Effect Of Prednisone On Guillain-Barré Syndrome In HIV Positive Patients

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Citation

Abstract
INTRODUCTION

Neurology is one of these medical disciplines in which many frustrating results due to a lack of proper curative treatment, are seen. However to see patients in progressive recovery from a complete paralysis of their four limbs and, inability to talk, swallow, and breath spontaneously, is very stimulating.

It is commonly observed in patients with Guillain-Barré Syndrome (GBS) under early treatment with IV Immunoglobuline and/ or Plasmapheresis, but what is expected for HIV patients with GBS where these facilities are not available? The answer probable is: “depends in what stage of the AIDS these patients are” but without doubt to identify and treat this condition in an early stage will help to our patients to afford further neurological complications in better conditions.

GBS is a acute autoimmune predominant polyradiculoneuropathy with a clinical presentation of flaccid paralysis with areflexia; although hyperreflexia is a controversial symptom in patients with GBS some of them may develop functional corticospinal tract involvement, also variable sensory disturbances including a sensory variant can be seen, and an elevated cerebrospinal fluid protein without pleocytosis is almost patognomic. GBS had been viewed as a group of syndromes with several distinctive subtypes these include the principal subtype prevalent in the Western world: Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and others like: Acute motor sensory axonal neuropathy (AMSAN), Acute motor axonal neuropathy (AMAN), Fisher syndrome (FS), and Acute panautonomic neuropathy (APN), which are also characterized by a rapid symmetrical involving of the longest pathways in the periphery often preceded by an antecedent event or trigger, most frequently an infection disease such as: Group A beta-hemolytic streptococcal infection in Fisher syndrome predominantly, HIV/AIDS, cytomegalovirus(CMV), CMV-infected fibroblasts express ganglioside-like epitopes that recognize specifically anti-GM2 antibodies induced by molecular mimicry between GM2 and antigens in CMV infection; Human parvovirus B19 infection, Mycoplasma pneumoniae infection; West Nile virus infection; varicella; Haemophilus influenzae infections can elicit an AMSN or an AMAN in those patients the recovery seemed to be better than those with GBS and Campilobacter jejuni (C jejuni) infection. C jejuni is the most frequently reported antecedent infection in association with GBS; the pure motor variant of GBS accounts for 10% to 20% of all cases and is highly associated to C jejuni infections (83%), the mortality rate in this group is also high and apart from more severe course, a more pronounce seasonal preponderance is observed.

Epstein-Barr virus infection can also influence on the neurophysiologic classification and clinical features of GBS. The importance of considering Toxoplasma infection as an etiology of GBS in the transplant setting has been reported. Herpes simplex infection is a rare antecedent infectious agent in Guillain-Barré syndrome and Bickerstaff’s brainstem encephalitis and an Acute motor axonal Guillain-Barré syndrome after Salmonella typhirium infection in HIV-AIDS patients with an associated cryptococcal meningitis has been also described recently.

Apart from the association of Guillain-Barré syndrome and before-cited gastroenteritis others has been reported such as: systemic lupus erythematous and Hairy cell leukemia after a single course of 2-Chlorodeoxyadenosine, hepatitis A in pregnancy organ transplant patients and bone marrow transplant patients whom have iatrogenically suppressed T-cell function supporting the notion that the humoral immune system is...
involved in the pathogenesis of GBS, an association between Vogt-Koyanagi-Harada disease and GBS has been also described.

Human immunodeficiency virus (HIV) infection an associated GBS was reported by Thornton CA, Ahmed S, et al in Zimbabwe among others. GBS may be due to different pathological substrates and most of health professionals consider that steroid medications does not provide additional benefits, however in places where IV immunoglobulin and plasmapheresis are not available and where the incidence of HIV is extremely high, looking into another way of treatment is mandatory.

METHODS

Patients: Thirty patients fulfilling the diagnostic criteria of GBS were identified prospectively for the study during a three-years period; all patients were studied at Umtata General Hospital which is a terminal hospital of the Former Transkei providing neurology service for 15 peripheral hospital with a population of 6.4 millions of people approximately. Almost all eligible patients had active disease characterized by progressive ascending muscle weakness no beyond four weeks.

An experienced neurologist evaluated all patients, none patients had no previous history of peripheral nerve disease and those with concomitant disease (myelopathy or evidence of central demyelination, hepatitis, Lyme disease, cancer, para proteinemia or Castleman’s disease) were excluded; pregnant women, and patients with elevated serum creatinine were also excluded. In all patients for testing the cerebrospinal fluid (CSF), lumbar punction was done. Because nerves conduction studies were not performed with the same protocol at the same stage of the process, with the same operator with the same uniformity, these results were not included for analysis in this report. We studied patients with almost all variants of GBS with only one common No patients receiving treatment for any disease requiring immunomodulatory agents (IVIg, cyclophosphamide, azathiopine, corticosteroids, tacrolimus, cyclosporine, OKT3, plasma exchange alpha, beta or gamma interferon) within the past six months were admitted to the study.

Additional outcome measures included the Hughes...
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Functional Disability Scale (HFDS) (0=normal; 1=minor symptoms capable of running; 2=able to walk up to 10 meters without assistance but unable to run; 3=able to walk 10 meter with assistance of one person, a walker or a cane; 4=unable to walk; 5=requires assisted ventilation; 6=death).

STATISTICS

Two –sided t-test were used to analyze the primary outcome measure, a change in QMT between baseline and the end of the treatment for both group of patients, secondary outcome measures used a similar approach and included change between baseline QMT and at the end of the treatment alone with changes in ability to holding head. The HFDS was assessed by classifying the patients by categories: better, worse, or no change The Pearson x test was used to compare the functional improvement between the groups. The percentage in the change in the scores obtained in the baseline up to the end of treatment was calculated for the 1) QMT of upper limbs; 2) QMT of lower limbs. Clinical bedside test for power were not include in this analysis for obvious reason.

RESULTS

Figure 2

Figure 1: Efficacy analysis

Efficacy analysis included 15 patients (9 women and 6 men, mean age 51 +_ 20 years, range 16 to 77) treated with predispose, and 14 (8 women and 6 men, mean age 50 + – 16 years, range 21 to 71) with placebo.

At baseline: no difference between Group P-treated with prednisone and group C with placebo (predispose 7.08 + or – 1.27 versus placebo 7.16 +/-1.20 p = 0.54) (table 2) was found. At the end of the treatment, improvement was seen in QMT when comparing group P with group C (mean SE, 0.62 +/-0.17 versus – 0.1 +/-0.1, 0.74 +/-0.26, mean difference +/-SE; p=0.006). 74% improved in strength in prednisone group. Patients receiving prednisone showed improvement that increases with time (day 14: prednisone: 0.41 +/-0.13 versus placebo 0.08 +/-0.7, mean +/-SE; mean difference +/-SE 0.38 +/-0.18; P = 0.054; and day 36: prednisone 0.48 +/-0.15 versus placebo 0.02 +/-0.13 mean +/-SE; mean difference +/-SE, 0.45 +/-0.23; p = 0.046),Table 1.

Table II: Change, %, SD of Quantitative Muscle Testing scores in patients randomized to prednisone or placebo

Functional performance was different using the HFDS at day 36 comparing prednisone and placebo group (exact p = 0.016). In the group P, 10 patients improved by at least one functional grade (8 patients by one grade and 2 patients by two grades), whereas no patients in this group regressed in functional capabilities. In contrast, only one patient improved by one grade in the group C; in fact this condition worsened and the rest remained unchanged, measurement muscles strength on the neck musculature showed similar results. Grades of disabilities beyond 36 weeks for this study was not established.

Discontinuation of the treatment was not reported. No follow-up data were available in one patient.

Flow chart of the randomized, controlled trial of prednisone and placebo on GBS in HIV positive patients:

Registered or Eligible Patients: N=30

DISCUSSION

The total QMT, clinical bedside assessment, and HFDS scores at baseline in both groups were similar securing adequacy of randomization. Our report provides documentation that prednisone is effective in untreated GBS in HIV positive patients. Using muscle strength (QMT) as the primary outcome variable we found a highly significant difference between prednisone and placebo. The differences were seen as early as 14 days and the gap between prednisone and placebo groups widened at day 36, as the prednisone group continued to improve and the placebo group stayed the same or worsened. Because it is difficult to measure QMT in functional terms, the HFDS, an established measure of efficacy in plasma exchange in Guillain-Barré
In the Thorton et al. series, those patients (GBS) test are not available yet. Culture, genotypic and phenotypic assays and other virology assays, Chiron bDNA v.3 Organon Teknika Nucliseno, viral (>200), plasma viral RNA load, ultra sensitive viral load confirmed by western blot test and had higher CD4 count infected with HIV

Peripheral nerve disorders are common in individuals has been described probable due to functional corticospinal tract involment how lymphocytosis and did no response to steroids medication examination an important protein elevation and mild A patient with generalized hyperreflexia showed on CSF showed poor response to prednisone therapy in this series. Lower limbs and autonomic cardiac dysfunction (2 cases) with regard to the CSF albumin-cytology dissociation are recognized. However the designation of these variants as falling within the limits of GBS is made because they retain the others essential features of this syndrome. Benator M and Eastman RW, in 2000 described an human immunodeficiency virus associated pure motor lumbosacral polyradiculopathy in 4 Xhosa-speaking African women with similar clinical an electrophysiological pattern seen in GBS but the presence of the CSF pleocytosis was characteristic, those patients presented early in the course of HIV infection (no acquired immunodeficiency syndrome-defining illness) and preserved CD4 cell counts and negative cytomegalovirus tests. Those patients showed spontaneous recovery.

In our study patients with pure sensory deficit showed better outcome that those with pure motor forms presentation from the subjective point of view, and other combined presentations such as facial diplegia with paresthesia (1case) lower cranial nerve palsies, sensory loss in glove-stocking distribution, albumin-cytologic dissociation with HIV seroconversion (1case), motor and sensory disturbance of the lower limbs and autonomic cardiac dysfunction (2 cases) showed poor response to prednisone therapy in this series.

A patient with generalized hyperreflexia showed on CSF examination an important protein elevation and mild lymphocytosis and did no response to steroids medication probable due to functional corticospinal tract involment how has been described. Peripheral nerve disorders are common in individuals infected with HIV our selected HIV patients were confirmed by western blot test and had higher CD4 count (>200), plasma viral RNA load, ultra sensitive viral load assays, Chiron bDNAv.3 Organon Teknika Nucliseno, viral culture, genotypic and phenotypic assays and other virology test are not available yet.

In the Thorton et al 25 series, those patients (GBS) seropositive (N=16) showed a remarkable difference regarding generalized lymphadenopaty, mechanically ventilated and coexistent CNS disturbances such as: neurosyphilis, transient encephalopathy, and myelopathy compared with seronegative GBS patients. In our series apart from hyperreflexia no other sign of CNS involvement was seen; however the common finding was pleocytosis in the CSF (92%) that can be present in non-proportional quantity with the muscle strength improvement. We had hypothesized also that cell count levels are cytokine related, based in other parallel experience.

A course of corticosteroids was given to 4 HIV seronegative and 9 seropositive patients in Thorton's series 25 but information about their results was not reported.

A cytokine-mediated mechanism has been suggested for HIV-associated distal sensory polyneuropathy (DSP) which is the most debilitating symptom in seropositive patients and can affect up to 50% of AIDS patients to differentiate HIV-DSP from BGS (AIDP) or Sensory GBS recordable sensory action potential can help, but the increased protein level and pleocytosis in CSF is confirmatory.

In 1997, Adnan et al. reported three immunocompromised patients with confirmed GBS, two of them were HIV positive and the third one had cardiac transplantation, was on azathiprine and cyclosporine, other eleven immunosupressed patients (5-post renal + high doses of corticosteroid, 2- cardiac transplant + azathiprine, 5- lymphoma + cytarabine, carboplatinum, etoposide, and steroids, and cyclosporine, 1-1-lymphoma + cytarabine, carboplatinum, etoposide, and steroids) had been previously reported therefore GBS is not a common problem in immunocompromised patients and almost all of HIV-positive patients develop GBS at the begining of infection before developing AIDS. It is the first study done on HIV-seropositive patients with confirmed GBS, two of them were HIV positive and the third one had cardiac transplantation, was on azathiprine and cyclosporine, other eleven immunosupressed patients (5-post renal + high doses of corticosteroid, 2- cardiac transplant + azathiprine, 5- lymphoma + cytarabine, carboplatinum, etoposide, and steroids, and cyclosporine, 1-1-lymphoma + cytarabine, carboplatinum, etoposide, and steroids). It is the first study done on HIV-seropositive patients with associated GBS under treatment with prednisone. Our results justify to use steroids, especially is not other therapeutic way is available. A recommendation that it be used as “first choice treatment” for HIV-Guillain-Barre syndrome must be
examined in comparison with other available therapeutic approaches.

References

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