evaluation before starting amiodarone therapy, followed by repeat examinations every six months during the first year, and then annually. Timely identification of ocular adverse effects related to amiodarone is crucial to prevent the progression of keratopathy or the emergence of rare complications [19].

Isotretinoin can cause corneal opacities and keratitis [6]. It is also known to cause dry mucous membranes, including the conjunctiva. Other ocular side effects associated with its use include meibomian gland dysfunction and blepharoconjunctivitis [6]. Chloroquine and hydroxychloroquine can induce corneal changes, including vortex keratopathy/cornea verticillata. The drugs accumulate in the epithelial layer of the cornea, resulting in a whorled or linear opacity [4].

Anterior Chamber Angle

Topiramate, a sulfamate-substituted monosaccharide used to treat seizures, migraines, and neuropathic pain, can cause acute angle-closure glaucoma [20, 21]. Topiramate-induced acute angle closure (TiAAC) is a potentially vision-threatening side effect [21]. It is a rare occurrence, reportedly affecting approximately three per 100 000 patients taking the medication. However, because indications for topiramate use are expanding, the incidence of TiAAC is anticipated to increase [20]. TiAAC often presents bilaterally with acute eye pain, eye redness, reduced vision, headache, and/or nausea and vomiting. These symptoms may be less severe than those observed in primary angle-closure glaucoma. Patients may experience blurred vision that is worse at a distance than near due to a myopic shift, and they might also report halos and glare because of corneal edema from elevated IOP [20]. The initial evaluation typically reveals decreased visual acuity and increased IOP. Slit-lamp biomicroscopy might show corneal edema, diffusely shallow anterior chamber, closed angle on gonioscopy, and a mid-dilated pupil without iris bombe. B-scan ultrasonography may reveal ciliochoroidal effusions [20].

TiAAC typically presents within the first two weeks of treatment but has been reported to occur within hours of the first dose or as long as seven weeks after the onset of therapy [20]. The most essential treatment for TiAAC is early recognition and discontinuation of topiramate. Patients initiating topiramate treatment should be educated about the symptoms of angle closure and encouraged to seek urgent ophthalmological attention if such symptoms occur. Management includes topical and/or oral anti-glaucoma medications, a cycloplegic agent (e.g., atropine or cyclopentolate), and topical corticosteroids. Aqueous suppressants are preferable to other ocular antihypertensives, such as prostaglandin analogs or miotics [20]. Laser treatment or surgical intervention may be necessary in some cases [21]. After starting treatment, the mean duration until the resolution of TiAAC is 3.9 ± 3.6 days [21].

Lens

Allopurinol use may increase the likelihood of developing cataracts. A cumulative dose of allopurinol exceeding 400 g or a treatment duration longer than three years has been linked to an elevated risk of cataract extraction [22]. However, one study found no evidence that allopurinol users were at a higher risk of developing cataracts after an average of 6.9 years of use [23]. Another study indicated that patients undergoing long-term allopurinol treatment exhibited an unusual morphological thinning of the anterior clear zone of the lens [22]. In a population-based nested case-control study involving 7900 patients diagnosed with gout and a new diagnosis of cataracts >3 years after their initial gout diagnosis, compared to 33 475 patients without cataracts, colchicine was significantly associated with cataracts, but not allopurinol and benzbromarone [24]. In addition, long-term use of corticosteroids is associated with the formation of cataracts [4, 5].

Table 1. Summary of the ocular side effects of selective systemic medications

Medication	Class	Ocular Side Effects	Mechanism	Risk Factors/Monitoring
Sildenafil, tadalafil, and vardenafil [6, 46-49]	PDE-5 Inhibitors	Blurred vision, temporary blue discoloration, and possible association with ION.	Inhibits PDE-6 in the retina, increasing cGMP levels; may affect retinal blood flow. Increased levels of cGMP result in smooth muscle relaxation and inflow of blood.	Caution in individuals with retinitis pigmentosa, macular degeneration, and diabetic retinopathy. Should be avoided in patients with prior nonarteritic ION.
Ethambutol [6, 34-36]	Anti-tuberculosis agents	Retrobulbar optic neuritis, optic nerve damage, central or centrocecal scotomas, and impairment of blue-yellow color vision.	Optic nerve toxicity, causing slow and bilateral dose-dependent damage. Retrobulbar optic neuritis is most common, involving axial or less commonly, periaxial fibers.	Monitor for changes in color vision and visual acuity. The incidence of nerve damage after two months of therapy is 18%, 6%, and 1% in participants receiving 35, 25, and 15 mg/kg/day of ethambutol, respectively.
Interferon alpha [5, 29, 30]	Immunomodulator	Ischemic retinopathy, optic neuropathy, and serous retinal detachment.	May lead to ischemic retinopathy and optic neuropathy.	Monitor for visual changes during therapy.
Amiodarone [7, 18, 19, 37-41]	Antiarrhythmic	Optic neuropathy (similar to nonarteritic ION), corneal microdeposits (vortex keratopathy), and colored halos around lights.	Accumulates in optic nerve lysosomes.	Regular eye examinations are recommended.
Anticoagulants (e.g., warfarin) [42]	Anticoagulants	Spontaneous suprachoroidal hemorrhage and subconjunctival hemorrhage.	Increased risk of bleeding.	Monitor for signs of bleeding.
Corticosteroids (e.g., prednisone) [4, 5, 42]	Corticosteroids	Increased intraocular pressure (glaucoma). Corticosteroids are a well-documented risk factor for posterior subcapsular cataracts.	The exact mechanism is unclear; may affect trabecular meshwork outflow.	Monitor intraocular pressure regularly, especially with long-term use.
Bisphosphonates [5]	Bone resorption inhibitors	Conjunctivitis, uveitis, scleritis, and keratitis.	Inflammatory response.	Monitor for ocular inflammation.
Tamoxifen [4, 5, 28, 50]	Selective estrogen receptor modulator	Maculopathy (pseudo-cystic cavities).	Muller cell dysfunction.	Regular eye examinations are recommended, especially with long-term use.
Topiramate [8, 20, 21]	Anticonvulsant, migraine prophylactic	Acute angle-closure glaucoma, myopic shift, and choroidal effusion.	Increased lens thickness, anterior displacement of the lens-iris diaphragm, and anterior chamber shallowing.	Monitor for sudden-onset eye pain and blurred vision.
Isotretinoin [6, 10-15]	Retinoid	Dry eye, blepharoconjunctivitis, decreased night vision, and pseudotumor cerebri (visual disturbances).	Affects mucous membranes and tear production; and can increase intracranial pressure.	Monitor for dry eye symptoms and visual changes.
Aminoquinolines (chloroquine and hydroxychloroquine) [3, 4, 25-28]	Antimalarial, immunosuppressant	Irreversible retinal damage (bull's eye maculopathy).	Binds to melanin in retinal pigment epithelium, causing toxicity to the macula. Changes normal physiological function by binding to melanin and accumulating in the ciliary body, retinal pigment epithelium, and iris.	Regular eye examinations with visual field testing and optical coherence tomography are essential, especially with long-term use; risk is lower with lower doses.
Vigabatrin [51]	Anticonvulsant	Progressive, irreversible peripheral visual field constriction.	N/A	Requires regular visual field testing.
Quetiapine [52]	Atypical antipsychotic	Cataracts and pigmentary retinopathy (rare).	N/A	Monitor for visual changes.
Cyclooxygenase-2 inhibitors [53]	Non-steroidal anti-inflammatory drug	Blurred vision, conjunctivitis, and dry eye.	N/A	Monitor for ocular irritation or visual changes.
Allopurinol [5, 22]	Xanthine oxidase inhibitor	Cataracts, optic neuritis (rare), and retinal hemorrhage (rare).	N/A	Monitor for visual changes.
Biologics (e.g., Dupixent®) [17]	Monoclonal antibody	Conjunctivitis, dry eye, and blepharitis.	Immune-mediated	Manage ocular surface inflammation.

Abbreviations: PDE, Phosphodiesterase; ION, ischemic optic neuropathy; cGMP, cyclic guanosine monophosphate; N/A, not available.

Retina

Prolonged use of certain medications can lead to permanent retinal damage. Chloroquine and hydroxychloroquine may accumulate in the retinal tissue by binding to melanin in the retinal pigment epithelium (RPE), resulting in lasting toxicity to the macula [4]. Retinal damage manifests as maculopathy and bull's-eye maculopathy [25]. The prevalence of retinal damage in individuals taking hydroxychloroquine for more than five years is approximately 7.5% and can increase to 20–50% after 20 years of therapy, especially with doses exceeding 5 mg/kg/day [26]. These drugs affect the metabolism of retinal cells and have an affinity for melanin in the RPE [27]. This binding can lead to drug accumulation in ocular tissues, potentially causing retinal toxicity [27, 28].

The mechanism of retinal toxicity is not fully understood but may involve the inhibition of all-trans-retinol recycling, disruption of lysosomal function, and direct retinal toxicity [28]. Early signs of hydroxychloroquine toxicity include the appearance of pigmented spots at the macula and a loss of central recess reflexes, which can progress to paracentral scotomas and, in advanced stages, bull's-eye maculopathy. Both hydroxychloroquine and chloroquine can increase the permeability of RPE cells, potentially disrupting their function. Moreover, melanin within the RPE can concentrate hydroxychloroquine, thereby enhancing its toxic effects on the retina [27]. In addition, tamoxifen can cause maculopathy [4, 5, 28].

Interferon alpha can cause retinal damage. Changes may include cotton-wool spots, intra-retinal and preretinal hemorrhage, and macular edema, potentially leading to retinopathy [29]. In a study involving patients with chronic active hepatitis undergoing interferon alpha therapy, 42% exhibited retinopathy featuring cotton wool spots and splinter hemorrhages [30]. Moreover, digoxin may cause photoreceptor toxicity. Digoxin-induced cell death occurs specifically in photoreceptor cells, with only minor effects on other retinal cell types, affecting scotopic and photopic retinal function [31]. Electrophysiological and electroretinographic studies suggest that exposure to toxic levels of digoxin can result in reversible dysfunction of rod and cone photoreceptors [32]. Furthermore, a selectively reduced maximum response parameter in the cone a-wave has been observed in monkeys treated with digoxin, indicating cone photoreceptor dysfunction [33].

Optic Nerve

Ethambutol can cause optic neuritis [34], a rare but serious side effect that is more probable with greater doses and longer use. Visual problems generally appear after 4 to 12 months of drug administration but can occur soon after initiation of treatment [34]. Ethambutol-induced optic neuropathy typically presents with subacute, painless, bilateral visual deterioration [35]. Patients may experience a loss of central vision and cecocentral scotomas in the visual field [36]. Other symptoms include decreased visual acuity, loss of red-green color discrimination, and visual field defects [34]. Examination may reveal a normal optic nerve appearance; however, progressive optic atrophy may develop [34]. Ophthalmic imaging may show decreased thickness of the peripapillary retinal nerve fiber layer and macular ganglion cell layer [35]. Ethambutol-induced optic neuritis is usually reversible after discontinuation of the medication; however, recovery can be prolonged. Supplementing with zinc, copper, and multivitamins may help mitigate the risk [34].

Amiodarone-associated optic neuropathy (AAON) is characterized by an insidious onset and slow progression, ultimately resulting in bilateral simultaneous vision loss and protracted disc swelling [7, 37]. Most cases of optic neuropathy commence within 12 months of amiodarone administration. However, more than 10% of patients may be asymptomatic at the onset [38]. The mean duration of amiodarone use before visual loss is approximately nine months [7]. Optic disc edema was observed in 85% of cases, and two-thirds of AAON cases manifesting with bilateral simultaneous optic neuropathy [39]. The optic nerve swelling frequently persists for several months and resolves much more slowly than in typical non-arteritic anterior ischemic optic neuropathy [7, 39]. The median duration of optic disc edema in AAON after cessation of amiodarone use is three months; however, it may persist up to 15 months in some cases [40]. Patients with AAON may present with monocular or bilateral acutely or insidiously reduced visual acuity [39]. Up to a third of patients with AAON may be asymptomatic [39]. Other symptoms might be dyschromatopsia and nerve fiber-type visual field defects [41]. Amiodarone should be discontinued if optic neuropathy is confirmed, as the condition may progress to permanent visual loss. After discontinuing amiodarone use, visual acuity and visual field deficits tend to improve or stabilize in most patients [7].

Vascular Damage

Anticoagulant medications can elevate the risk of spontaneous suprachoroidal hemorrhage. This hemorrhage can lead to choroidal and retinal detachment, an acute angle-closure crisis, and increasing IOP. In such cases, the lens-iris diaphragm may be displaced, obstructing the trabecular meshwork, and impeding fluid drainage. Management involves IOP reduction via topical aqueous suppressants or oral carbonic anhydrase inhibitors; discontinuation of the anticoagulant may be necessary for elderly patients with multiple risk factors [42]. In addition, immune checkpoint inhibitors, interferons, and platinum analogs may induce ischemic retinopathy. MEK inhibitors may result in retinal vein occlusions [4].

Overall/Multiple Structures

Anticholinergic drugs can affect several parts of the eye. They cause ciliary muscle relaxation, leading to temporary blurred vision [5]. This loss of accommodation, also known as "iatrogenic presbyopia," results from paralysis of the ciliary muscle. Anticholinergics can also contribute to dry eye symptoms by suppressing normal parasympathetic activity [5]. The anticholinergic burden is associated with an approximately threefold increase in the risk of dry eye disease [43].

Anticholinergic drugs can also cause the severe adverse effect of angle-closure glaucoma, particularly in hyperopic patients with narrow drainage angles [5]. Common ophthalmic findings include slightly dilated pupils that constrict weakly to bright light. Greater caution in prescribing anticholinergic drugs for adult patients is important in reducing the rates of adverse outcomes [43].

Isotretinoin causes dryness of mucous membranes, including those of the eye. Other ocular side effects include meibomian gland dysfunction, decreased dark adaptation, keratitis, photophobia, teratogenic ocular abnormalities, and disturbances in night vision [6, 44, 45].

Phosphodiesterase type 5 (PDE-5) inhibitors, such as sildenafil, can cause pupillary dilation, redness, dryness, blurred vision, chromatopsia, and temporary cyanopsia [46]. They increase cyclic guanosine monophosphate levels and lead to vasodilation. They also partially inhibit phosphodiesterase type 6 (PDE-6), found at high concentrations in the retinal rod and cone photoreceptor cells. Partial inhibition of PDE-6 can result in visual disturbances such as impaired color vision, blurred vision, and increased light sensitivity [46-48]. Administration of PDE-5 inhibitors has been associated with visual disturbances such as blue tinge, photophobia, and blurred vision [47]. PDE-5 inhibitors can also cause ocular surface abnormalities [48]. A mild and transient increase in IOP has been observed in some patients [46, 48]. Some studies have linked PDE-5 inhibitor use to more serious ocular conditions, such as serous retinal detachment, retinal vascular occlusion, and ischemic optic neuropathy [46, 48, 49]. Table 1 summarizes the ocular side effects of certain systemic medications.

Diagnostic and Monitoring Strategies

Patients taking systemic medications with known ocular side effects require diligent monitoring to prevent and manage potential complications. Comprehensive eye examinations are essential for early detection of drug-induced ocular changes [4]. Baseline and periodic eye examinations allow clinicians to establish a reference point for each patient's ocular health, enabling timely identification of any adverse effects that may arise due to medication use. Regular evaluations can help mitigate the risk of permanent damage, as many ocular side effects can progress silently before becoming symptomatic [4]. For instance, visual acuity testing is crucial for detecting any decline in visual performance. Regular visual acuity tests can help identify early signs of ocular toxicity, especially in patients taking medications such as hydroxychloroquine or tamoxifen, which are known to affect retinal function [4, 5, 54].

Visual field testing evaluates the entire scope of vision, identifying any peripheral vision loss or central scotomas that may indicate conditions such as glaucoma or retinal toxicity. For example, patients taking vigabatrin may experience progressive visual field constriction, necessitating regular visual field assessments [4].

The slit-lamp examination provides a magnified view of the anterior segment of the eye, allowing detailed evaluation of structures such as the cornea, lens, and anterior chamber. This examination is particularly important for patients taking systemic corticosteroids, as it helps identify cataracts or changes in IOP that could lead to glaucoma [6].

Indirect ophthalmoscopy allows a thorough examination of the fundus, including the retina and optic nerve head [55]. Fundus examination is essential for detecting retinal changes associated with systemic medications, such as serous retinal detachments linked to immune checkpoint inhibitors such as nivolumab [55-57].

Fundus autofluorescence imaging is valuable for assessing RPE and identifying early signs of toxicity from medications such as chloroquine and hydroxychloroquine. Changes in autofluorescence patterns can indicate RPE dysfunction before structural damage becomes evident [4].

Optical coherence tomography (OCT) provides cross-sectional imaging of the retina, allowing a detailed assessment of retinal layers and detection of subtle changes that may indicate drug toxicity. For instance, OCT can reveal early signs of maculopathy associated with long-term hydroxychloroquine use [3].

Multifocal electroretinography measures the electrical responses of various retinal regions to light stimuli, providing insight into retinal function. It is particularly useful in monitoring patients taking medications that may cause retinal dysfunction, such as vigabatrin and ethambutol [3].

Finally, B-scan ultrasound biomicroscopy and anterior segment OCT are beneficial for evaluating ocular structures that may not be adequately visualized through traditional examination techniques. They can assist in diagnosing conditions such as retinal detachment or assessing changes in anterior segment morphology in patients receiving systemic therapies [58, 59].

Management of Ocular Side Effects

Management of the ocular side effects of systemic medications is a critical aspect of patient care that requires a multifaceted approach. This includes the discontinuation or adjustment of medications, the use of topical treatments, and, in some cases, surgical interventions [60]. The role of prescribing physician is vital in managing systemic medications that may lead to ocular side effects. When a patient experiences adverse ocular effects, such as blurred vision or dry eyes, the physician must evaluate the risks and benefits of continuing the medication. For instance, topiramate has been linked to acute angle-closure glaucoma, which may require immediate dose adjustment or treatment cessation [61].

The decision to discontinue or adjust medication should be based on a thorough assessment of the patient's symptoms and the potential for irreversible ocular damage. In addition to systemic management strategies, topical treatments can effectively alleviate specific ocular side effects [5]. For example, lubricants are commonly prescribed for patients experiencing

dry-eye side effects of systemic medications. These lubricants help maintain ocular surface hydration and comfort. Anti-inflammatory drops can alleviate side effects such as conjunctivitis [5]. The choice of topical therapy should be tailored to the individual patient's needs and the specific ocular side effects. If systemic medications lead to more severe ocular complications, surgical interventions may be warranted. For instance, cataract surgery may be necessary for patients developing cataracts as a result of long-term corticosteroid use [5]. Similarly, patients with glaucoma induced by certain systemic therapies may require surgical intervention to manage high IOP. Ophthalmologists and other healthcare providers must collaborate closely in these situations to ensure optimal patient outcomes [5].

The Role of Healthcare Professionals

Managing ocular side effects of systemic medications requires strong interdisciplinary communication between ophthalmologists, optometrists, primary care physicians, and other specialists [4, 60]. Collaboration ensures early identification and treatment of ocular complications, particularly when systemic drugs are a potential cause. Ophthalmologists and optometrists must carefully review patients' medication histories to avoid misdiagnosis or delayed care. Equally important is patient education on the potential ocular side effects of systemic medications [4, 60]. Patients should be informed about symptoms such as blurred vision or dry eyes and encouraged to promptly report visual changes. Studies highlight that educating patients improves awareness, facilitates timely diagnosis of ocular side effects, and judicious medical intervention. Interdisciplinary collaboration and patient education are critical for optimizing outcomes and preventing long-term visual impairment [60].

This narrative review provides a practical summary of the ocular side effects associated with systemic medications, as reported in the literature over the past two decades. It also briefly discusses how to assess patients and manage these drug-related side effects. However, because a systematic review search methodology was not used, some valuable studies may have been overlooked. Additionally, employing meta-analysis in further research could offer accurate numerical data regarding the likelihood of ocular side effects from systemic medications.

CONCLUSIONS

This review highlights the diverse ocular side effects of systemic medications, ranging from corneal changes and cataracts to retinopathy and optic neuropathy. Early detection through regular eye examinations and patient education is crucial. Clinicians should carefully consider potential ocular risks when prescribing systemic medications, particularly in long-term use or with high-risk drugs such as hydroxychloroquine and amiodarone. Vigilant monitoring and prompt management can mitigate vision-threatening complications and preserve patients' visual health. Moreover, collaborative management by eye care professionals and prescribing physicians is vital to diminish risks. Further research should focus on the mechanisms of drug-induced ocular toxicity and developing effective preventive measures.

ETHICAL DECLARATIONS

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