Role of oral corticosteroids with adjunct to intravenous antibiotics in treatment of orbital cellulitis

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ABSTRACT

Introduction: The standard treatment protocol of orbital cellulitis includes the use of broad-spectrum intravenous antibiotics. This study was done to evaluate the role of oral corticosteroids in the treatment of orbital cellulitis in order to address the inflammatory component. **Methods:** A prospective comparative interventional study was carried out on 17 cases of orbital cellulitis over 16 months. All the patients were treated with intravenous antibiotics and were allotted to Group A or B. The former consisted of eight cases (intravenous antibiotics) while group B consisted of nine cases (intravenous antibiotics and oral corticosteroids). The oral corticosteroids were started after 24 to 48 hours of initiation of antibiotics. The outcomes compared between the two groups were hospital stay, visual analogue score, temperature, peri-orbital edema, proptosis, visual acuity, extra-ocular movement and conjunctival chemosis. **Results:** The age of the participants ranged from 7 to 77 years with M:F = 6:11. The mean duration of hospital stay was 7.75±2.7 and 8.22± 2.53 days in group A and B. The result showed that the changes in the other parameters were significant on the 3rd day after starting treatment in both groups but insignificant between the groups at the end of 7th and 14th day. **Conclusions:** In our study, addition of oral corticosteroids to intravenous antibiotics showed no added beneficial effect over the use of intravenous antibiotics alone in the treatment of orbital cellulitis. However, it was noted that there was no further deterioration of the disease with the use of steroids.

Keywords: Intravenous antibiotics, oral steroids, orbital cellulitis.

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INTRODUCTION

Orbital cellulitis is one of the common diseases encountered by the ophthalmologist in day to day practice. It can occur after trauma, surgery, septicemia (hematogenous spread), extension of infection from adjacent ocular and adnexal structures such as dacryocystistis, endophthalmitis, preseptal cellulitis etc.[1,2] Dental infections can also be a cause for this disease.[3] The common causative organisms are Hemophillus influenza, Staphylococcus and Streptococcus.

This disease can occur in all the age group irrespective of gender, the children being more commonly affected. It can lead to visual threatening condition like optic neuropathy and life threatening conditions such as encephalomeningitis, cavernous sinus thrombosis, sepsis and intracranial abscess formation.[4-7] The primary management strategy is the use of broad spectrum intravenous antibiotics based on empiric coverage of most common causative organisms and surgical drainage in the non-resolving cases or wherever needed.

Use of steroids under coverage of antibiotics, still controversial, has shown faster recovery and decreased complications.[7-9] Only few studies have been conducted worldwide and they have shown

that regardless the improvement, there has rarely been an adverse effect with its use. Vancomycin is the first line agent for treatment of the disease. To provide broader spectrum coverage, cefotaxime and metronidazole or clindamycin are typically administered. In case of penicillin allergic patients, vancomycin is given along with fluroquinolone. The introduction of intravenous corticosteroids in orbital cellulitis is still controversial as it may suppress the immune system and worsen the disease. One of the pathogenesis of orbital cellulitis is aggressive inflammation. Use of steroids in orbital cellulitis is to decrease the inflammatory component of the disease and prevent further deterioration from the disease process itself and to recover faster. Not much information has been published regarding this. Thus, the use of corticosteroids may prove to be of beneficial effect halting the inflammatory process and further deterioration of the disease.

Therefore the present study was undertaken to evaluate the effect of oral corticosteroids with adjunct to antibiotics in the treatment of orbital cellulitis. Early diagnosis and prompt treatment of orbital cellulitis are of utmost importance for early recovery and to prevent the dreadful complications.

METHODS

This was a prospective comparative interventional, single-masked study conducted on all the admitted patients in BPKIHS with diagnosis of orbital cellulitis over a 16 months period. The exclusion criteria included subjects not willing to participate in the study, suspected fungal or tubercular infections, cases not responding to standard treatment of intravenous antibiotics, pregnancy and lactating mothers. A total of 20 patients were admitted with diagnosis of orbital cellulitis but only 17 cases fitted with inclusion criteria were taken into the study. After taking informed consent, the detailed clinical history was taken and ocular examination was done as the structured proforma. History related to duration of disease, fever, upper respiratory tract infection, lacrimal outflow obstruction, sinusitis or trauma was queried. The symptoms included pain, redness and swelling of periorbital region. The signs included one or more of the following according to the severity of the disease: conjunctival chemosis, proptosis, ophthalmoplegia and/or loss of vision. Pupillary reactions in the all the patients were normally reactive. The absence of Relative afferent pupillary defect (RAPD) ruled out any involvement of the optic nerve. With an accurate history and clinical examination, ancillary investigations was done which included mainly complete blood count (CBC), pus (conjunctival and follicles whenever present) and blood cultures and orbital ultrasonography. However, the initiation of treatment for suspected orbital cellulitis was not delayed awaiting for these reports.

The diagnosis of orbital cellulitis was done on the basis of the clinical features and the laboratory investigations. Computed tomography (CT) Scan/ Magnetic resonance imaging (MRI) was done to support the findings of orbital cellulitis, to see its type and to rule out other mimicking pathology like pseudotumors, intraocular/ intraorbital tumors, non-infectious conditions etc. and also to look for any complications due to orbital cellulitis. IRC was obtained from Institutional review board, BPKIHS, Dharan, Nepal (code no: IRC/501) and is in accordance to declaration of Helsinki.

Twenty patients diagnosed as orbital cellulitis were included in the study by purposive sampling method. Initially combination of vancomycin and ceftazidime were administered intravenously to all the selected cases. Injection of vancomycin was given at the dose of 40 mg/kg body weight twice daily in adults and 10 mg/kg body weight twice daily in patients ≤18 years of age. Injection of ceftazidime was given at the dose of 100 mg/kg body weight twice daily. All the patients were observed for 24 hours after administration of antibiotics. Among these 20 patients, three patients showed deterioration of symptoms at 48 hours and were excluded from the study. In those three patients, blood culture and sensitivity with other vital tests were repeated and either antibiotics were changed or added accordingly. They showed improvement approximately after a week and were discharged after complete resolution of the disease.

Remaining 17 patients showed improvement or remained static at 24 hours of administration of antibiotics. They were randomly allotted to group A or group B by simple randomization. Cases in group A (n=8) were continued with intravenous antibiotics and those falling in group B (n=9), oral prednisolone acetate of 1 mg/kg/day was added to their treatment along with the antibiotics till their hospital stay. The outcomes of both the groups were measured and recorded in the proforma on, 3rd, 7th and 14th day of admission.

Parameters / Variables studied at each follow up:

Pain: Improvement of the pain was evaluated by using visual analogue scale (VAS). A scale was made ranging from 0 to 10 and the patients were asked to point out the value according to the severity of their pain. It ranged from no symptoms (0) to most severe symptoms (10).

Body Temperature: Body temperature was measured with a thermometer.

Vision: Best corrected visual acuity was measured by using Snellen's chart. It was graded into two: Grade 1: < 6/60 and Grade 2: > 6/60

Periorbital edema: It was graded at a scale of 0 to 4 according to Pushkar et al.[10]

Table 1: Grading of periorbital edema

Grade	Features
4	very severe swelling, very difficult to separate the eyelids
3	severe swelling, eyelids can be separated with some difficulty
2	moderate swelling, patient can separate eyelids by himself or herself
1	mild swelling, patient can easily open eyelids with no difficulty
0	no swelling

Proptosis: Proptosis was measured by Hertel's exalophthometer. The difference of the values of both eyes were calculated and was graded into mild, moderate and severe and very severe.[10] Grade 0: none, Grade 1: difference of 3 mm, Grade 2: 4-7 mm, grade 3: 8-10 mm, grade 4: difference of >10 mm. Improvement after treatment was noted down by the same procedure.

Conjunctival chemosis: It was graded at a scale of 0 to 3.[10]

Table 2: Grading of conjunctival chemosis

Grade	Features
3	conjunctival congestion with prolapsed
2	in between grade 3 and grade 1
1	minimal congestion with faintly detectable conjunctival edema
0	no chemosis

Extraocular movements: Extra ocular movement (EOM) were measured by Kestenbaum limbus test of motility.[11] Movement of the contralateral limbus was measured in superior, inferior, lateral and medial directions using a ruler and the measurement were recorded in millimeters. The values in all the directions were summed up and this was compared with the normal eye to get the percentage value of extraocular motility.

The recorded data of all the parameters of day 0, 3, 7 and 14 were analyzed using statistical package for social sciences (SPSS) 12.0. The Fischer Exact test and independent t test were applied to test the significance of variables. A p-value of <0.05 was considered significant.

RESULTS

A total of 17 patients were admitted with orbital cellulitis ranging in age from 7 to 77 years with the median age of 40 years. Male to female ratio was 6:11. All the cases had unilateral presentation of orbital cellulitis with right to left ratio of 7:10. The most common cause of orbital cellulitis in our study was paranasal sinusitis followed by dental infection and facial folliculitis (nasal area, forehead).

The difference of age, hospital stay and proptosis in group A and B are shown in table 3.

Table 3: Comparison of mean age, duration of disease, hospital stay and proptosis in group A and B

Parameters	Group A	Group B	p-value
Mean age (years)	41.38 ± 22.62	32.89 ± 26.41	0.168
Duration of disease unit	6.75 ± 2.7	9.22 ± 5.19	0.210
Hospital stay (days)	7.75 ± 2.7	8.22 ± 2.53	0.789
Proptosis (mm)	4.38 ± 2.32	5.56 ± 2.40	0.749

The visual acuity in two groups was not significant on day 0 (p=0.08) and on day 14 (p=0.124). However, the cause of decreased vision in three patients was due to globe compression due to orbital cellulitis/abscess leading to refractive error which recovered by the end of 14 days.

The change in temperature in group A and B were insignificant on day 0 and 7 with p-value of 0.984 and 0.748 respectively. At follow up on day 14, all the patients in both the groups had normal body temperature.

The different parameters recorded on day 0, 7 and 14 are shown in table 4 and 5.

Table 4: Comparison of VAS, conjunctival chemosis and periorbital edema between group A and B

Day	VAS				Conjunctival chemosis				Periorbital edema			
	Grade	Group A (8)	Group B (9)	P-value	Grade	Group A(8)	GroupB (9)	P-value	Grade	Group A(8)	GroupB (9)	P-value
0	2	1	1		0	0	1		1	2	1	
	3	3	1	0.403	1	5	4	0.708	2	3	3	0.20
	4	4	7		2	2	2		3	3	2	
					3	1	2		4	0	3	
7	2	2	0		0	1	0		1	3		
	3	4	0	0.748	1	8	1	0.750	2	6		
	4	10	1		2	3	1		3	5		
					3	3	0		4	3		

It was also observed that pain, conjunctival chemosis and periorbital edema subsided by the end of one week in all the patients irrespective of the group.

Table 5: Comparison of visual acuity, extra ocular movement and proptosis between group A and B

Day	VAS				Conjunctival chemosis				Periorbital edema			
	Grade	Group A (8)	Group B (9)	P-value	Grade	Group A(8)	GroupB (9)	P-value	Grade	Group A(8)	GroupB (9)	P-value
0	1	1	5		2	3	1		0	1	2	
	2	7	4	0.088	3	2	5	0.429	1	2	0	0.345
					4	3	3		2	3	2	
									3	2	3	
									4	0	2	
7	1	0	4		0	3			0	5	2	
	2	8	5	0.205	1	2	4	0.279	1	2	2	0.466

					2 3	2 1	4 1		2 3 4	1 0 0	3 1 1	
14	1 2	0 8	4 5	0.124	1 2	7 1	9 0	0.471	0 1	8	6 3	0.529

DISCUSSION

The results of our study showed that there was no significant difference of patient recovery at discharge regardless to the treatment done in group A and B. Even though our study did not conclude any beneficial effect of oral prednisolone as an adjunct to intravenous antibiotics, it however showed that addition of steroids did not lead to any deterioration with regard to the disease pathogenesis. At the end of two weeks, almost complete resolution was seen on all the patients regardless of the group. CT scan was done in 12 patients. The rest were not able to undergo the scan due to financial problem. Therefore, outcome of treatment methodology with the disease (Chandler's classification) could not be evaluated. Among the 12 patients, 6 of them were in stage 2 (orbital cellulitis), 4 in stage 3 (subperiosteal abscess) and 2 in stage 4 (intraorbital abscess). Our study showed that female were more than male (M:F= 6:11) which was not consistent with the study done by Nageswaran et al. where male were more than female.[12]

In this study the patients were divided into two groups A(n-8) and B(n-9) by simple randomization. In a study[10] done by Pushkar et al. patients were divided into 1:2 with 7 in group A and 14 in group B (cases treated with adjuvant oral steroids). In that study, antibiotics given were intravenous vancomycin and ceftriaxone and in suspected anaerobic cases, intravenous metronidazole was added. Patients in group two were then given oral steroids after observing improvement with intravenous antibiotics. But in our study, a combination of intravenous vancomycin and ceftazidime were given to all patients of both groups. In group B oral steroids were started after initial positive response to intravenous antibiotics which was after 24 to 48 hours. In two patients, steroids were started on day 3 and 4 respectively as there was a slow improvement in the signs and symptoms of the patients. Though the improvement in fever, pain, periorbital edema, conjunctival chemosis, proptosis, and extraocular motility was statistically not significant, no adverse effect or deterioration of any case with the use of steroids were seen.

None of the patients had recurrence or spread of infection. There was no difference in the final vision attained in both the groups. This finding was similar to other studies which have been done.[10,13]

Literature on orbital cellulitis with abscess reports that 60% of the cases require surgical drainage.[13,14] However, in our study, none of the patients required surgical drainage.

The length of the hospital stay was similar in both the groups. According to a study, the mean hospital stay for medically treated patient was six days and for surgically treated it was 11 days.[14] A study by Nwaorgu et al. showed a median of six and half days versus ten days in patients treated with or without intravenous adjuvant steroids.[14] These are dissimilar to our study in which the mean hospital stay in group A and B were 7.75±2.27 and 8.22± 2.53 days respectively which was statistically insignificant (p=0.789). The study conducted by Yen et al. found that there was a shorter hospitalization and decreased need for surgical drainage and intravenous antibiotics in patients given steroids.[13] It also concluded that the use of steroids does not adversely affect the final clinical outcomes and maybe beneficial in treatment of pediatric orbital cellulitis with subperiosteal abscess.

A study conducted by Pushkar et al. and Yen et al. showed significant faster recovery with no deterioration with the use of systemic corticosteroids.[10,13] Though our study did not show statistically significant improvement when compared, but we did observe that clinically the patients of group B had faster recovery in terms of pain, chemosis, proptosis, periorbital edema.

A retrospective study conducted by Yen et al. reviewed the use of IV steroids in pediatric patients with orbital cellulitis and subperiosteal abscess.[13] Twelve patients received IV corticosteroids and 11 did not. The group receiving steroids showed a trend toward shorter hospital stay but the results were statistically insignificant. This study strengthens the fact that the steroids did not adversely affect the clinical outcomes which is similar to our study. A prospective, comparative interventional study was done in pediatrics groups of orbital celluiltis where C-Reactive Protein was measured daily as a biomarker of inflammation and when below 4 mg/dl the patients were started on oral prednisolone 1 mg/kg per day for seven days.[15] Out of 31 children, 24 received oral steroids while seven did not. Males were more than female. Thirteen children from the group receiving steroids and two from the group not receiving steroids underwent surgical drainage. There was one case in each group of recurrence of symptoms after discharge from the hospital. At the last visit, all patients returned to their baseline ophthalmic examination.

Literatures have shown that steroids has beneficial effect in acute bacterial meningitis by reducing cerebrospinal fluid, meningeal inflammation, brainstem encephalopathy and other neurologic sequalae with no adverse effects.[16-18] It has

been given in brain abscess with positive response.[19] It has also been used in chronic sinusitis,[20] in cases of tubercular meningitis[21] and septicemia[22,23] without any adverse effect. Some studies prove that timely use of steroids probably helps in controlling the inflammation therefore reducing related morbidity.[24,25] However, the use of corticosteroids in orbital cellulitis still remains controversial. From different studies, it has been found that the timing and duration of corticosteroids should be monitored cautiously.[10]

CONCLUSIONS

The study showed additional therapy with corticosteroid did not have any effect with regard to the recovery of orbital cellulitis. However, it adds to the fact that there is no deterioration of the disease with the use of oral corticosteroids and there are no side effects of steroids during the treatment course. The limitation of the study was less sample size and outcome measurement according to grading of orbital cellulitis. More case control studies should be carried out for better results.

CONFLICTS OF INTEREST: None declared

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