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LONGITUDINAL CLINICAL STUDIES

Dr. Jacques Delarue and colleagues from the University Hospital of Nancy conducted a longitudinal clinical study on 18 patients with multiple sclerosis over a period of 1 year. The study aimed to evaluate the safety and efficacy of interferon-ß1a in the treatment of this disease.

Methods

The study was a double-blind, placebo-controlled trial. Patients were randomized to receive either interferon-ß1a or placebo. The primary endpoint was the determination of the occurrence of new clinical deficits and changes in neurological examination scores.

Results

The results showed that interferon-ß1a significantly reduced the number of new clinical deficits compared to placebo. Additionally, there was a trend towards improved neurological examination scores in the interferon-ß1a group. The safety profile of interferon-ß1a was found to be comparable to the placebo group.

Conclusion

Interferon-ß1a is an effective and safe treatment for multiple sclerosis, as evidenced by the reduction in new clinical deficits and improved neurological examination scores. Further studies are needed to confirm these findings and to explore the long-term effects of interferon-ß1a in multiple sclerosis.

References

3. Rentschler Biotechnology, Laupheim, Germany

Identity of Interferon-ß1a Product in Multiple Sclerosis Study

Wieland W. Wolf, PhD

We extend sincere congratulations to Dr. Jacobs and colleagues for the successful conclusion of their study of recombinant interferon-ß1a (rIFN-ß1a) in patients with multiple sclerosis (MS). The impressive results showed that 6 million international units of rIFN-ß1a applied once weekly via the intramuscular route was safe and effective in patients with relapsing-remitting MS.

For all its merits, we are compelled to point out an error in the article [1]. Dr. Jacobs' designation of the study material as Avonex is incorrect and misleading. The only rIFN-ß1a used in this study was not as stated in the study, i.e., the substance with the trade name Avonex, produced by Biogen Inc., Cambridge, Massachusetts, but the Chinese hamster ovary-derived rIFN-ß1a developed and produced by Bioferon Biochemische Substanzen GmbH (Bioferon) in Laupheim, Germany. Today all product rights of the clinically tested product are held by Dr. Rentschler Biotechnologie GmbH (Rentschler), which is continuing the development of its proprietary rIFN-ß1a product.

According to a public statement by an FDA official, the marketed Biogen product Avonex is only "comparable" with [2] but not identical to the Bioferon product used in the trial by Dr. Jacobs. The FDA obviously decided that the clinical data derived from the use of Bioferon's product supports licensure of Biogen's product. However, according to our knowledge, an identity or comparability between the two molecules in terms of safety and efficacy in MS has not been proved in a pivotal trial.

Rentschler Biotechnology, Laupheim, Germany

References


Central Nervous System Whipple's Disease

Wim J. M. Verhagen, MD, PhD,* Patrick L. M. Huygen, PhD,† and Johanna E. Dalman, MD*

We read with interest the report by Louis and colleagues [1] on guidelines for diagnostic screening and treatment in central nervous system (CNS) Whipple's disease (WD). Recently, we reported on a similar patient [2]. CNS involvement is reported in about 10 to 43% of the WD patients [1, 3]. However, CNS involvement is not infrequent [4, 5]. The clinical presentation is variable, ranging from subtle cognitive dysfunction to severe psychomotor retardation [3]. CNS involvement is often seen [2, 5]. It is also important that oligoclonal banding and an increased IgG level in the CSF are often seen [1, 3], as is a decrease in IgG after treatment [2, 3].

The most effective antibiotic treatment regimen for WD is still under discussion. Even clinical and jejunal histological improvement after drug treatment does not guarantee an uncomplicated clinical course [2]. Fleming and co-workers [4] mentioned relapses in 31 of 88 WD patients. Oral tetracycline alone had been the initial treatment in 9 of the 30 patients who developed CNS relapse. Tetracycline does not cross the blood–brain barrier well, unless there is meningeval inflammation [5]. Keinath and associates [6] stated that ini-
tial treatment with double-dose sulfamethoxazole-trimethoprim (ST), given twice daily for 1 year, might be the best approach. Because folate deficiency is a potential complication of such treatment, supplementation is recommended [5]. In many studies, there was no improvement in CNS involvement during treatment with tetracycline alone, or in combination with other antibiotics [2]. Gaze paresis and nystagmus were most responsive to treatment, and dementia was arrested in patients with WD confined to the nervous system (for review, see Reference 2). Remarkable improvement in the organic psychosyndrome was noted when using ST and slight improvement when using ceftriaxone [2]. The optimum duration of antibiotic treatment is unknown. In the initial stage of WD, it appears wise to prescribe ST for a period of about 1 year [3]. Several of the CNS relapse patients had been undergoing treatment for about a year or more [2], although Fleming and co-workers [3] stated that the duration of treatment did not have any substantial effect on the outcome. We prefer long-term treatment [2]; our patient has now been treated for 32 months without having a relapse.

*Department of Neurology, Canisius-Wilhelmina Hospital; and †Department of Otolaryngology, University Hospital, Nijmegen, The Netherlands

References


Treatment Guidelines in Central Nervous System Whipple's Disease

P. J. Schneider, MD, E. C. Reisinger, MD, T. Berger, MD, G. J. Krejs, MD, and E. Aufl, MD

We read with interest the review by Louis and colleagues [1] on the diagnostic guidelines in central nervous system Whipple's disease (WD). The authors presented guidelines for diagnostic screening and selection for biopsy by reviewing 84 cases of cerebral WD. For antibiotic treatment the authors refer to a review by Keinath and colleagues on antibiotic treatment in WD (including only a few with cerebral WD) published in 1985 [2]. The authors stated that guidelines for treatment of cerebral WD have not been proposed so far. We recently published treatment guidelines for cerebral WD, but our results were published when Louis' paper was already submitted for publication. We reviewed the literature and contacted all authors who had reported on cerebral WD within the past 10 years [3]. The data published by Louis support our findings and treatment guidelines.

While antibiotic therapy achieves good results in patients with gastrointestinal involvement in WD, the outcome is poor with central nervous system (CNS) involvement. On the basis of empirical observations, trimethoprim and sulfamethoxazole (TMP-SMX) have been recommended for patients with WD to prevent spread to the CNS involvement [2]. In our report some of the reviewed patients responded well to TMP-SMX, but others did not. Three of 5 patients developed CNS involvement while on TMP-SMX therapy [3]. Third-generation cephalosporins were successful in preventing CNS involvement in all 4 patients in whom it was used [3–5]. Patients initially treated with penicillin and streptomycin showed a better long-term outcome than patients treated with penicillin alone [3]. Louis and colleagues reported on 1 patient with cerebral WD who relapsed after initial improvement while on TMP-SMX. When diarrhea developed, ceftriaxone (2 g IV daily) for 1 month led to improvement. After the patient was switched to doxycycline, a second relapse occurred; the patient was again successfully treated with ceftriaxone [1]. Another patient improved after ceftriaxone (2 g IV daily), and supranuclear gaze palsy and lethargy recurred after the patient was switched to TMP-SMX therapy [1]. The outcome in these 2 patients supports our findings that TMP-SMX neither prevents nor cures CNS involvement in all patients with WD. TMP-SMX reaches high intracellular concentrations, but it is bacteriostatic and therefore cannot destroy pathogens in possibly defective macrophages [6]. Third-generation cephalosporins have been shown to be effective in the treatment of cerebral WD that did not respond to TMP-SMX [1, 3]. However a low dose of ceftriaxone (2 g IV daily) might be responsible for the CNS relapses after discontinuation of ceftriaxone [1]. Based on our own long-term follow-up study and the results of Louis and colleagues, we suggest initial treatment of WD with intravenous ceftriaxone (instead of penicillin), 2 g twice daily, plus streptomycin, 1 g once daily for 2 weeks, or alternatively intravenous TMP-SMX, 960 mg twice daily for 1 to 2 weeks. Follow-up treatment for 1 year should consist of oral TMP-SMX, 960 mg twice daily, or oral cefixime, 400 mg once daily.

*Division of Neurological Rehabilitation, Department of Neurology, University of Vienna; and †Division of Infectious Diseases, Department of Medicine, Karl Franzens University, Graz, Austria

References

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