Abstract

Background: Multiple sclerosis (MS) is a chronic autoimmune, inflammatory neurological disease of the central nervous system (CNS). It attacks the myelin sheaths in the CNS, destroying the myelin and the axons to varying degrees. It is diagnosed based on supporting evidence from tests like the magnetic resonance imaging (MRI) of the brain. Contrast enhancing lesions (CELs) are marked by relapses or exacerbations of symptoms followed by periods of remission, when symptoms improve or disappear. Multiple sclerosis (MS) is a chronic autoimmune, inflammatory neurological disease of the central nervous system (CNS) that attacks the myelin sheaths in the CNS, destroying the myelin and the axons to varying degrees. It is diagnosed based on supporting evidence from tests like the magnetic resonance imaging (MRI) of the brain. Contrast enhancing lesions (CELs) are marked by relapses or exacerbations of symptoms followed by periods of remission, when symptoms improve or disappear. Contrast enhancing lesions (CELs) are marked by relapses or exacerbations of symptoms followed by periods of remission, when symptoms improve or disappear. Contrast enhancing lesions (CELs) are marked by relapses or exacerbations of symptoms followed by periods of remission, when symptoms improve or disappear.

Methods: The analyses performed in this study complement these findings, indicating that the use of IFN-beta-1b reduces the formation of new CELs but does not prevent disappearance of already-formed CELs. These results suggest that the design of optimal therapies combining IFN-beta-1b and steroids might affect the occurrence and resolution of inflammation more effectively.

Results

1. Data: (Figures 1A and 1B)

Different intervals were calculated from the observed data with a decreasing step of 10 starting from the 90% interval. Darker grey colors represent smaller intervals.

Solid black line shows the observed median for the CELs.

Red dashed line indicates the beginning of the treatment period.

2. Effect of IFN-beta-1b in the model:

Effect of IFN-beta-1b was evaluated on the model parameters, JL, PDV, PPDV, and PVDV.

3. Estimated JL and λ:

Different intervals were calculated using the estimated parameters and the final model with a decreasing step of 10 starting from the 90% interval. Darker grey colors represent smaller intervals.

Solid blue line shows the median of JL (left) and λ (right).

Red dashed line indicates the beginning of the treatment period.

4. Predicted interval of Visual Numerical Predictive Check:

Different dynamic descriptors were compared for the observed and simulated data based on the selected model. For each of the descriptors, 10th and 90th percentiles were calculated with an increasing step-size of 5. Solid black line shows the observed median. The 95% predicted interval is represented by the red area and the simulated median is represented by the dashed red line.

5. Simulated accumulated CELs using combinations of varying number of doses of IFN beta-1b and steroids

Based on the selected model, accumulated CELs were simulated for a 5 year (60 months) therapy period for several treatment combinations of IFN beta-1b and steroid.

IFN beta-1b treatments: Subcutaneous administration of 250 μg IFN beta-1b every other day for the treated months: (a) every month (60 months); (b) every 2 months (30 months); (c) every 4 months (15 months); (d) every 8 months (12.5 months).

Steroid administration: A single dose every: (a) 0 months (0 dose administrations); (b) 3 months (20 dose administrations); (c) 6 months (10 dose administrations); (d) 12 months (5 dose administrations).

Simulated accumulated CELs for the 1st (Figure 5A), 2nd (Figure 5B) and 3rd years (Figure 5C) are shown as surface plots. The blue, red and green surfaces represent the 10th, 50th and 90th percentiles, respectively.

Discussion

The analyses performed in this study indicate that the use of IFN beta-1b reduces the formation of new CELs but does not promote disappearance of already-formed CELs.

A previous study (4) indicated that the use of steroids contributes to the resolution of existing CELs, but does not reduce the development of new CELs.

These results suggest that the design of optimal therapies combining IFN beta-1b and steroids might affect the occurrence and resolution of inflammation more effectively.

References