UNIVERSITY „LUCIAN BLAGA” OF SIBIU

FACULTY OF MEDICINE

THE MANAGEMENT IN EXPOSURE KERATOPATHY

Summary

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Summary

INTRODUCTION

The management of exposure keratopathy is an extremely complex process and today multiple therapeutic options are available.

To ensure the success of the therapeutic process it is important to know the main cause and the gravity of the disease. Frequently, a multidisciplinary approach is required for an efficient management.

Exposure keratopathy is a condition which cause is linked to an excessive evaporation of the lacrimal film due to some eyelid occlusion abnormalities which will result in the dehydration of superficial layers of the cornea.

Exposure keratopathy is a clinical diagnosis based on the patient's history and physical examination. Ophthalmic examination in case of patients with presumed dry eye syndrome diagnosis reveals the fact that the exposure of the cornea is the main etiology.

Common symptoms include pain, ocular foreign body sensation, blurry vision, epiphora, photophobia. Signs include incomplete eye blinking ,lagophtalmos, changes of the lacrimal film, formation of corneal filaments, epithelial defects, corneal edema with corneal thinning and perforation in severe cases.

The etiology of exposure keratophathy includes : **facial nerve paralysis** of multiple causes: idiopathic (Bell's palsy), strokes ,tumors (acoustic neuromas, epidermoid and dermoid tumors), demyelination, sarcoidosis, trauma, sectioning surgery, otitis, Ramsey–Hunt syndrome, Guillan-Barre syndrome, Lyme disease, **eyelid malpositions** : nocturnal lagophtalmos, ectropion,defect of eyelid margin, surgical ptosis overcorrection, **orbital diseases**: proptosis, thyroid opthamopathy ,reduced muscular tone: general anesthesia, profound coma, Parkinson disease, tetanus.

The management of exposure keratopathy requires the management of paralytic lagophthalmos, eyelid malpositions, thyroid opthamopathy and that of the conditions which determine the reduction of the muscle tone.

PERSONAL RESEARCH

Proper eyelid closure as well as a normal blink reflex are essential to maintain the integrity of the corneal surface and a stable tear film.

Lower lubrication of the ocular surface due to lagophthalmos or due to the lower rate of blinking will cause corneal exposure and subsequent keratopathy which may develop corneal ulceration and infectious keratitis.

The diagnosis and treatment of exposure keratopathy is based on the patient's history data as well as clinical examination. A careful history should be performed to determine the etiology of lagophthalmos and it should contain information related to trauma, surgery of the face or eyelids, suggestive symptoms for thyroid disease, previous infection with herpes zoster, history of obstructive sleep apnea.

The most frequent cause of lagophthalmos is paralysis of the facial nerve, usually idiopathic (Bell's palsy) but it can be a cause of trauma,infection, strokes, eyelid surgery, various tumor formation or even surgical techniques to have them removed. It can also represent of a particular thyroid disease, a tumor,acoustic neuroma.

Another variant of lagophthalmos is nocturnal lagophthalmos which is a more discreet form of bilateral lagophthalmos. .It can become obvious while the patient is sleeping and as a result it is a disease which is difficult to diagnose as patients are hardly aware of the fact they may be sleeping with their eyes half-open. A slight decrease in the action of the orbicularis is noticeable.

Patient exam includes:

-Eyelid inspection in order to evaluate possible malposition. The eyelids should be examined for ectropion, entropion or retraction.

-Eyelid and globe testing

-The patient is asked to look down and to slightly close both eyes. Lagophthalmos is present when a space remains between the upper and lower eyelid margins. The degree of lagophthalmos is quantified by measuring the latter space, in millimeters, with a ruler.

- Determination of the blinking rate

- Determination of the presence and quality of Bell's palsy

- Assessing muscular power of the orbicular according to the generated force in the attempt of eye closing

-Testing the corneal sensitivity by applying soft cotton without the instillation of anesthetics

- Tear secretion evaluation through Schirmer test and the breaking time of the tear film

- Slit lamp examination using vital dyes to highlight the extent of corneal damage

The method of treatment varies according to the etiology, the severity and estimation of the duration of lagophthalmos and should be individualized for each patient.

Therapeutic means are multiple, some of which are temporary if lagophthalmos is discreet and functional recovery is anticipated , while some are permanent if lagophthalmos is severe and carries on more than initially anticipated.

Starting from the premise that lagophthalmos and secondary keratopathy is an extremely severe condition for patients with impact on life quality and socio-professional integration because of the symptoms determined by the affected eye area as well as the major esthetic changes, this his paper aims to examine the therapeutic point of view of the conservative one and surgery.

Aim of study

1. To evaluate the most appropriate therapeutic procedure,conservative or surgical in managing exposure keratopathy while taking into account the etiology and degree of functional loss.

2. To emphasize the effectiveness of the technique of gold weights implant within the upper eyelid as the main method of surgery performed for exposure keratopathy and persistent lagophthalmos.

3. To observe the evolution of patients with exposure keratopathy at varying intervals depending on the chosen therapeutic method.

Material and Method

A retrospective observational analytical study was conducted using a number of 62 hospitalized with exposure keratopathy, treated in January 2006-december 2015 in the Department of Ophthalmology of the Clinical Hospital Sibiu.

Material:

The considered parameters were:

-Patient's demographic data

-Cause of exposure kerathopaty based on patient's personal history

-Family history of exposure keratopathy and other associated pathology (thyroid disease, diabetes, high blood pressure)

-The length of time form the onset of lagophthalmos until the moment of finding

From all the patients, the main cause of exposure keratopathy and lagophthalmos in 53 patients was facial nerve paralysis, of which 32 cases were Bell palsy and 21 cases of facial paralysis of other etiologies , in 4 cases thyroid ophthalmopathy and in 5 patients involutive ectropion.

Patient's ophthalmic examination included:

-Evaluation of lagophthalmos degree in presentation, measured in millimeters with a ruler from the margin of the upper lid to the margin of the inferior lid in pupillary vertical plan, with the eyes opened to determine the height of eye fissure and with closed eyes for lagophthalmos .For patients with paralytic ectropion ,the measurement was performed form the margin of the upper eyelid to the lower limbus.

-Corneal sensitivity was determined by applying soft cotton over the cornea without previous anesthetic instillation

-Lacrimal secretion was measured with Schirmer tests

-Exoftalmometry measured with Hertel exoftalmometer in case of patients with thyroid disease

-Slit lamp examination of the anterior pole was performed using fluorescein stain to determine the grade of the exposure keratopathy:

Mild - punctate epithelial inferior epithelial erosions or paracentral in proptosis

Moderate-persistent epithelial defect

Severe-corneal ulcer

Method of study

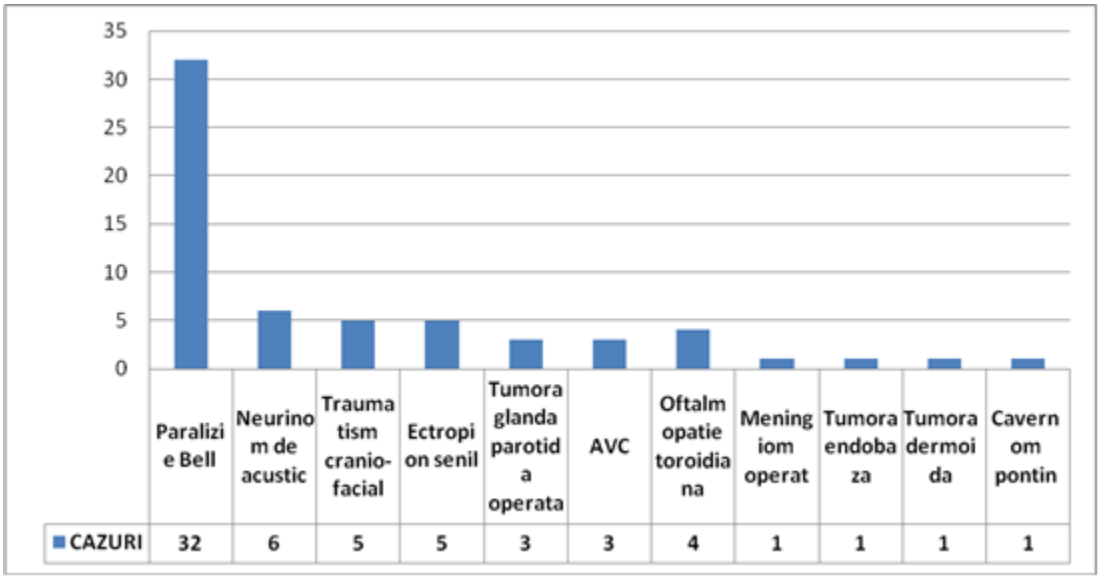
The elected treatment for each patient included the cause, the duration and the severity of lagophthalmos.

Weeks	**Months**	**Prolonged/Permanent**
Topical Antibiotics	External palpebral weight	Gold weight implantation
NSAD's	Temporary tarsorrhaphy	Ectropion correction
Artificial tears and		
Ointments		
Corneal lubricants		
Therapeutic contact lenses		

Results and discussion

During January 2006-december 2015 within the department of Ophthalmology of the Clinical Hospital in Sibiu, 62 cases of exposure keratopathy were hospitalized and treated.

Based on the patient's personal history it has been established for each patient the determinant cause of exposure keratopathy.



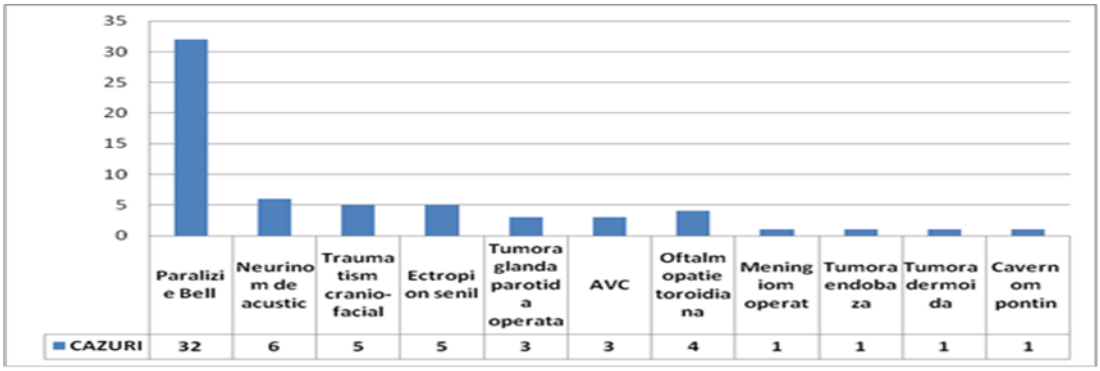
Distribution of etiology for EK

The main cause of exposure keratopathy in the studied group was paralysis of facial nerve of various etiologies and a smaller proportion of cases with palpebral malformations –senile ectropion and thyroid ophthalmophaty.

The extensive etiologie of facial nerve paralysis prevents the accurate estimation of the incidence of facial nerve palsy of a certain cause.

The most frequent cause of facial nerve palsy was idiopathic palsy, also known as Bell's palsy, representing 51% according to Rahman (2007), followed by trauma 22% and Ramsey-Hunt syndrome 7 %. According to Hohman (2014), Bell's palsy represents 38% of facial nerve palsy surgery for acoustic neuromas 10%, tumors 7%, iatrogenic lesions 7%, Ramsey-Hunt syndrome, 7%,benign lesions 5%,congenital paralysis 5% ,Lyme disease 4 % .

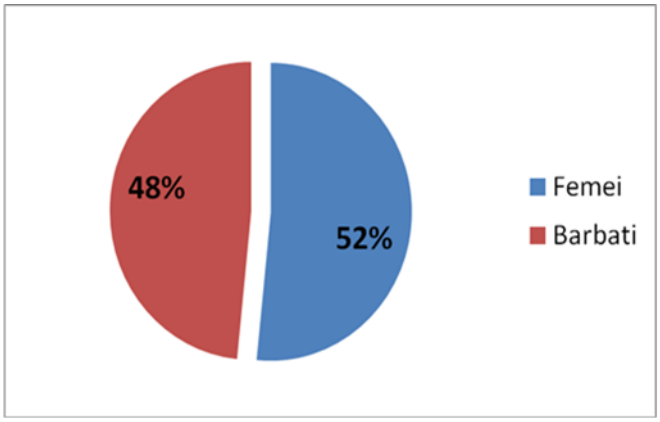
In our studied group, Bell's palsy resulted in 62.75% of the facial nerve paralysis cases, followed by tumor causes and an equal percentage of 5.88 of traumas and stroke causes.



FNP etiology

Facial nerve paralysis affects all categories of population irrespective of age, gender or rase. So far, there is no consensus if it mainly affects males or females.

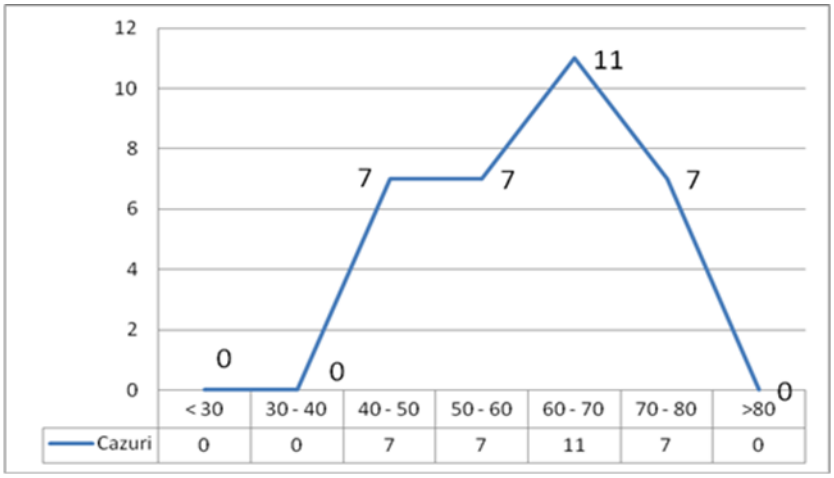
In case of our study group, gender distribution of patients was relatively equal with a slight predominance of female gender.



Gender distribution of EK

In most cases, Bell's palsy occurs among adults according to some studies with a slight predominance of patients over 65 with an incidence of 59 cases per 100.000 inhabitants as opposed to children under 13 presenting an incidence of 13 cases per 100.000 inhabitants. Other studies have recorded the maximum of Bell's palsy between 15-45 years. Arie J.Nemet and co. have exposed in a different study that there is a clear incidence of age related with a marked increase in incidence with each decade but with a slight decrease in incidence after the age of 85 as a result of possible case underreporting.

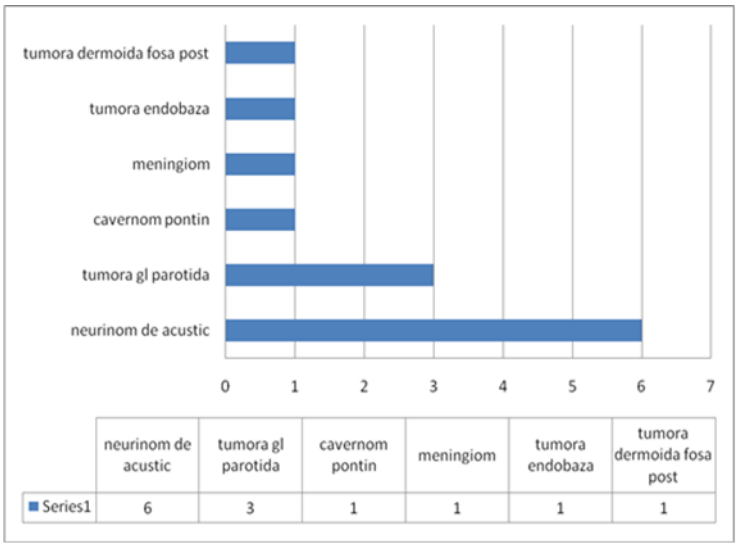
A similar result can be seen in case of studied patients, which incidence reaches a maximum for the 60-80 age group and quite lower for the 40-60 age group.



Age distribution for BP

The most frequent tumors which affect the facial nerve are the acoustic neuromas, facial tumors (cholesteatomas ,dermoid cyst, hemangiomas, meningiomas) and parotid gland tumors .

According to Mathies and Samii ,17 % of patients with acoustic neuroma showed facial nerve dysfunction before surgical removal.



Tumor cause in FNP

Both non-penetrating and penetrating trauma can cause facial nerve injury.

Car accidents cause 31% of the facial nerve damage which results in temporal bone fractures, followed by accidents caused by falls.

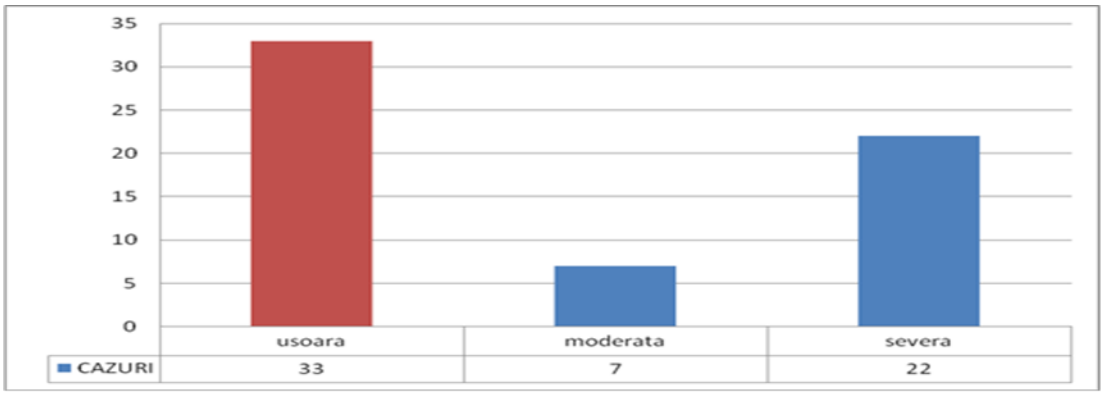
Thyroid ophthalmopathy was present as the cause of exposure keratopathy in 4 of the studied cases. All cases were females aged between 40 and 60 .Three of which presented with hyperthyroidism , only one case was in euthyroid state. Two of the patients were smokers.

The disease is more common in women F/M=4/1, yet the proportion of men affected increases as the severity is higher. Male/female ration is 9.3/1 in mild forms of impairment, 3.2/1 in moderate forms and 1.4 /1 in severe ophthalmopathy.

Senile ectropion was the cause of 6 exposure kerathopathy cases of the studied group. Patients were included in age groups of 70-80 years, four case of which were of male gender and two of female gender. This particular form of senile ectropion was reported as 2.9 % to 5.1 % in male gender and 1.5% in female gender.

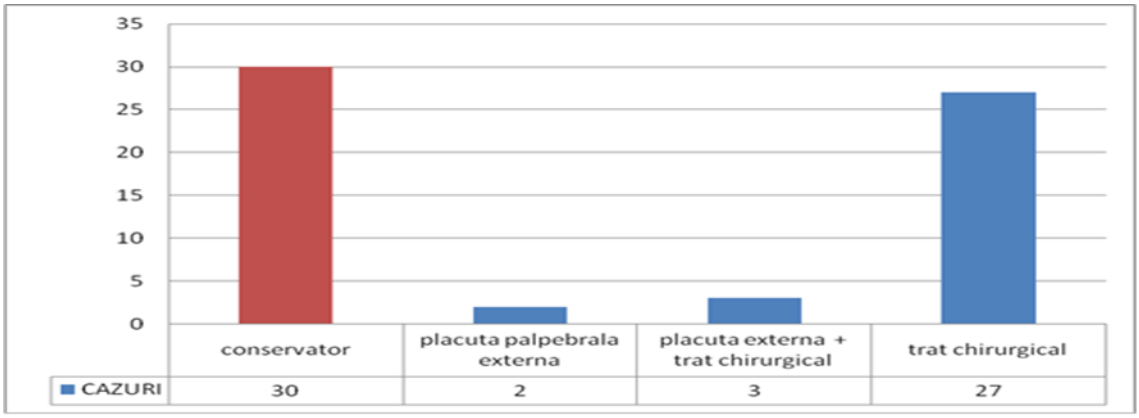
Management of the patients with exposure keratopathy was different depending on the etiology, its degree as well as its duration in early recovery.

The degree of exposure keratopathy was determined for all patients by the use of fluorescent stain and slit lamp as examination means ,thus being classified in mild (33 cases),moderate (7 cases) and severe (22 cases).



Classification of EK

The management of patients includes a wide range of therapeutic possibilities ranging from conservatory methods to treat symptoms of dry eye to complex surgical techniques depending on the gravity.



Therapeutic options in patients with EK

Management of exposure keratopathy caused by paralyitic lagophtalmos

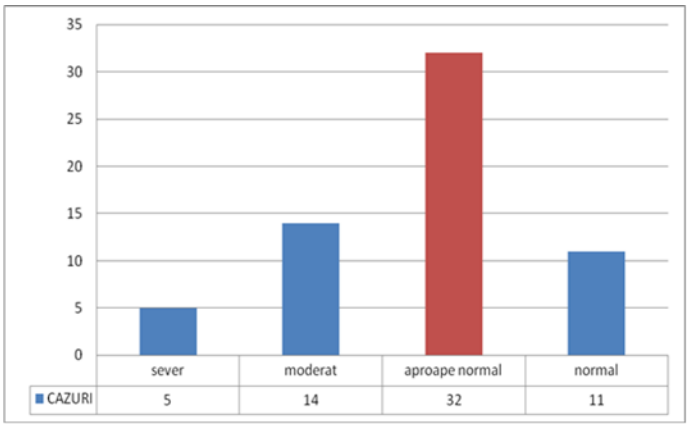
Proper treatment for corneal protection in case of patients with facial nerve paralysis depends on the estimated duration of functional recovery of the functional nerve and corneal risk level, determined by the degree of lagophtalmos, the presence of Bell's palsy and the presence or absence of paralytic ectropion.

1. Conservative treatment

Of all 52 patients with facial nerve paralysis and paralytic lagophtalmos, 29 cases of idiopathic etiology (Bell palsy)presented mild form of exposure keratopathy and discreet lagophtalmos with functional recovery outlook in a short amount of time. The patients received only conservative treatment, corneal protector and were monitored every two weeks until complete lagophtalmos remission.

Conservative treatment consisted of frequent administration of lubricating ointments such as artificial tears during the day, NSAID's , topical antibiotics, trophic corneal ointments and more binding ones during the night.

Tear test was performed in all cases using the Schirmer test to determine the degree of dry eye, mild, moderate or severe.



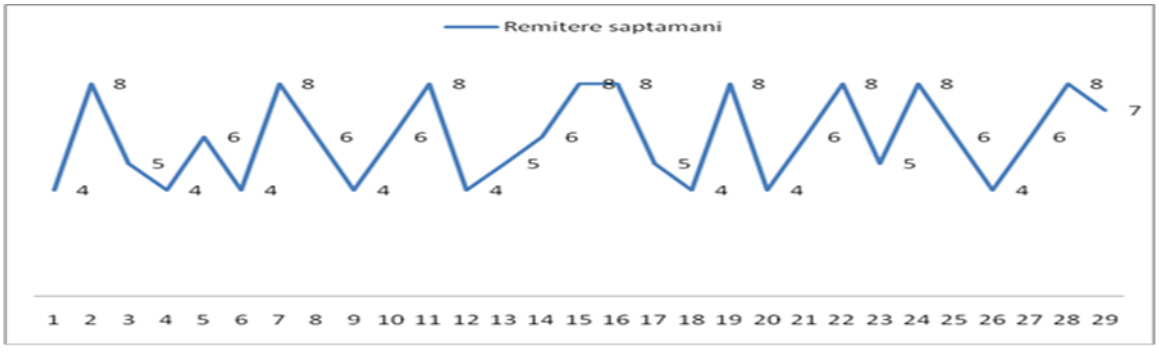
Dry eye syndrome degree

Improvement of the quality of the tear film can be made by administrating artificial tears frequently, improvement of lipid component by applying warm compress or by oral administration of products containing Omega 3 fatty acids, according to some studies.

Scleral contact lenses were described as being an alternative to tarsorrhaphy for patients with exposure keratopathy and corneal anaesthesia , thus providing effective protection in an optimizing esthetic manner and visual function.

Injecting botulinum toxin is a good temporary method with a low risk with an effect which lasts up to 48 days is considered to be an alternative method for postoperative facial nerve paralysis when the facial nerve is anatomically intact.

From a number of 29 patients with Bell's palsy who received only conservative treatment, all of them achieved complete functional recovery without consequence in varying intervals of time, the average recovery being estimated in 6 weeks.



The evolution of Bell's palsy with conservative treatment

Complete and spontaneous recovery of Bell's palsy is produced in 70% of cases. Usually, remission starts within 3-4 weeks, with complete recovery up to 6 months.

Patients who presented incomplete forms of paralysis, had obtained complete spontaneous recovery in 93-98 %of cases.

Long-term complications may occur just after facial nerve paralysis which include synkinesis, crocodile tear syndrome and seldom facial spasm.

2. **External palpebral weights**

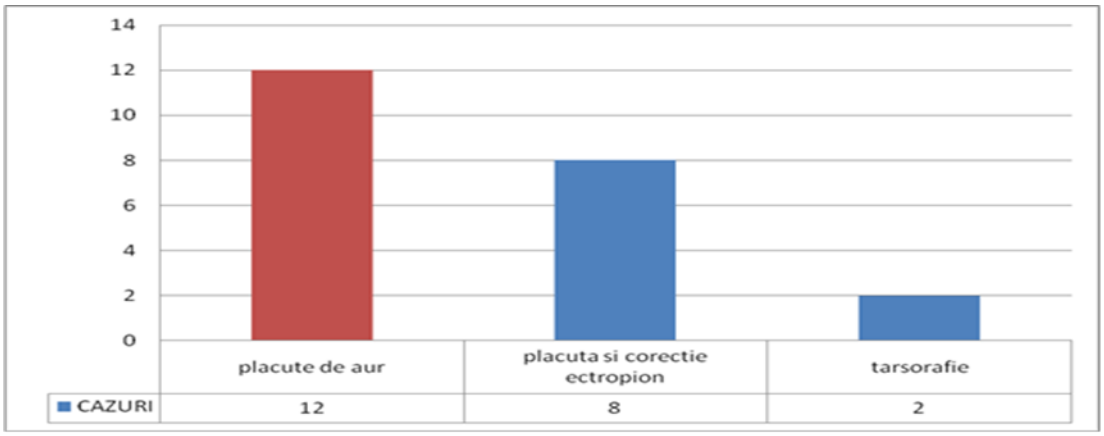
Temporary treatment with external palpebral weights was assessed by Seiff and co. and had been shown to be effective in most cases.

These weights work by passive eyelid closure and supports patient's less frequent use of artificial tears and ointments. They are proven to be effective in management of paralysis with short term recovery and were used over much more extensive periods in some cases. They are also affective as a temporary treatment method until temporary surgery.

External palpebral weights was a therapeutic option in 5 of the studied cases.

3. **Surgery**

In 22 of the studied cases of exposure keratopathy and paralytic lagophtalmos, the degree of corneal damage and anticipated functional recovery required surgery as a management method.



Surgical techniques

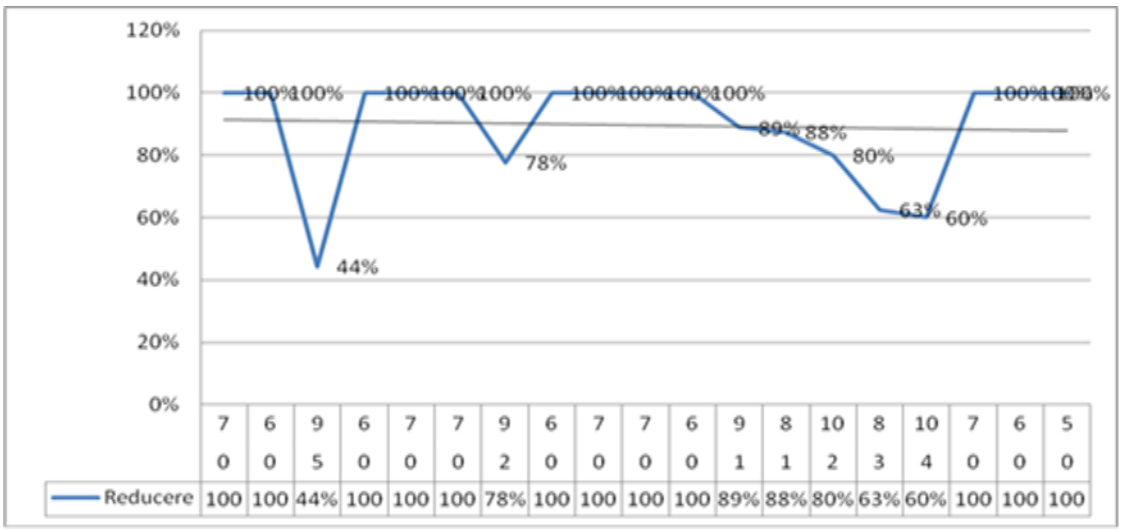
The implantation of gold weight in the upper eyelid was the preferred surgical technique in managing exposure keratopathy ,accentuated paralytic lagophtalmos with the perspective of recovery, being conducted in 20 of the studied cases together with the correction of the paralytic ectropion in 8 cases.

The concept of weight implantation in the upper lid was first introduced in 1950.

It is a relatively easy technique to perform which has a low rate of complications and is effective both in the initial stages as well as in the advanced facial palsy and is completely reversible if functional recovery of facial nerve is obtained.

The weights were individually manufactured in 24 karat gold by a local jeweler. Implanted weights varied between 1.2 and 1.6 grams.

The success of surgery was estimated on the measurement of lagophtalmos in millimeters one month post-op. The results were compared to the results obtained preop, aiming as a criteria for successful intervention to reduce the degree of lagophtalmos by 50%.None of the presented cases showed overcorrection one month post-op, which was by the absence of ptosis for more than 2 millimeters.



Reduction of lagophthalmos

Statistical regression	
Multiple R	**0,772218**
R Square	0,59632
Adjusted R Square	0,572574
Standard error	0,955166
Observations	19

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	22,91125	22,91124871	25,11258	**0,000107031**

Residual	17	15,5098	0,912341407
Total	18	38,42105	

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95,0%*	*Upper 95,0%*
Intercept	6,676471	0,259006	25,77731634	4,57E-15	6,130016437	7,222925	6,130016	7,222925
Reduction	0,730392	0,145751	5,011245588	**0,000107**	0,422885229	1,037899	0,422885	1,037899

A significant positive parallel is highlighted between the degree of post-op lagophtalmos by Pearson coefficient r= 0,772218 and p= 0,000107031 which is <0.05 and which rejects the null hypothesis that assumes the existence of statistical significance.

All patients with gold weight implant which were included in our study had had a positive development .There were no infectious complications, migration or extrusions. Only one case required explanation due to complete functional recovery 3 months post-op.

In eight cases, surgical correction of paralythic ectropion was carried out simultaneously with the gold weight implantation, using Duverger modified technique in all cases.

There were no intraoperative complications in any cases such as bleeding or post-op infection, wound dehiscence, or persistence of ectropion.

All patients with gold weight implant were immediately evaluated after surgery from one month to a year.

Post-op outcome was evaluated as satisfactory after gold weight implant after the patients were questioned regarding the persistence of pain symptoms, ocular redness, tearing degree, cosmetic appearance.

Management of keratopathy determined by thyroid ophtalmopathy

The management of patients with thyroid ophtalmopathy aimed at managing acute inflammatory phase, stabilizing the lacrimal film and the management of upper limbic keratoconjunctivitis.

In the inflammatory stage with congestive exophtalmia, all patients received medical treatment with systemic corticosteroids administered orally and gastric protection.

Stabilization of the tear film is essential for the protection of the ocular surface in patients with thyroid ophtalmopathy. All patients included in our study received topical treatment with lubricants such as artificial tears instilled frequently during the day and overnight application of ointments.

Superior limbic keratoconjuctivitis management included frequent artificial tears instillation and corneal lubricants.

All patients had a positive evolution after topical and systemic treatment with the remission of inflammatory phenomena. Patients were monitored regularly both ophthalmic and endocrinologic.

Exposure keratopathy management associated with senile ectropion

In 6 of all studied cases, exposure keratopathy was secondary to senile, involutional ectropion, which is considered to be the main clinical form of presentation of ectropion.

Patients with involutional ectropion and exposure kerathopathy received conservative treatment with artificial tears and corneal lubricants.

Surgery of ectropion was performed in all cases due to chronic ocular surface irritation despite topical treatment, the presence of exposure keratopathy , hiperlacrimation due to lacrimal punctum eversion in some cases or reflex in others due to the chronic irritation of the ocular surface.

Postoperative results were positive in all cases, there were no intraoperative or postoperative complications, no residual ectropion with adequate coverage of the ocular surface.

Conclusions :

1. Exposure keratopathy is a clinical diagnosis, based on the patient's history,the data provided by ophthalmologic examination. It is a condition which left untreated can lead to complications threatening the visual function.

2. Management of exposure keratopathy should be individualized for each patient and should consider the underlying cause, the anticipated length of recovery, the degree of lagophtalmos and the function of the orbicularis,the patient's age ,the presence of Bell's palsy, corneal sensitivity.

3. The causes of exposure keratopathy vary, the most common cause of the studied group was facial nerve paralysis of different etiology with the predominance of Bell's palsy,eyelid malformations. These were expressed in the studied group by senile ectropion and some cases of thyroid opthalmopathy.

4. A great variety of techniques can be used to protect the ocular surface, both conservative and surgical depending on the gravity of exposure keratopathy and its main cause.

5. Cases of light degree of exposure keratopathy received only conservative treatment, protector of ocular surface and consisted of frequent instillation of artificial tears during the day, corneal lubricants, ointments at night and topical antibiotics.

6. External eyelid weights represented an effective nonsurgical treatment in cases were function recovery was anticipated in the short but also an adjunct therapy conservative treatment until the moment of surgery in other cases ,as it is an easier and more comfortable for patients lowering the frequency of topical treatment use.

7. Cases of severe exposure keratopathy and persistent lagophtalmos in which functional recovery was not anticipated in short term, benefited from surgery, static procedures as gold weight implant on the upper lid , tarsorrhaphies and corrective surgery for ectropion were performed.

8. Implant of gold weights on the upper eye lid was the preferred method for patients who required surgery, a relatively easy technique to use, using local anesthesia. It is reversible, it causes a reduction in the degree of lagophtalmos ensuring adequate protection of the corneal surface, and was devoid of complications within the studied group.

9. Implant of gold weights in the upper lid improved subjective symptoms which decreased frequency of topic treatment administration. It increased the satisfaction of patients regarding eyelid closure during the day and during the night, also giving a satisfactory cosmetic appearance.

10. Tarsorrhaphy is an effective therapeutic method, ensuring adequate protection of the cornea, but with little usage because of the poor cosmetics and limited field of vision.

11. Surgery correction for paralytic ectropion,through Duverger modified method was successfully used as an adjuvant and simultaneous method to gold weight implant in some cases, improving postop outcome.

12. Management of thyroid opthalmopathy aimed the stabilization of the tear film, increasing ocular surface lubrication, topical control of inflammation for protecting the tear film from excessive evaporation and protecting the cornea., in association with systemic corticosteroid treatment.

13. Surgical correction of the involutional ectropion using Kunt- Szymanovski method was found to be effective in protecting the eye surface in all cases of exposure keratopathy due to this type of eyelid malposition.

BIBLIOGRAPHY

1. Fatemeh Rajaii, MD, PhD, and Christina Prescott, MD, PhD. Management of Exposure Keratopathy; EyeNet Magazine; April 2014

2. Dumitrache Marieta, Tratat de oftalmologie, vol I,II,III , Editura universitara Carol Davila 2012

3. De Neil J. Friedman,Peter K. Kaiser. Essentials of Ophthalmology ; Pg. 180

4. Michael Giese, OD, FAAO . Revisiting Exposure Keratopathy; NorthWest Eye Surgeons; April 2015

5. Jimmy D. Bartlett,Siret D. Jaanus. Clinical Ocular Pharmacology. Pg. 508

6. Khurana. Ophthalmology. Pg.130

7. Ahmed E. Comprehensive Manual of Ophthalmology. Pg. 185

8. Joana Portelinha , Maria Picoto Passarinho, João Marques Costa. Neuro-ophthalmological approach to facial nerve palsy. Saudi Journal of Ophthalmology (2015) 29, 39–47

9. Rahman I, Sadiq SA. Ophthalmic management of facial nerve palsy: a review. Surv Ophthalmol 2007;52(2):121–44

10.Dumitrache Marieta, Neurooftalmologie, Editura universitara Carol Davila 2013, Pg 193-222

11. Colbert S, Coombes D, Godden D, Cascarini L, Kerawala C, Brennan PA. How do I manage an acute injury to the facial nerve? Br J Oral Maxillofac Surg 2014;52(1):67–71

12. Lee V, Currie Z, Collin JR. Ophthalmic management of facial nerve palsy. Eye (Lond) 2004;18(12):1225–34.

13. Mavrikakis I. Facial nerve palsy: anatomy, etiology, evaluation, and management. Orbit 2008;27(6):466–74.

14. McAllister K, Walker D, Donnan PT, Swan I. Surgical interventions for the early management of Bell's palsy. Cochrane Database Syst Rev 2013;10:CD007468

15. Murakami S, Mizobuchi M, Nakashiro Y, Doi T, Hato N, Yanagihara N. Bell palsy and herpes simplex virus: identification of viral DNA in endoneurial fluid and muscle. Ann Intern Med 1996;124(1 Pt):27–30.

16. Murai A, Kariya S, Tamura K, Doi A, Kozakura K, Okano M, et al. The facial nerve canal in patients with Bell's palsy: an investigation by high-resolution computed tomography with multiplanar reconstruction. Eur Arch Otorhinolaryngol 2013; 270(7):2035–8.

17. Zandian A, Osiro S, Hudson R, Ali IM, Matusz P, Tubbs SR, et al. The neurologist's dilemma: a comprehensive clinical review of Bell's palsy, with emphasis on current management trends. Med Sci Monit 2014;20(20):83–90

18. Kim C, Lelli Jr GJ. Current considerations in the management of facial nerve palsy. Curr Opin Ophthalmol 2013; 24(5):478–83.

19. James DG. All that palsies is not Bell's. J R Soc Med 1996; 89(4):184–7.

20. Scott D. Lawrence, MD, and Carrie L. Morris, MD. Lagophthalmos Evaluation and Treatment. EyeNet Magazine april 2008

21. Yash Shah. Thyroid Ophthalmopathy. Supplement to Japi, January 2011, vol. 59

22. Ing E, Abuhaleeqa K. Graves' Ophthalmopathy (thyroid-associated orbitopathy). Clinical and Surgical Ophthalmology 2007; 25:386-92

23. Rajat Maheshwari and Ezekiel Weis. Thyroid associated orbitopathy. Indian J Ophthalmol. 2012 Mar-Apr; 60(2): 87–93

24. Rootman J. A Multidisciplinary Approach. Hagerstown: Lippincott Williams and Wilkins; 2003. Diseases of the Orbit.

25. Bartley GB, Fatourechi V, Kadrmas EF, Jacobsen SJ, Ilstrup DM, Garrity JA, et al. The incidence of Graves' ophthalmopathy in Olmsted County, Minnesota. Am J Ophthalmol. 1995; 120:511–7. [PubMed]

26. Wiersinga WM, Bartalena L. Epidemiology and prevention of Graves' ophthalmopathy. Thyroid. 2002; 12:855–60. [PubMed]

27. Tellez M, Cooper J, Edmonds C. Graves' ophthalmopathy in relation to cigarette smoking and ethnic origin. Clin Endocrinol (Oxf) 1992; 36:291–4. [PubMed]

28. Garrity JA, Bahn RS. Pathogenesis of graves ophthalmopathy: Implications for prediction, prevention, and treatment. Am J Ophthalmol. 2006; 142:147–53 [PubMed]

29. Wiersinga WM, Kahaly GJ.Graves orbitopathy: A multidisciplinary approach. Basel: Karger; 2007.

30. Rajendram R, Bunce C, Adams GG, Dayan CM, Rose GE. Smoking and strabismus surgery in patients with thyroid eye disease. Ophthalmology. 2011 Dec. 118(12):2493-7. [Medline].

31. Krassas GE, Wiersinga W. Smoking and autoimmune thyroid disease: The plot thickens. Eur J Endocrinol. 2006;154:777–80. [PubMed]

32. Brix TH, Kyvik KO, Christensen K, Hegedus L. Evidence for a major role of heredity in Graves' disease: A population-based study of two Danish twin cohorts. J Clin Endocrinol Metab. 2001;86:930–4. [PubMed]

33. Lee HB, Rodgers IR, Woog JJ. Evaluation and management of Graves' orbitopathy. (6).Otolaryngol Clin North Am. 2006;39:923–42. [PubMed]

34. Bartley GB, Fatourechi V, Kadrmas EF, Jacobsen SJ, Ilstrup DM, Garrity JA, et al. Clinical features of Graves' ophthalmopathy in an incidence cohort. Am J Ophthalmol. 1996;121:284–90. [PubMed]

35. Frueh BR, Musch DC, Garber FW. Lid retraction and levator aponeurosis defects in Graves' eye disease. Ophthalmic Surg. 1986;17:216–20. [PubMed]

36. Neigel JM, Rootman J, Belkin RI, Nugent RA, Drance SM, Beattie CW, et al. Dysthyroid optic neuropathy. The crowded orbital apex syndrome. Ophthalmology. 1988;95:1515–21. [PubMed]

37. Saks ND, Burnstine MA, Putterman AM. Glabellar rhytids in thyroid-associated orbitopathy. Ophthal Plast Reconstr Surg. 2001;17:91–5. [PubMed]

38. A Grixti, M Sadri & MT Watts 2013, 'Corneal Protection during General Anesthesia for Nonocular Surgery', The Ocular Surface, vol. 11, no. 2, pp. 109-18

39. S Contractor & JG Hardman 2006, 'Injury During Anaesthesia', Continuing Education in Anaesthesia, Critical Care & Pain, vol. 6, no. 2, pp. 67-70

40. VK Grover, KV Kumar, S Sharma & SP Grewal 1998, 'Comparison of Methods of Eye Protection under General Anaesthesia', Canadian Journal of Anesthesia, vol. 45, no. 6, pp. 575-7

41. PN Nair & E White 2014, 'Care of the Eye During Anaesthesia and Intensive Care', Anaesthesia and Intensive Care Medicine, vol. 15, no. 1, pp. 40-43

42. E White 2004, 'Care of the eye during anaesthesia', Anaesthesia and Intensive Care Medicine, vol. 5, pp. 302-3

43. Hernandez EV, Mannis MJ: Superficial keratopathy in intensive care unit patients. Am J Ophthalmol 1997; 2:212-216

44. Mercieca F, Suresh P, Morton A, et al: Ocular surface disease in intensive care unit patients. Eye 1999; 13:231-236

45. Ezra DG, Healy M, Coombes A. Assessment of corneal epitheliopathy in the critically ill. Intensive Care Med 2005; 31:313

46. Maurice DM: The Von Sallmann Lecture 1996: An ophthalmological explanation of REM sleep. Exp Eye Res 1996; 66:139-145

47. Ommeslag D, Colardyn F, De Laey JJ: Eye infections caused by respiratory pathogens in mechanically ventilated patients. Crit Care Med 1987; 15:80-81

48. Cunningham C, Gould D: Eye care for the sedated patient undergoing mechanical ventilation: The use of evidence-based care. Int J Nurs Stud 1998; 35(1-2):32-40

49. Maurice DM: The Von Sallmann Lecture 1996: An ophthalmological explanation of REM sleep. Exp Eye Res 1996; 66:139-145

50. Jamie B. Rosenberg, MD; Lewis A. Eisen, MD; Eye Care in the Intensive Care Unit: Narrative Review and Meta-analysis; Crit Care Med. 2008;36(12):3151-3155.

51. V. C. Reddy, S. V. Patel, D. O. Hodge, and J. A. Leavitt, "Corneal sensitivity, blink rate, and corneal nerve density in progressive supranuclear palsy and parkinson disease," Cornea, vol. 32, no. 5, pp. 631–635, 2013

52. A. Labbé, Q. Liang, Z. Wang, et al., "Corneal nerve structure and function in patients with non-sjögren dry eye: clinical correlations," Investigative Ophthalmology & Visual Science, vol. 54, no. 8, pp. 5144–5150, 2013

53. Anushree Sharma and Holly B. Hindman ; Aging: A Predisposition to Dry Eyes; Journal of Ophthalmology Volume 2014 (2014)

54. Muddappa T M, Srinivasa Rao P N. Ocular tetanus. Indian J Ophthalmol 1982;30:163-5

55.Pereira MV, Gloria AL. Lagophthalmos. Semin. Ophthalmol. 2010 May; 25(3):72-8

56. Robinson C, Tantri A, Shriver E, Oetting T. Temporary eyelid closure appliqué. Arch Ophthalmol. 2006; 124(4):546-549.

57. Yücel OE, Artürk N. Botulinum toxin-A-induced protective ptosis in the treatment of lagophthalmos associated with facial paralysis. Ophthal Plast Reconstr Surg. 2012 Jul-Aug;28(4):256-60

58. K Boboridis, NG Ziakas, C Bunce, N Georgiadis, NT Stangos; Management Of Lagophthalmos In Facial Nerve Palsy With Botulinum Toxin . Invest. Ophthalmol., 2002, volume 43, issue 13

59. M. P. Gavin, E. G. Kemp & C. M. Kirkness. Botulinum toxin-A in the management of paralytic lagophthalmos; Orbit,1995 volume 14 issue4

60. Ellis MF, Daniell M. An evaluation of the safety and efficacy of botulinum toxin type A (BOTOX) when used to produce a protective ptosis. Clin Experiment Ophthalmol. 2001:394-399.

61. Mancini R, Taban M, Lowinger A, Nakra T, Tsirbas A, Douglas RS, Shorr N, Goldberg RA. Use of hyaluronic acid gel in the management of paralytic lagophthalmos: the hyaluronic acid gel "gold weight". Ophthal Plast Reconstr Surg. 2009;25(1):23-6.

62. Alan Kahana, Mark J Lucarelli : Tarsorraphy and lacrimal occlusion. Cornealsurg. ; 2008 Chap 29

63. Schmitzer S, Pop M, Ungureanu R, Chiţac F. Lagoftalmia Paralitică, Metode De Tratament. Oftalmologia. 2004; 48(2): 62-4

64. Ghid de neuro-oftalmologie. Adriana Stănilă, Ioan Ştefan Florian, 2007, pg 116

65. Muller-Jensen K. Lid load operation in facial palsy. Indian J Ophthalmol 1994; 42:153-6

66. C. C. Ciocan – Pendefunda, Carmen Vicol, Eugenia Popescu, V. V. Costan. Tratamentul chirurgical al lagoftalmiei paralitice postparotidectomie. Jurnalul de Chirurgie, Iaşi, 2011, Vol. 7, Nr. 2

67. Schrom T. Lidloading in facial palsy. Laryngorhinootologie. 2007 Sep;86(9):634-8

68. . Berghaus A, Neumann K, Schrom T. The platinum chain: A new upper lid implant for facial paralysis. Arch. Facial Plast. Surg. 2003; 5(2): 166-170

69. Baheerathan N, Ethunandan M, Ilankovan V. Gold weight implants in the management of paralytic lagophthalmos. Int J Oral Maxillofac Surg. 2009 Jun;38(6):632-6

70. El Shazly M, Guindi S. Static management of lagophthalmos following facial nerve paralysis using standardized weights. Rev Laryngol Otol Rhinol (Bord). 2008;129(4-5):263-6.

71. Jayashankar N, Morwani KP, Shaan MJ, Bhatia SR, Patil KT. Customized gold weight eyelid implantation in paralytic lagophthalmos. J Laryngol Otol. 2008 Oct;122(10):1088-91

72. Aggarwal E, Naik MN, Honavar SG. Effectiveness of the gold weight trial procedure in predicting the ideal weight for lid loading in facial palsy: a prospective study. Am J Ophthalomol 2007 Jun; 143(6): 1009-1012

73. Tuna SH, Gumus HO, Hersek N. Custom-made Gold Implant for Management of Lagophthalmos: A Case Report. Eur J Dent. 2008; 2(4): 294-8

74. Dinces EA, Mauriello JA Jr, Kwartler JA, Franklin M. Complications of gold weight eyelid implants for treatment of fifth and seventh nerve paralysis. . Laryngoscope. 1997 Dec;107(12 Pt 1):1617-22.

75. Preeti J. Thyparampil; Seongmu Lee; Michael Yen. Outcomes And Complications Of Eyelid Gold Weight Implantation For Facial Paralysis. IOVS, march 2012,volume 53, issue 14

76. Pickford MA, Scamp T, Harrison DH: Morbidity after gold weight insertion into the upper eyelid in facial palsy. Br J Plast Surg 1992;45:460-464.

77. Seigel RJ. Palatal grafts for eyelid reconstruction. Plast Reconstruct Surg 1985; 76: 411–414.

78. Anderson RL, Gordy DD. The tarsal strip procedure. Arch Ophthalmol 1979; 97: 2192–2196

79. Gunter JP, Hackney FL, Hester Jr TR, Codner MA, Paul MD. Evolution of the lateral canthoplasty. Techniques and indications. Plast Reconstruct Surg 1997; 100: 1396–1408.

80. Hassan AS, Frueh BR, Elner VM: Müllerectomy for upper eyelid retraction and lagophthalmos due to facial nerve palsy. Arch Ophthalmol 2005; 123:1221-1225

81. Krassas GE, Heufelder AE. Immunosuppressive therapy in patients with thyroid eye disease: an overview of current concepts. Eur J Endocrinol 2001;144:311-8.

82. Bartalena L, Tanda L. Immunotherapy for Graves' orbitopathy: easy enthusiasm but let's keep trying. J Endocrinol Invest 2006;29:1012-6.

83. Tanikawa T, Okada Y, Tanaka Y. Inravenous cyclophosphamide pulse therapy is effective for refactory Graves' ophthalmopathy. J Uoeh 2006;28:185-91.

84. Wakelkamp IM, et al. Orbital Irradiation for Graves' Ophthalmopathy: Is it Safe? A Long Term Follow Up Study Ophthalmology 2004;111:1557-62

85. Hohman MH, Hadlock TA. Etiology, diagnosis, and management of facial palsy: 2000 patients at a facial nerve center. Laryngoscope 2014; 124(7):E283–93.

86. Adour KK, Byl FM, Hilsinger Jr RL, et al. The true nature of Bell's palsy: analysis of 1,000 consecutive patients. Laryngoscope 1978; 88:787–801.

87. El Tallawy HN, Farghaly WM, Abo-Elfetoh N, et al. Epidemiology of Bell's palsy in Al-Kharga district, New Valley, Egypt. Neurol Res 2013; 35:663–70.

88. Arie Y. Nemet , Shlomo Vinker. Considerations and complications after Bells' palsy. Journal of Clinical Neuroscience 22 (2015) 1949–1953

89. Rowhani-Rahbar A, Baxter R, Rasgon B, et al. Epidemiologic and clinical features of Bell's palsy among children in Northern California.Neuroepidemiology 2012;38:252–8.

90. Peitersen E. Bell's palsy: the spontaneous course of 2,500 peripheral facial nerve palsies of different etiologies. Acta Otolaryngol Suppl 2002; 549: 4–30.

91 Zandian A, Osiro S, Hudson R, Ali IM, Matusz P, Tubbs SR, et al. The neurologist's dilemma: a comprehensive clinical review of Bell's palsy,with emphasis on current management trends. Med Sci Monit 2014;20(20):83–90.

92. Devriese PP, Schumacher T, Scheide A, et al: Incidence,prognosis and recovery of Bell's palsy. A survey of about1000 patients (1974--1983). Clin Otolaryngol Allied Sci 15:15--27, 1990

93. Prescott CA: Idiopathic facial nerve palsy (the effect of treatment with steroids). J Laryngol Otol 102:403--7, 1988

94. Matthies C, Samii M. Management of 1000 vestibular schwannomas (acoustic neuromas): clinical presentation. Neurosurgery 1997;40(1):1–9, Discussion 9–10.

95. Rinaldi V, Casale M, Bressi F, Potena M, Vesperini E, De Franco A,et al. Facial nerve outcome after vestibular schwannoma surgery: our experience. J Neurol Surg B Skull Base 2012;73(1):21–7.

96. Bartley GB, Fatourechi V, Kadrmas EF, et al. Clinical features of Graves' ophthalmopathy in an incidence cohort. Am J Ophthalmol 1996;121:284-90

97. Bartley GB, Fatourechi V, Kadramas EF et al. Long-term follow-up of Graves' ophthalmopathy in an incidence cohort. Ophthalmology 1996;103:958-62

98. Damasceno RW1, Osaki MH, Dantas PE, Belfort R Jr. Involutional entropion and ectropion of the lower eyelid: prevalence and associated risk factors in the elderly population. Ophthal Plast Reconstr Surg. 2011 Sep-Oct;27(5):317-20

99. Mavrikakis I. Facial nerve palsy: anatomy, etiology, evaluation, and management. Orbit 2008;27(6):466–74

100. Gire A, Kwok A, Marx DP. PROSE treatment for lagophthalmos and exposure keratopathy. Ophthal Plast Reconstr Surg 2013;29(2):e38–40.

101. Weyns M, Koppen C, Tassignon MJ. Scleral contact lenses as an alternative to tarsorrhaphy for the long-term management of combined exposure and neurotrophic keratopathy. Cornea 2013;32(3):359–61.

102. Prell J, Rampp S, Rachinger J, Scheller C, Alfieri A, Marquardt L, et al. Botulinum toxin for temporary corneal protection after surgery for vestibular schwannoma. J Neurosurg 2011;114(2):426–31.

103. Zandian A, Osiro S, Hudson R, Ali IM, Matusz P, Tubbs SR, et al. The

neurologist's dilemma: a comprehensive clinical review of Bell's palsy,with emphasis on current management trends. Med Sci Monit 2014;20(20):83–90.

104. Yamamoto E, Nishimura H, Hirono Y. Occurrence of sequelae in Bell's

palsy. Acta Otolaryngol Suppl 1988;446:93–6.

105. Seiff SR, Boerner M, Carter SR. Treatment of facial palsies with external eyelid weights. Am J Ophthalmol 1995;120:652-7.

106. Orin M. Zwick, M.D., and Stuart R. Seiff, M.D. Supportive care of facial nerve palsy with temporary external eyelid weights.Optometry (2006)77,340-342

107. Sheehan JD: Progress in correction with facial palsy with tantalum wire and mesh. Surgery 27:122--9, 1950

108. Abell KM, Baker RS, Cowen DE, et al: Efficacy of gold weight implants in facial nerve palsy: quantitative alterations in blinking. Vision Res 38:3019--23, 1998

109. Smellie GD: Restoration of the blinking reflex in facial palsy by a simple lid-load operation. Br J Plast Surg 19:279--83, 1966

110. Snyder MC, Johnson PJ, Moore GF,Ogren FP. Early versus late gold weight

implantation for rehabilitation of the paralyzed eyelid. Laryngoscope 2001:111: 2109–2113

111. Choo PH, Carter SR, Seiff SR. Upper eyelid gold weight implantation in

The Asian patient with facial paralysis. Plast Reconstr Surg 2000: 105: 855–

859.

112. Jobe R: The use of gold weights in the upper lid. Br J Plast Surg 46:343, 1993

113. Rofagha S, Seiff SR. Long term results for the use of gold eyelid load weights in the management of facial palsy. Plast Reconstr Surg 2010; 125: 142

114. Lessa S, Nanci M, Sebastiá R, Flores E: Treatment of paralytic lagophthalmos with gold weight implants covered by levator aponeurosis. Ophthal Plast Reconstr Surg 2009; 25:189-193.

115. Egemen O, Ozkaya O, Uscetin I, Akan M: Covering the gold weight with fascia lata graft in paralytic lagophthalmos patients Br J Oral Maxillofac Surg 2012; 50:369-372.

116. Silver AL, Lindsay RW, Cheney ML, et al. Thin-profile platinum eyelid weighting: a superior option in the paralyzed eye. Plast Reconstr Surg 2009; 123 :1697

117. Schrom T, Goldhahn A, Berghaus A. The use of gold weight in facial palsy lagophthalmos. Eur J Plast. Surg.2000; 23:72-77

118. Berghaus A Neumann K, Schrom T. The platinum chain: a new upper-lid implant for facial palsy. Arch Facial Plast Surg. 2003 Mar-Apr; 5(2):166-70.

119. Ahmet Sonmez, Nurdan Ozturk, Nihal Durmusx , Mehmet Bayramicli, Ayhan Numanoglu. Patients' perspectives on the ocular symptoms of facial paralysis after gold weight implantation. Journal of Plastic, Reconstructive & Aesthetic Surgery (2008) 61, 1065-1068

120. Bordaberry M, Marques DL, Pereira-Lima JC, et al. Repeated peribulbar injections of triamcinolone acetonide: a successful and safe treatment for moderate to severe Graves' ophthalmopathy.Acta Ophthalmol 2009;87 :58-64

121. Holly FJ, Lamberts DW. Effect of nonisotonic solutions on tear film osmolality. Invest Ophthalmol Vis Sci 1981; 20 :236-45

122. Gupta A, Sadeghi PB, Akpek EK. Occult thyroid eye disease in patients presenting with dry eye symptoms. Am J Ophthalmol 2009; 147 : 919-23

123. Kabat AG. Lacrimal occlusion therapy for the treatment of superior limbic keratoconjunctivitis. Optom Vis Sci 1998; 75:714-8

124. Passons GA, Wood TO. Conjunctival resection for superior limbic keratoconjunctivitis. Ophthalmology 1984; 91:966-8