Interferon-α2b May Impair Myelinization of Rat Optic Nerve

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ABSTRACT

This study investigated the effects of interferon-alpha-2b (IFN-α2b) on the optic nerves of 17 adult male Wistar albino rats. Animals were divided into 3 groups: 6 rats (group 1) received 7.5 units (5 mIU/m²) IFN-α2b—a normal treatment dose, and 6 (groups 2) received 30.0 units (20 mIU/m²)—a high dose; 5 rats (control group) received 0.5 mL saline. Test substances were delivered by intraperitoneal injection 3 times a week for 3 weeks with animals under inhalation anesthesia. After the rats were sacrificed, their optic nerves were dissected, sectioned, and examined under an electron microscope. The mean thicknesses of the basal membranes of blood vessels were 86.354 nm in the control group, 104.297 nm in group 1, and 140.181 nm in group 2. Basal membrane changes in IFN groups were dose dependent. Mitochondrial swelling, degeneration, increased diameter of vacuoles, and vacuolization in the cytoplasm of oligodendrocytes and astrocytes were also observed. IFN-α2b has histopathologic effects on blood vessels and cells of the optic nerve.

Keywords: interferon-α; optic neuropathy; adverse effect; electron microscopy; histopathology; optic nerve
INTRODUCTION

Interferon-alpha (IFN-α) is a natural glycoprotein that is produced and secreted by immune cells in response to viral infection. With antiviral, antiproliferative, antiangiogenic, and immunomodulatory effects, it has been widely used for treatment in many systemic disorders, especially of viral and neoplastic origins.1,2 Despite its therapeutic ability, however, IFN-α produces adverse effects that are mediated by antiviral antibodies or immune complexes, including pathologic autoimmune consequences.2,3 The mild to severe adverse effects of IFN-α include flulike syndrome and anosmia, as well as an array of hematologic, infectious, cardiovascular, renal, otologic, neurologic, and psychiatric disturbances.2,4-7 Retinal hemorrhage and vision loss may also occur. The most common clinical manifestations of ocular toxicity are retinopathy and anterior ischemic optic neuropathy.8,9 These adverse effects are believed to result from vasculitis that affects small arterioles.5

This study investigated the effects of 2 dose regimens of IFN-α on the optic nerve of rats.

MATERIALS AND METHODS

Study Design

The study involved 17 adult male Wistar albino rats, weighing between 240 and 280 g, that were maintained on a cycle of 12 hours of light and 12 hours of darkness. The Ethics Committee on Animal Research at our institution approved the protocol, which ensured appropriate care and use of the animals.

Rats were divided into 3 groups: group 1 (n=6) received 7.5 units (5 mIU/m 2) of IFN-α2b (Intron® A; Schering Corporation, Kenilworth, NJ, USA), which is considered a normal treatment dose; group 2 (n=6) received 30.0 units (20 mIU/m2) of IFN-α2b, which is considered a high dose; group 3 (control, n=5) received 0.5 mL of saline. All test substances were delivered through intraperitoneal injection 3 times a week for 3 weeks with the animals under inhalation anesthesia.

After 30 days, the rats were sacrificed by means of a pentobarbital overdose (200 mg/kg), and craniotomy was performed. The optic nerves were dissected from 1 mm behind the sclera to the optic chiasm and resected.

Optic nerve tissues were fixed with 2.5% glutaraldehyde, postfixed with 1% osmium tetroxide, dehydrated in a graded alcohol series, cleared with propylene oxide, and embedded in epon. A Leica® UCT 125 instrument (Leica Microsystems, Allendale, NJ, USA) was used to cut 50- to 70-mm sections, which were stained with uranyl acetate and lead citrate and examined and photographed under an electron microscope (JEOL JEM-1011; JEOL USA, Inc., Peabody, Mass, USA). A soft imaging system was used to measure the thickness of each of the basal membranes of blood vessels found in the sections. Two or 3 vessels were evaluated in each grid of each animal. Five measurements were taken of each blood vessel, and average values were estimated.

Statistical Analysis

The average thicknesses of basal membranes were compared by means of a 1-way analysis of variance post hoc test. A P value <.05 was accepted as significant.