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Case Report

L-lysine as a Possible Supplement for Treatment of Herpetic Epithelial Keratitis: A Case Report and Literature Review

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Abstract

Herpetic Epithelial Keratitis is characterized by a corneal dendritic lesion, and prolonged or recurrent medication such as acyclovir, raises the possibility of resistant strains, necessitating the search for new therapies. An 84-year-old woman, phototype III, reported severe discomfort in the left eye. The presence of a dendritic ulcer was confirmed. Acyclovir therapy (oral—1.6 g/day and topical—seven days) was initiated and replaced by famciclovir (oral–1.5 g/day—seven days; topical acyclovir discontinued). Every three months, a new recurrence occurred. Famciclovir treatment (seven days) was subsequently supplemented with L-lysine (3 g—loading dose + 500 mg/day per 30 days) with L-arginine intake control. After amino acid supplementation, the clinical signs of the active lesion were reduced compared to previous treatment. Furthermore, a longer interval between recurrences was observed until they ultimately stopped. The patient is controlling L-arginine intake. When necessary, L-lysine supplementation is associated. Additional investigation is needed on the proposed supplementary therapy for Herpetic Epithelial Keratitis, which could help reduce side effects and resistance to antiviral drugs. However, as documented in this case report, amino acid supplementation can be recommended for controlling herpesvirus infection with no risk of adverse effects

Introduction

Herpetic Epithelial Keratitis (HEK) is considered a common condition but it has a high potential to cause blindness due to recurrent infections resulting in corneal damage. Successful treatments reduce the recurrence and the duration of the disease, and prevent the formation of progressive and repetitive scarring, which is the main cause of vision loss.[1]

The corneal disease is caused by herpesvirus infection (*Alphaherpesvirinae*, a subfamily of the *Herpesviridae*). The three members of this subfamily are herpes simplex virus type-1 (HSV-1), herpes simplex virus type-2 (HSV-2), and varicella-zoster virus.[2] Keratitis caused by herpes simplex virus (HSV) initially produces a dendritic lesion in the corneal epithelium (HEK), a pathognomonic eye lesion observed on slit lamp examination. With this finding alone, the diagnosis can be conclusive. Rarely, the corneal epithelium is scraped and subjected to a PCR test.[3]

Acyclovir is the most prescribed antiviral medication, being a potent drug used for treatment or prophylaxis. Oral and topical antivirals are prescribed as soon as the HEK diagnosis is confirmed,[2] but the actual antiviral therapies are not capable of interfering with latent viruses such as herpesviruses; they can only interfere with viral particle adhesion and fusion in the host or with viral protein production, playing an important role in epidemiology and viral control, particularly at the beginning of infection.[4]

It is also known that viral particles cannot replicate or express genetic material without the amino acid L-arginine (L-Arg) available in the initial phase of infection, during viral replication. Infected cells deprived of arginine do not exert cytopathogenic effects or show viral replication; when arginine is replenished, infection is rapid and extensive. Lysine is not necessary but has a partial inhibitory effect on viral replication.[5]

Some studies have shown that viruses controlled by acyclovir, *e.g.,* HHV-1 (*herpes simplex*) and HHV-6/7 (*Pityriasis rosea*),

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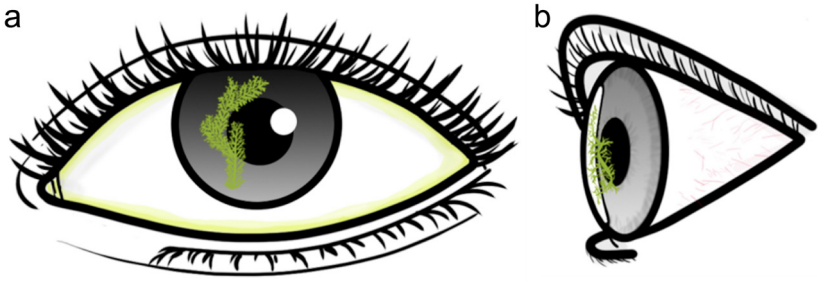

Fig. 1. Schematic drawing of an eye with a typical dendritic ulcer on the cornea, resembling branches of a tree with the greenish-yellow color of fluorescent eye drops. (a, b) Front and side views.

could also be controlled by the amino acid L-lysine (L-Lys) used concomitantly with a reduction in dietary or supplemental amino acid L-Arg.[6,7]

Various nutritional factors linked to the host can favor both the multiplication and control of many viruses because all protein foods contain the amino acids in question. Therefore, a balanced diet and/or amino acid supplementation, such as their depletion, can be a prophylactic and/or therapeutic alternative against the virus. L-Lys, with its competitive antagonism and interference in the production of renal arginase, depletes arginine, disrupting the formation of the capsid and viral DNA.[8]

In 2020, Moshirfar *et al*. questioned: "Is there any role for lysine in herpetic keratitis?"[9] Coincidentally, a patient taking L-Lys was being monitored; thus, this study aimed to present a review of the pathology and the use of amino acids as antiviral therapy, as well as to report an unprecedented case of recurring HEK (HSV) controlled with amino acid balance, with a four-year follow-up (April 2019-April 2023).

Case presentation

Written consent was obtained from the patient for the case publication, including clinical information and photos. The report was composed in accordance with CARE 2013 guidelines.

An 84-year-old woman with phototype III, who has had glaucoma for 34 years controlled with latanoprost 0.005% 125mcg/2.5ml (1 drop/q.h.s.—before sleeping), dorzolamide hydrochloride 2% associated with timolol maleate 0.5% (1 drop/b.i.d—morning and night) and sodium hyaluronate gel lubricant (1 drop/q.i.d.). The patient also reported experiencing a herpes zoster episode more than 20 years ago.

In 2015, she sought a cornea specialist ophthalmologist due to symptoms that started 24 hours prior, including tearing, conjunctival irritation, visual clouding, photophobia, and pain in the left eye. She denied complaints in the right eye. Based on the clinical record, the patient's complaints, and the ophthalmological examination using a slit lamp and fluorescein eye drops, which identified a dendritic ulcer in the corneal epithelium, the HEK diagnosis was concluded, possibly caused by HSV due to the ulcer characteristics (Fig. 1a, b). Confirmatory tests such as viral cultures or polymerase chain reactions were not requested due to the pathognomonic presence of a dendritic ulcer, the patient's complaints, and clinical records.

Antiviral therapy was initiated with acyclovir 400 mg, an acyclic guanosine analogue, DNA polymerase inhibitor (1,600 mg/day—q6hr—seven days) along with topical acyclovir (three times daily) for seven days. At the reassessment visit, seven days after starting treatment, the patient reported an improvement in symptoms, and by day 10, she was asymptomatic. The absence of the dendritic ulcer at the 15-day follow-up confirmed the diagnosis (Fig. 2).

Recurrences occurred every three to four months, averaging three to four per year, with the acyclovir protocol being reinstated each time. In 2018, during a recurrence, the antiviral protocol was changed to oral famciclovir 500 mg (1,500 mg/day—q8hr—seven days), and topical acyclovir was discontinued. However, new recurrences continued. In early April 2019, due to the frequent quarterly recurrences, L-Lys 500 mg capsules were prescribed. Along with the famciclovir protocol (seven days), a 3 g loading dose of L-Lys was administered at the first clinical signs (pain, tearing, turbidity, and photophobia). It was kept (500 mg/day), in fasting condition, with a water glass, for 30 days. Concurrent with L-lysine supplementation and famciclovir protocol, the food intake containing rich L-arginine (chocolate, granola, almonds, orange and grape) was reduced.

While following this protocol (Famciclovir protocol + L-Lys protocol + L-Arg reduction), symptoms such as pain, tearing, and turbidity disappeared between the second and third day of treatment. By day seven, the patient was asymptomatic, and the ulcer had disappeared. The patient reported that, after the introduction of

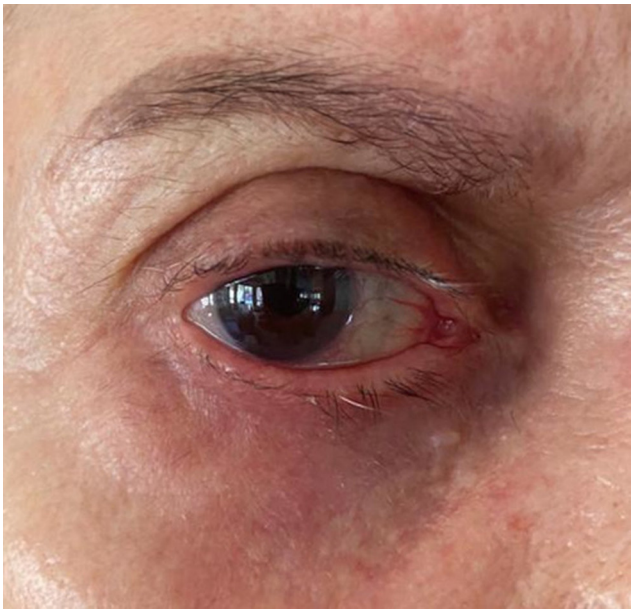

Fig. 2. Patient's left eye with full resolution of keratitis. Redness caused by glaucoma eye drops.

Table 1. Timeline of herpetic keratitis events and treatment

Year	Manifestation	Signs & symptoms	Treatment protocol	Injury resolution
2015	First episode of herpetic keratitis	Tearing, conjunctival irritation, visual clouding, photophobia, and pain in the left eye.	Antiviral therapy was initiated with acyclovir 400mg (acyclic guanosine analogue, DNA polymerase inhibitor) (1,600 mg/day—q6hr—7 days) + topical acyclovir (3× daily) for 7 days.	After 10 days, she was already asymptomatic.
2015; 2016; 2017	New outbreaks occurred with a frequency of one manifestation every 3 months, with the acyclovir protocol being reinserted	Tearing, conjunctival irritation, visual clouding, photophobia, and pain in the left eye.	Antiviral therapy was initiated with acyclovir 400mg (acyclic guanosine analogue, DNA polymerase inhibitor) (1,600 mg/day—q6hr—7 days) + topical acyclovir (3× daily) for 7 days.	After 10 days, she was already asymptomatic.
2018	New outbreaks every 3 months. The protocol was changed however, relapses did not decrease	Tearing, conjunctival irritation, visual clouding, photophobia and pain in the left eye.	The antiviral protocol was changed to oral famciclovir 500 mg (1,500 mg/day—q8hr—7 days) and topical acyclovir was discontinued.	After 8–10 days, she was already asymptomatic.
2019 April	New outbreak Early April	Tearing, conjunctival irritation, visual clouding, photophobia and pain in the left eye.	Oral famciclovir protocol + L-lysine 3 g loading dose in the first clinical signs + 500 mg/day until completing 30 days + the control of dietary intake of L-arginine	Pain, tearing and turbidity disappeared between the second and third day of treatment, unlike the previous outbreaks. After 7 days, the patient was already asymptomatic
2019 August	New outbreak. End of August. Almost 5 months interval after amino acid balance	Tearing, conjunctival irritation, and pain in the left eye. (lighter)	Famciclovir protocol + L-lysine + (L-arginine control intake protocol)	After 4 days, she was already asymptomatic.
2020 February	New outbreak. End of February 6 months interval after amino acid balance	Tearing, conjunctival irritation, and pain in the left eye. (lighter)	Famciclovir protocol + L-lysine + (L-arginine control intake protocol)	After 4 days, she was already asymptomatic.
2020 March to 2023 April	NO OUTBREAKS		The patient maintains regular control of L-arginine intake and, in the face of possible reactivation triggers, any symptoms or prodromal signs L-lysine 3g + (500 mg/day) for 30 days	

the new protocol, the keratitis episodes became milder, lasted for a shorter duration, and had longer intervals for recurrences than with the isolated use of famciclovir, which brought comfort. Following this protocol, a new herpetic relapse occurred in late August 2019 (almost a five-month interval). Another recurrence occurred after six months (February 2020). In both recurrences, the protocol (Famciclovir protocol + L-Lys protocol + L-Arg reduction) was used.

Since February 2020, the patient has been controlling the dietary L-Arg intake (Table 1). When facing potential triggers for reactivation or experiencing any symptoms or prodromal signs, the patient initiates the L-Lys protocol. She reported that after a few hours, the signs and symptoms disappeared, but even so, she maintained the lysine (500 mg) for the full 30 days. No new relapses have been reported since then.

Discussion

Forty-one articles were included that could, briefly, base the discussion on the pathology, treatments and the applicability of amino acid balances as antivirals. As of the literature review, there is no narrative or systematic review, clinical trials or case studies evaluating L-Lys therapy in HEK manifestations. This case report indicated that after amino acid supplementation, the clinical signs of the active lesion were reduced compared to the previous treatment. Furthermore, a longer interval between recurrences was observed until they ultimately stopped.

It is estimated that 95% of ocular herpesvirus infections are caused by HSV/HHV-1, except in cases of neonatal eye infections, which are largely caused by HSV-2 contracted during passage through an infected birth canal. The diagnosis of HEK is based on clinical signs such as conjunctivitis and/or blepharitis, patient-reported symptoms such as eye pain, photophobia, excessive tearing, blurred vision, and local irritation with a foreign body sensation,[2] and on examination with a slit lamp, the presence of dendritic lesions in the corneal epithelium (HEK).[3] These signs and symptoms were observed in the patient in this report, aiding the diagnosis.

The diagnosis of HSV herpetic keratitis can be suggested only

by the presence of multiple dendritic epithelial ulcers with terminal bulbs stained with fluorescein, as observed through the slit lamp.[10]

Corneal samples are believed to assist in guiding therapeutic interventions by reducing disease progression and drug resistance. However, current staining and culture methods have limited sensitivity in viral cases and long response times, which generally do not alter the clinical decision, making cultures less essential for management.[11] PCR testing can confirm the initial diagnosis in atypical or complicated cases. While viral culture is considered the gold standard for HEK, its use is limited in clinical settings due to low sensitivity, the need for a qualified technician, and slow response time (up to 10 days).[1]

In some cases, the detection of HSV-1 by PCR from epithelial scrapings or tear samples would have been useful to confirm the diagnosis,[12] despite the sensitivity of the test being 55.8% for HSV.[13] However, due to the patient's age, associated comorbidities, classic clinical signs and symptoms, and the professional's experience, additional analyses were not requested, and antiviral therapy was initiated with positive results.

Regarding the severity and frequency of HEK episodes in this report, the host's susceptibility to the virus is determined by its immune status and inherited or acquired conditions, such as age and atopy. These factors increase the frequency of disease recurrence. Local corneal susceptibility also plays a role in recurrence and can be affected using medication and frequent trauma, which results in inflammation. Medications such as prostaglandin agonists to control intraocular hypertension and local corticosteroids can increase the risk of recurrence.[10,12] In our case report, factors such as age, medication for intraocular hypertension control, and consumption of arginine-rich foods would account for the recurrences.

The most commonly used therapeutic drugs in clinical practice are nucleoside analogues (DNA polymerase inhibitors) that disrupt DNA synthesis, halting its chain extension. They are effective against active virus replication, especially during multiplication in the early post-infection stages,[14] as stipulated in the lysine protocol presented in this case.

Acyclovir is the most commonly prescribed antiviral and is a potent drug used for treatment or prophylaxis. However, in immunocompromised patients, prolonged treatment, repeated use or discontinuation from the therapeutic protocol results in strains resistant to it due to mutations in thymidine nucleoside kinase (TK) or DNA polymerase.[2,14] This could be another hypothesis to explain the relapses in this case report, but switching to famciclovir showed no changes in the disease's progression or in controlling relapses.

The deficiency of acyclovir, the current gold standard therapy for HSV, was investigated. The results suggested the need for new therapies using natural products to control HSV infection and to supplement L-Lys and control with L-Arg.[15]

Other researchers reinforce the importance of developing alternative methods for controlling these viruses and even capable of eradicating latent infections.[9,16,17] Although current antivirals are still viable treatments for active herpetic diseases such as keratitis, controlling recurrence and the virus in the latent phase remains a challenge due to a virus in its latent state being resistant to all antiviral drugs.[14,16–18]

Vaccines targeting this viral group have not yet been developed, which increases the need for effective therapies that not only safely treat active herpesvirus infection, but also aim to prevent latent infection. Understanding the pathogenesis and virulence characteristics of herpesviruses can lead to new therapeutic targets to prevent the virus from entering, spreading and replicating.[18]

Genetic engineering is also striving for herpesvirus control, with one promising direction being the development of CRISPR/Cas systems for safe and relatively effective long-term control of HSV-1 infection. Plasmids encoding the CRISPR/Cas9 system from Streptococcus pyogenes can completely suppress HSV-1 infection in Vero cell lines within 6 days and provide substantial protection within nine days. The Cas9 protein without sgRNAs attenuates herpesvirus (HSV-1) infection. While administered CRISPR/Cas systems may be promising therapies for HSV-1 control,[17] they are not as accessible as amino acid balancing, which serves as a complementary therapy.

The most recent guideline for treating HSV keratitis was published in 2014. The evidence supporting the addition of debridement to antiviral treatment is weak and lacks coherence. Therefore, the guideline only recommends the use of antiviral agents. For the initial treatment of this disease, it is recommended to avoid topical corticosteroids. Instead, three systemic antiviral agents are available and actively used for HEK treatment: acyclovir (400 mg/3–5 times daily), famciclovir (250 mg/2–3 times daily), and valacyclovir (500 mg/twice daily) for one to two weeks. However, there is currently no consensus on the optimal treatment for HEK.[19] With our report and results, perhaps the association of the amino acid L-Lys with the control of L-Arg intake is a safe and promising option.

Viruses go through several phases during their replication after entering the host cell. In one of these phases, amino acids have been implicated as adjuvants that participate in the production of viral proteins and, interestingly, when a cell is infected by a herpesvirus, there is greater absorption of the amino acid L-Arg.[20,21] Reducing the availability of arginine has therefore been proposed for the control of herpesviruses and currently for the control of SARS-CoV-2.[5,20,22,23]

Kaplan and collaborators inferred that viruses gain strength and increase their multiplication when arginine is available[21] and lysine, as a competing antagonist for the same carriers, would help reduce arginine levels, interfering with the availability of this important amino acid for viral replication[8] that occurs in the initial phase of infection.[20,21]

This competitive antagonism can be explained by the similarity between the chemical structures of the amino acids.[8] L-Lys (K), a (S)-2,6-diaminohexanoic acid (C6H14N2O2), and L-Arg (R), a 2-amino-5-guanidino-pentanoic acid (C6H14N4O2), are structurally related molecules and can compete for the same transporters during intestinal absorption and transport across cell membranes (Table 2).[8,24]

L-Lys supplementation has already been shown to be a safe therapeutic alternative for reducing the frequency of HSV recurrences on the lips (herpes simplex) and could play an important role in the treatment of ophthalmic herpes simplex infections; however, evidence is needed to support this hypothesis.[9]

To control herpesviruses such as HHV-1 (oral herpes simplex) and HHV-6/7 (pityriasis rosea), which are also controlled by acyclovir, L-Lys supplementation therapy has been proposed along with a reduction in arginine-rich foods such as peanuts, almonds, dark chocolate, grapes, oranges, granola, and walnuts, among others. This therapeutic protocol was started in the early stages of viral replication.[6–8,25]

This protocol, with more lysine and less arginine, has not been previously described for keratitis treatment in humans, but it was coincidentally suggested by Moshirfar and collaborators in 2020[9] as it was already being applied in 2019 in this case report showing positive results.

While this study is limited to a single case report, other clinical

Table 2. Pharmacological information—L-arginine and L-lysine

Amino acid	Abbreviation/Symbol	pKa values			pI **	Hydropathy index	Occurrence in proteins (%) *
		pK_1 (-COOH)	pK_2 (-NH3+)	pK_3 (R group)			
Arginine	Arg/R	2.17	9.04	12.48	10.76	(–) 4.5	5.1
Lysine	Lys/K	2.18	8.95	10.53	9.74	(–) 3.9	5.9

*Average occurrence in more than 1,000 proteins, ** Isoelectric point—is the pH at which the amino acid has an equal charge (0). Source: Adapted from Nelson & Cox, 2017,[24] and Pedrazini *et al*., 2022.[8]

studies on herpetic keratitis have also indicated the importance of arginine depletion in viral control. Patients with herpetic keratitis could not be cured by traditional antivirals until they reduced both arginine supplementation and arginine-rich foods.[26,27]

This explains why controlling arginine-rich foods concomitantly with lysine supplementation during prodromal signs and symptoms of relapse showed positive results in the case presented, suggesting that HSV keratitis could be another frontline for the use of L-Lys. The improvement in the patient's health indicated the potential of the proposed protocol.

As antiviral prophylaxis (HSV), L-Lys (500 mg/day/30 days) can be supplemented in the event of possible reactivation triggers such as periods of stress, exposure to the sun or cold, reduced immunity, menstrual periods prior to activation of the immune system by vaccines and local trauma. Studies indicate that this amino acid can prevent the virus from emerging from its dormant state by competing with the absorption of ingested arginine.[6,28]

In viral manifestation, a loading dose of lysine (3 g) at the first signs and symptoms, maintaining therapy with lower doses (500 mg-1 g/day) for a limited period (15 to 30 days), can prevent the viral disease from progressing, even disappearing in the prodromal phase or reducing the cycle of lesions, as well as a late recurrence.[6,7,28] The balance between lysine and arginine will control viral multiplication and expression, promoting shorter and milder cycles.[25,28] It has been debated whether dietary amino acid balance alone is sufficient to control relapses,[8] and in this case report, as of February 2020, it appears that dietary balance was able to prevent relapses.

Thus, the balance of amino acids as an antiviral therapy can occur through dietary choice, selecting foods with more lysine and less arginine.[29,30]

Lysine belongs to the group of essential amino acids, which are only acquired through food, whereas arginine is considered "semi-essential" because it is synthesized in the body. As it is totally consumed, it becomes indispensable in the diet.[24]

The literature is full of foods rich in lysine, arginine, or with equivalent amounts of both amino acids (Table 3), so it's easy to make dietary choices.[8,29,30]

Coincidentally, lysine has been studied as an additional component to antivirals, such as penciclovir, an antiviral for herpes simplex, with the hypothesis that it could potentiate the antiviral effects without pharmacological damage. Designing new formulations and strategies is crucial in combating viral diseases and combining drugs with amino acids could be an alternative.[31] This study corroborates the positive results of combining lysine with famciclovir in this case report.

Faced with the emergence of so many viral threats, new solutions and alternatives must be better investigated. The amino acid L-Lys has been a focus of research for decades.[32,33] Its potential as an antiviral therapy has shown promising results showing that L-Lys, alone or in the form of a polycationic nanopolymer, is an effective antiviral against a variety of viruses.[33]

Protease inhibitors are also potent antiviral drugs and as a result of the screening assay for commercially available amino acids, researchers have designed and synthesized several potent protease inhibitors derived from L-Lys, also yielding promising results.[34]

The varicella-zoster virus, also from the herpesvirus family, causes another type of corneal disease known as zoster stromal keratitis. In acute cases of the disease, pharmacotherapy includes newer drugs such as topical ganciclovir for patients who do not respond to oral antiviral therapy alone.[35]

Some patients may not respond to conventional oral antivirals because they are ingesting a high amount of the amino acid arginine, either through their diet or supplements. This observation should be made by ophthalmologists because, given this fact, control of the viral disease is not achieved.[26,27] This hypothesis corroborates this clinical case, which only showed control of HEK after dietary arginine (dark chocolate, nuts, granola, almonds, orange and grape) along with supplementary L-Lys. Therefore, in cases of ocular zoster, L-Lys could also help and further studies should be carried out.

The balance between lysine and arginine has also been discussed in patients with dry eyes. Tear hyperosmolarity promotes dry eye and increases the risk of co-infections, including viral infections (such as HSV and zoster virus, among others). The conjunctival proteome of patients with dry eyes shows reduced biosynthesis of the amino acid lysine and increased expression of arginine (a marker) depending on the degree of osmolarity. Although further investigation is required, the increased biosynthesis of L-Arg in the conjunctiva of patients with tear hyperosmolarity and consequent dry eye, may be controlled by lysine supplementation.[36] L-Lys, due to its antagonism with L-Arg,[8] would be a promising therapy for controlling both osmolarity and latent viruses in patients with dry eyes.

An *in vivo* study inducing ocular herpes in rabbits with herpesvirus hominis also showed a greater expression of arginine in the tears of the animals, which guaranteed viral multiplication. The main source of arginine was the squamous epithelium of the infected cornea, which, when worn down, reduced arginine levels in tears and viral expression. The same result was obtained using eye drops with homologous arginase, an enzyme that degrades arginine, taken from the animals' livers. It has been suggested that to reduce arginine in the eyes, eye drops could be supplemented with arginase, which would result in control of the herpetic process by suppressing arginine.[37] Following this reasoning, eye drops with lysine compounds, also known as arginine suppressants,[8] could be tested in a pre-clinical *in vivo* study.

Another *in vitro* study, following the same logic, used a recombinant human arginase (peg-arg1) to control HSV. This arginase promoted arginine depletion and, consequently, a decrease in viral expression. The comparison between peg-arg1 and different doses of acyclovir showed that the results were better with the use of arginase,[38] which corroborates the previous study.[37] These findings illustrate that metabolic pathways associated with host arginine

Table 3. L-Arginine/L-Lysine ratio in food with proteins

Food	Amount (g)	Qty of arginine (mg)	Qty of lysine (mg)	Ratio of arg/lys
Low arginine to lysine ratio				
Yogurt Plain	100	104	311	0.34
Margarine	10	2	6	0.34
Figs Fresh	50	8	14	0.57
Whole Milk	250	298	652	0.46
Mango	250	32	70	0.46
Apple	150	8	17	0.47
Cheese	85	600	1,650	0.36
Salmon	85	1,309	2,014	0.65
Chicken	85	1,584	2,232	0.71
Liver, beef	85	1,363	1,671	0.82
Pork	85	1,470	1,586	0.93
Balanced arginine to lysine ratio				
Oatmeat flakes	90 g	600	600	1
Medium Egg	51 g	400	400	1
Pumpkin	200 g	78	78	1
Mayonnaise	185 g	1,400	1,400	1
Beet greens	100g	52	52	1
High arginine to lysine ratio				
Orange	200 g	94	68	1.38
Grapes	100 g	48	15	3.2
Almonds	16 g	683	145	4.7
Brazil nuts	100g	2,392	541	4.42
Peanuts	100 g	3,269	1,036	3.15
Chocolate	100 g	4,000	2,000	2
Cashews	21 g	481	185	2.6
Wheat Flower	100 g	422	248	1.7
Granola	100 g	925	500	1.85

Source: Adapted from "Amounts of L-lysine and L-arginine amino acids in foods": https://www.traditionaloven.com/tutorials/l-lysine_rich_foods.html, and Pedrazini *et al*., 2022.[8] Qty, quantity.

are an effective means of controlling viral replicative processes. Further exploration is necessary to assess the range of viruses inhibited by increased arginases and their ability to suppress pathophysiological disease processes associated with arginine-associated viruses.[38]

There is currently no consensus on the dosage of L-Lys as a prophylactic antiviral protocol. Doses vary between 312 and 3,000 mg per day. A recommended safe and effective dose for prophylaxis would be between 500 and 1,000 mg/day for a limited period, with higher doses (3,000 mg/day) reserved for active relapses as an attack dose for a limited period.[7,8,32]

Some precautions regarding high doses or prolonged use of L-Lys supplementation have been described. Excessive doses or chronic administration of L-Lys can be harmful as they interfere with arginine, which is essential for cell metabolism. Doses exceeding 6 g/day can immediately cause gastrointestinal discomfort.[39,40] Limited doses of lysine for short periods during active viral infections or as prophylaxis against possible viral triggers have been shown to be safe and effective,[7,28] as also observed in the case presented where the L-Lys protocol improved HEK, as questioned in other studies.[9] In relapse events, the amino acid balance rapidly promotes regression of prodromal symptoms, as demonstrated in cases of herpes simplex labialis.[7]

The concomitant control of arginine intake is also important, being a differential in viral control, as discussed in other studies where ocular herpetic infection could not be controlled with antivirals such as acyclovir as long as the supply of arginine was not removed/reduced,[26,27] which corroborates the results of this case report.

The importance of the balance between L-Lys and L-Arg has been reported in several viruses, including SARS-CoV-2, as one possible antiviral therapy.[20] Therefore, in herpetic keratitis, this may be a promising treatment as suggested but requires further clinical studies.[9]

New methods to prevent herpesvirus infections could have a considerable impact on public health, reducing the incidence of herpetic eye diseases and associated morbidity, such as visual impairment.[41]

Conclusions

The supplementation of L-Lys along with the control of L-Arg intake for prophylaxis or associated with allopathic antiviral for the active HEK treatment is interesting and shows a positive result in the case presented with the reduction in clinical signs in the active lesion, as well as spacing and controlling the reactivation. However, further studies should be carried out with this protocol or even with the use of amino acid balance alone, without allopathic antivirals, thus reducing adverse effects and drug resistance. While these studies are not developed, the amino acid balance protocol can be considered a safe option for controlling herpesvirus infections at recommended doses, without the risk of toxicity and/or adverse effects.

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Conflict of interest

The authors declare no competing interests.

Author contributions

Study concept and design (MCP), acquisition of data (MCP, LFGO), analysis and interpretation of data (MCP, MHS, LFGO), drafting of the manuscript (MCP), critical revision of the manuscript for important intellectual content (MHS, FCG), administrative, technical, or material support (MCP), and study supervision (MCP, LFGO). All authors have made a significant contribution to this study and have approved the final manuscript.

Ethical statement

The study was conducted in accordance with the guidance from the Committee on Publication Ethics (COPE) and as outlined in the Declaration of Helsinki as revised in 2013. Written consent was obtained from the patient for the case publication, including clinical information and photos.

Data sharing statement

The health record data used is restricted to protect patient privacy. When appropriate, certain data from health records are included verbatim in the article. Data used in the discussion were sourced from peer-reviewed journals and previously published case reports. Appropriate citations and references are included in the article.

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