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Original Article

Acyclovir and Prednisolone Combined Treatment for Bell's Palsy

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ABSTRACT

Aim: To evaluate the efficacy of acyclovir and prednisolone combination in treating patients with Idiopathic Facial Nerve Paralysis (Bell's palsy). Methods: This is a prospective study, conducted between June 2010 and February 2013 on 150 patients with Bell's palsy in Royal Medical Services hospitals in Jordan, who were treated within 7 days of the onset with a combination of acyclovir (dosage, 400 mg five times daily for 5 days) and prednisolone 1mg/kg daily. Results: Using the House-Brackmann Scale system, recovery from the palsy was defined as grade (I or II). Patients were followed until complete recovery occurred or for 6 months in cases with incomplete recovery . The rate of patient recovery in those treated with acyclovir and prednisolone (A+P) (92.5%) was significantly better ($p < 0.05$) than the rate in those treated with prednisolone alone (P) (83.7%). Conclusion: Acyclovir combined with prednisolone therapy was more effective in treating idiopathic facial nerve paralysis, than the conventional prednisolone therapy alone.

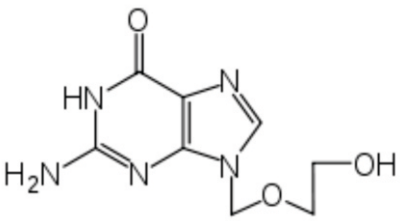
1. Introduction

Bell's palsy is found to be the most common etiology of facial nerve palsy(1), it has an estimated incidence of 11-40 cases per 100,000 people (2). Although the natural course of this disease is generally benign in that around 70% of patients show complete recovery with no sequelae (3). Treatment with corticosteroids proved its efficacy in improving the outcome of this disease; however, more than one tenth of patients failed to resume normal facial nerve function, and around 5% of those patients suffers from severe complications like residual facial paralysis, facial contracture, synkinesis and spasm (4).

Although the exact pathology of this disease is still unknown; viral pathogenesis has been postulated (5,6). advanced molecular biology investigations presented some evidences regarding the role of herpes simplex virus (HSV) infection in the etiology of the disease. In addition to that investigation of geniculate ganglia of facial nerve in human autopsy with past history of Bell's palsy also showed the presence of latent HSV genomes by polymerase chain reaction (PCR) (7,8). Also active HSV sequences have been explored in the endoneurial fluid of the facial nerve during decompressive surgery of facial nerve in patients with Bell's palsy (9). In a study conducted by Takahashi et al. (10) on mice, facial nerve paralysis was induced in 20% of them through reactivating the HSV. These results strongly suggest the role of reactivated HSV within the geniculate ganglion in the pathogenesis of idiopathic peripheral facial nerve paralysis (Bell's palsy), Which in turn suggests a role of an antiviral medications for the treatment of this disease (11).

Acyclovir, is synthetic guanosine analogue antiviral drug, its chemical name is acycloguanosine (figure 1),

Figure 1, chemical structure of acyclovir



It is the most commonly used anti viral medication and it is very active against the herpes viruses, including herpes simplex (HSV), varicella-zoster (HZV), and Epstein-Barr virus (EBV). HSV consists of a relatively large double-stranded, linear DNA genome encased within a protein called the capsid. Acycloveir is considered to be a prodrug which is converted into acyclo-guanosine monophosphate by the viral thymidine kinase , further phosphorylation takes place coverting it into the active form, acyclo-guanosine triphosphate which incorporates into viral DNA resulting in premature chain termination.

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This study was designed as a prospective trial to explore the effects of oral administration of acyclovir plus conventional prednisolone treatment on the outcome of facial palsy in patients with Idiopathic peripheral facial nerve paralysis. There was no financial interest for this study.

2. Methods

Between June 2010 and February 2013, all patients with idiopathic peripheral facial nerve paralysis attending the ophthalmology clinic at royal medical services hospitals in Jordan were enrolled in this study. All patients younger than 14 year, those who received treatment after 1 week of the disease onset, those who had already received treatment for the palsy, those who could not receive corticosteroids, those who had past history of similar attack and those with known causes for the facial palsy like trauma, tumours, or otitis media were excluded from the study,

After taking the approval of the ethical committee and the patient's consent corticosteroids in the form of prednisolone 5mg tablet was given in a dose of 1mg/kg with acyclovir (Zovirax) at 400 mg tablets 5 times daily for 5 days . Improvement was assessed using the House-Brackmann Scale system (12); this score ranges from I (normal) to VI (no movement) as shown in table 1.

Table 1. House-Brackmann Scale system

Grade	Definition
I	Normal symmetrical function in all areas
II	Slight weakness noticeable only on close inspection Complete eye closure with minimal effort Slight asymmetry of smile with maximal effort Synkinesis barely noticeable, contracture, or spasm absent
III	Obvious weakness, but not disfiguring May not be able to lift eyebrow Complete eye closure and strong but asymmetrical mouth movement with maximal effort Obvious, but not disfiguring synkinesis, mass movement or spasm
IV	Obvious disfiguring weakness Inability to lift brow Incomplete eye closure and asymmetry of mouth with maximal effort Severe synkinesis, mass movement, spasm
V	Motion barely perceptible Incomplete eye closure, slight movement corner mouth Synkinesis, contracture, and spasm usually absent
VI	No movement, loss of tone, no synkinesis, contracture, or spasm

The grading is performed by ophthalmologist aided by photographs taken during the patient each visits, all the patients were treated at the outpatient clinic and received follow-up at least once per month until complete recovery occurred or for 6 months after the paralysis.

3. Results

The mean age of the patients was 40.6 year (range 15 to 65 years), 77 of them were males with male to female ratio 1.1:1 severity of the facial palsy, the average time of starting treatment form the onset of the disease was 2.8 days, table 2 shows the outcome of assessment using the House-Brackmann Scale system at the time of attendance to the ophthalmology clinic.The most common grade found among patients was grade III followed by grade II, no patients were reported to have grade VI, at 6 months 96% of patients showed complete recovery.

Table : grades of Bell's palsy at 1,2,4 and 6 months after treatment.

Number of patients at presentation	Number of patients at 1 months	Number of patients at 2 months	Number of patients at 4 months	Number of patients at 6 months
0(0%)	7 (4.7%)	14(9.3%)	64(42.7%)	144(96%)
45(30%)	52 (34.7%)	55 (36.7%)	58(38.7%)	3(2%)
54(36%)	60 (40%)	65 (43.3%)	15(10%)	2(1`.3%)
33(22%)	21(14%)	6(4%)	5(3.3%)	1(0.6%)
18(12%)	10(7%)	10(7%)	8(5.3%)	0(0%)
0(0%)	0(0%)	0(0%)	0(0%)	0(0%)

A part from mild gastrointestinal upset in 7 patients no adverse effects were recorded. The rate of patient's recovery at 1, 2, 4 and 6 months are summarized in table 2 and the outcome at 3 and 6 months in regard to the time of starting treatment is summarized in table3.

Table 3, the grades of facial palsy in regard to the onset of starting treatment

Onset of treatment after presentation (days)	Number of patients at presentation	Number of patients at 3 months with complete recovery	Number of patients at 6 months with complete recovery
1	7	5/7(71%)	7/7(100%)
2	50	31/50(62%)	50/50(100%)
3	66	33/66(50%)	66/66(100%)
4	14	6/14(43%)	13(93%)
5	10	4/10(40%)	6/10(60%)
6	3	1/3(33%)	1/3(33%)
7	0	0(0%)	0(0%)

4. Discussion

Only few studies investigated the efficacy of anti-viral medications on the outcome of Bell's palsy; for example, a retrospective study conducted by Axelsson et al. (13) revealed a significantly better outcome in patients with Bell's palsy who were treated with valacyclovir and prednisone compared with patients receiving no medical treatment , Also Hato et al. (14) reported that the use of combined valacyclovir and prednisone was significantly more effective than the use of combined placebo and prednisone . in this study the results suggest that the combined use of antiviral agents and prednisolone is efficient. However other studies showed that there was no statistical significance regarding the outcome of using antiviral agents in treating Bell's palsy. (15, 16)

The pathophysiology of Idiopathic Facial Nerve Paralysis (Bell's palsy) may give a logic explanation regarding the use of is antiviral agents. With the primary infection, HSV most probably travel through the axons of the sensory nerves and latently infect the cells within the geniculate ganglion (17). This latent HSV infection may reactivated at any time by different factors, like physical fatigue, psychological stress, common cold, exposure to cold and dental manipulation. upon reactivation, the virus result in demyelinization of the facial motor fibers during the process of virus replication, which will result in inflammatory reaction that induces edema of the nerve and damages the nerve fibers. Acyclovir acts by preventing the replication of HSV by interfering with the DNA polymerase of the virus. Therefore, it cannot destroy or retrieve the viruses that have already replicated (18). Thus, the early administration of the antiviral agent is required to prevent progressive nerve degeneration. Given that corticosteroids are potent agents for reducing the inflammatory reaction and edema of the nerve (19), it is logical to use an antiviral agent and a corticosteroid in a combined therapy for the treatment of the disease. This study showed that early therapy with acyclovir and prednisolone resulted in a better prognosis than that resulting from therapy without acyclovir. Also it was clearly noted in our study that early treatment of Bell's palsy (within 3 days of onset) is more effective in the management of Bell' palsy , this was also noted and obtained by many studies done worldwide .for example Hato et al. (20,21)and Sullivan et al. (22) showed a significantly better outcome in the treatment of patients with Bell's palsy within 3 days of onset compared to those who received treatment after 3 days. These results suggest that combined therapy with Acyclovir and prednisolone should be recommended for early treatment, preferably within 3 days of onset of the palsy.

5. Conclusion

Acyclovir and prednisolone combination therapy was very effective in treating idiopathic facial nerve paralysis, therefore it should be recommended for early treatment, preferably within 3 days of onset of the palsy.

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