IONTORETINA®

Somministrazione di luteina direttamente alla macula tramite iontoforesi oftalmica

L'obiettivo principale del lavoro è valutare la tollerabilità e gli esiti funzionali della somministrazione di luteina tramite iontoforesi trans-sclerale in pazienti affetti da degenerazione maculare senile (AMD) iniziale o intermedia.

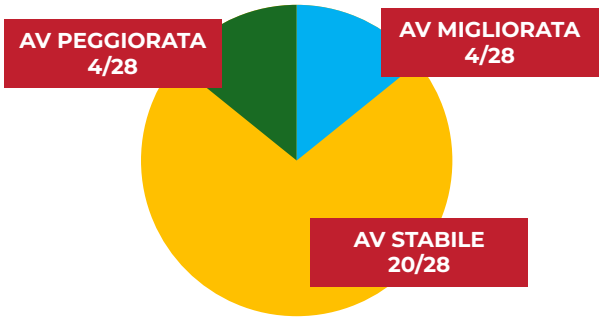
La tecnica di iontoforesi è stata impiegata per migliorare la biodisponibilità retinica della luteina, nota per le sue proprietà antiossidanti e fotoprotettive, evitando le barriere sistemiche.

Lo studio, condotto su 43 pazienti, non è ancora concluso, ma le prime evidenze indicano che il trattamento iontoforetico è tanto più efficace quanto più precoce è il suo inizio rispetto all'evoluzione della patologia, ***"fornendo una valida strategia preventiva contro la progressione dell'AMD".***

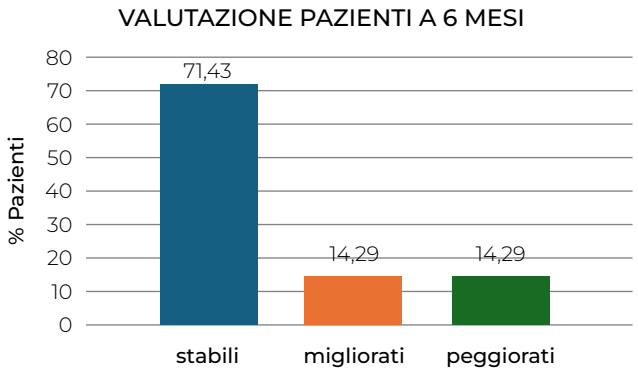
È importante notare che, al momento della presentazione dei dati (risalenti a luglio 2025), lo studio era ancora in corso e i risultati conclusivi a lungo termine (12 mesi) non erano ancora disponibili.

Sono stati presentati dati di follow-up significativi a 6 mesi (180 giorni) dal primo trattamento.

I RISULTATI PRELIMINARI A 6 MESI SUGGERISCONO CHE LA LUTEINA TOPICA SOMMINISTRATA TRAMITE IONTOFORESI TRANS-SCLERALE PUÒ CONTRIBUIRE A PRESERVARE L'ACUITÀ VISIVA NEI PAZIENTI AFFETTI DA AMD INIZIALE O INTERMEDIA.



Andamento dell'acuità visiva dopo la prima rivalutazione eseguita 6 mesi dopo la prima somministrazione di luteina tramite iontoforesi trans-sclerale.



Tra i 28 pazienti che hanno completato la rivalutazione a 180 giorni dopo il primo trattamento:

- **Il 71,43% (20 su 28)** ha mantenuto la propria acuità visiva (AV) rispetto al basale.
- **Il 14,29% (4 su 28)** ha mostrato un miglioramento dell'acuità visiva di almeno 2/10 rispetto al basale.
- **Il 14,29% (4 su 28)** ha mostrato un peggioramento dell'acuità visiva di almeno 2/10 rispetto al basale.

Nei pazienti che hanno mantenuto o migliorato la loro acuità visiva, gli esami strumentali (in particolare OCT, OCT-A e BAF) hanno ***"mostrato una sostanziale stabilità, senza segni di progressione della AMD".***

- I pazienti che hanno mostrato un peggioramento erano soprattutto coloro che all'inizio dello studio presentavano i segni e i sintomi più gravi di AMD nonché alcune delle acuità visive più basse. Questo suggerisce che **quanto prima i pazienti vengono individuati, tanto più efficace può essere il trattamento**.

I RISULTATI PRELIMINARI A 6 MESI SUGGERISCONO CHE IL TRATTAMENTO È BEN TOLLERATO E POTRÀ CONTRIBUIRE A PRESERVARE L'ACUITÀ VISIVA E GLI ESITI DEGLI ESAMI STRUMENTALI NELLA MAGGIOR PARTE DEI PAZIENTI ARRUOLATI.

OFFHEALTH

Trans-scleral iontophoresis for non-invasive ocular delivery of lutein as a prevention strategy in patients with age-related macular degeneration

Università degli Studi di Perugia - Azienda Ospedaliera di Perugia

Clinica Oculistica - Scuola di Specializzazione in Oftalmologia

A. Caricato, P. Mazzei, P. Menduno, M. Giugliano, G. Mirabella, C. Cagini

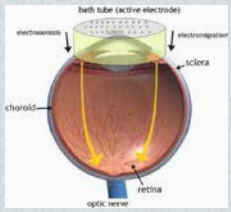
INTRODUCTION & OBJECTIVES

Age-related macular degeneration (AMD) is the main cause of legal blindness in industrialized countries, with a prevalence that can reach 25% in people older than 60 years[1,2]. In its early stages, AMD may cause little or no visual disturbance, but progression to geographic atrophy or choroidal neovascularization often results in irreversible loss of vision[3]. The disease shows a marked tendency towards bilaterality: in patients with advanced AMD in one eye, the cumulative 5-year risk of fellow-eye involvement may exceed 50%, particularly in the presenc of large drusen or retinal pigment epithelium (RPE) pigmentary abnormalities[4]. This underscores the importance of early treatment of the fellow eye at an early or intermediate stage in patients with contralateral advanced disease.

Since the vitality and function of the RPE are central to preventing disease progression in the early stages of AMD, interventions aimed at protecting these cells provide a particularly strong biological rationale. Among these, lutein stands out for its antioxidant and photoprotective properties, especially when delivered directly to target tissues through innovative approaches such as trans-scleral iontophoresis. Trans-scleral iontophoresis is a non-invasive technique that employs a low electrical current to transport charged molecules into the posterior segment, thus bypassing gastrointestinal and systemic barriers. Both preclinical and clinical studies have confirmed its safety in the human eye[5]. Applied to lutein, this approach could enable direct and targeted delivery to the retina, enhancing local bioavailability while reducing interindividual variability. The aim of the present study was to evaluate the tolerability and the functional outcomes of lutein administration by scleral iontophoresis in a prospective cohort of 43 patients with early or intermediate AMD, followed-up for 12 months by the Ophthalmology Clinic of the "University of Perugia - S. Maria della Misericordia Hospital".

MATHERIALS & METHODS

The present study recruited 43 patients diagnosed with Age-related Macular Disease in one eye and signs of early or intermediate AMD in the fellow eye, with the purpose of evaluating the functional outcome of lutein administration by scleral iontophoresis in the aforementioned second eye. Among the exclusion criterias, there were BVCA under 1/10 in the best eye, any kind of opacitiy of the dioptrics that could cause eyesight impairment (e.g.: hypermature or brunescent cataracts), uncompensated ocular hypertension and/or high-score glaucoma, poor compliance or any condition that on behalf of the examinator could interfere with the evaluation. All the patients have been subjected to a comprehensive eye examination, both clinical and instrumental: the latter specifically included Macular OCT, OCT-Angiography, Blue Autofluorescence and Ultra Wide Field funduscopy (*Tab. 1*). In case the patients met the set criterias, they have received all the informations and they have signed the consent form both for the treatment and for the collection and the use of the findings for the present study.



After the initial assessment, all the enrolled patients have been treated with a first administration of lutein by scleral iontophoresis; they have been then invited for a check-up in the following 24 hours to ensure they had not experienced any severe adverse effect after the treatment. Starting from the date of the first treatment, the patients underwent follow-up visits scheduled 30 days, 90 days and 180 days after the first treatment. During these visits, the visual acuity of the patients has been re-evaluated; the enrolled patients also underwent a panel of instruental examinations including Macular OCT, Blue Autofluorescence and Ultra Wide Field funduscopy. Six months after the first treatment, the patients underwent a comprehensive re-assessment and a second administration of lutein via scleral iontophoresis was performed: once again, a check-up in the following 24 hours has been arranged to exclude any immediate adverse effect. Finally, the schedule includes one last assessment (again: both clinical and instrumental) to be performed 180 days after the second subministration on lutein by scleral iontophoresis.

Both the treatment sessions and the visits have been performed in an out-patient setting at the Ophthalmology Department of the Hospital "Santa Maria della Misericordia" in Perugia. Our study was made possible by the unconditional contribution of OffHealth S.p.A., who supplied the "IontoRetina" kit including one dose of liposomal solution of lutein, one ocular electrode for scleral iontophoresis, one return electrode and the electrical current generator.

RESULTS

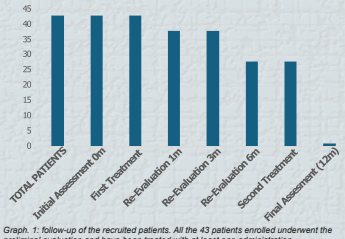
To date (July 2025), all the 43 patients recruited underwent the initial assessmentn and have been treated with at least one administration of lutein by scleral iontophoresis. Of the 43 patients: 38 of them underwent the first re-evaluation (30 days after the first treatment) and the second re-evaluation (90 days after the first treatment), while 28 of them underwent the re-assessment visit planned 180 days after the first treatment. The same 28 patients mentioned earlier have been treated once again with a second administration of lutein by scleral iontophoresis. To date (July 2025), no one of the enrolled patients have reached the final assessment (12 months after the first treatment) (*Graph. 1*).

20 out of 28 patients (71.43%) mantained their visual acuity ±1/10 comapred to baseline, 4 out of 28 patients (14.29%) have shown an improvement in visual acuity of at least 2/10 compared to baseline and 4 out of 28 patients (14.29%) have shown a worsening in terms of visual acuity of at least 2/10 compared to baseline (*Graph.* 2). The visual acuity has been evaluated measuiring the refraction of each patient during the initial assessment visit; and the same refractive correction has been using throughout all the phases of the follow-up.

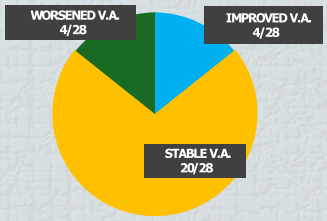
The patients that during the re-assessment visit mantained or improved their visual acuity compared to the baseline, showed a substantial stability of the findings during the instrumental examinations, with particular reference to OCT, OCT-A and BAF, without signs of progression of the Age-related Macular Disease (*Fig. 1*). On the other hand, patients who exhibited a worsening of their visual acuity compared to the baseline have also shown progression signs of the Age-related Macular Disease (e.g.: worsening of drusens, thinning of the RPE. develop of nvAMD) (*Fig.* 2). It is worth noticing that the present study did not find anything that might suggest that scleral iontophoresis of lutein could speed up the progression of AMD.

It is also worth noticing that the majority of the patients who exhibited a worsening trend were the ones who exhibited the most severe signs and symptoms related to AMD during the initial assessment, as well as some of the lowest visual acuities among all the patients: this could suggest that the earlier the patients are caught during their periodic eye examinations, the more effective the administration of lutein by scleral iontophoresis in the fellow-eye could be.

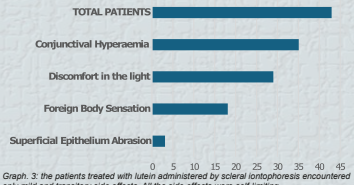
The administration of lutein via scleral iontophoresis proved not to give medium and long term adverse effects, showing only mild and transitory side effects. After the treatment session: 35 out of 43 patients (81.4%) shown conjunctival hyperaemia, 29 out of 43 patients (67.44%) felt a mild discomfort in the direct sunlight, 18 out of 43 patients (41.86%) have complained about about foreign body sensation and 3 out of 43 patients (6.98%) has been affected by a superficial abrasion of the corneal epithelium *(Graph. 3*). All the side effects described above were self-limiting and they healed without leaving scars and/or any other outcome of any sort. As a matter of fact, during the re-assessment at 6 months from the initial treatment no side effects were to be found.



Graph. 1: follow-up of the recruited patients. All the 43 patients enrolled underwent the preliminial evaluation and have been treated with at least one administration.



Graph. 2: trending of visual acuity after the first re-assessment performed 6 months after the first administration of topical lutein via scleral iontophoresis.



Graph. 3: the patients treated with lutein administered by scleral iontophoresis encountered only mild and transitory side effects. All the side effects were self-limiting.

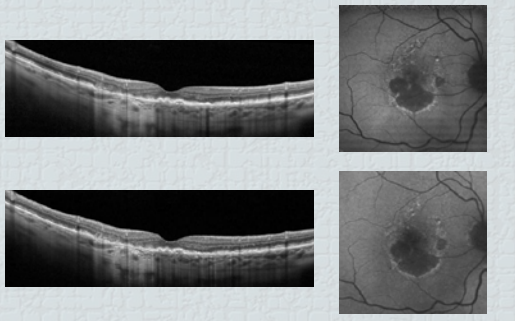


Fig. 1: OCT and BAF in patients with stable or slightly improved visual acuity compared to baseline expressed no signs of progression of AMD.

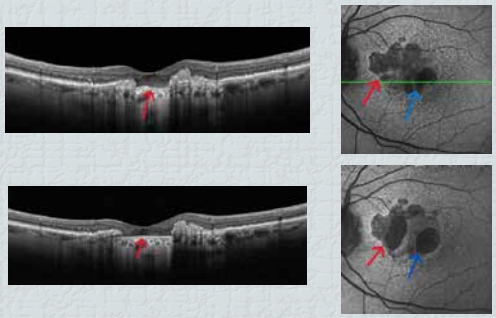


Fig. 2: patients who exhibited a worsening of their visual acuity have only shown signs related to the natural history of AMD (in this case mainly increase in drusens, thinning of the EPR and enlargement of the areas of atrophy) without any collateral and/or adverse findings.

	BLue AF	IR + OCT	Wide-Field Fundus Photography	OCT-A	Treatment
Initial Assessment (0m)	●	●	●	●	○
First Treatment	○	○	○	○	●
Re-Evaluation after 1m	●	●	●	○	○
Re-Evaluation after 3m	●	●	●	○	○
Re-Evaluation after 6m	●	●	●	●	○
Second Treatment	○	○	○	○	●
Final Assessment (12m)	●	●	●	●	○

Tab. 1: the patients recruited for the present study underwent a series of instrumental examinations as per the schedule resumed in this table. In particular, OCT Angiography has been performed at the Initial, Intermediate and Final Assessment to exclude pre-existing and/or newly developed nvAMD forms.

CONCLUSIONS

The early findings of the present study seems to suggest that topical lutein administered with the help of scleral iontophoresis can contribute to the preservation of the visual acuity in patients affected with early and/or intermediate Age-related Macular Disease, as well as preventing the onset of AMD in those who are mostly at risk of developing it. This seems to be particularly important given the ability of scleral iontophoresis to overcome sistemic conditions statistically increased among older people (e.g.: malabsorption, transporter deficiencies, etc.) that could results in poor uptake of dietary supplements when they are administered orally; and since AMD is typically a disease to be found in the elderlies, iontophoresis could be a winning and successful formula if strategically adopted. In the end, it is also worth remembering that a single administration of lutein by scleral iontophoresis promises to be as effective as a continuous intake of oral dietary supllements; but since the present study is still, to date, in progress, it will be necessary to wait for the end of the assessments before achieving some conclusive results.

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