ORIGINAL ARTICLE

Treatment with Interferon Beta-1b Improves Quality of Life in Multiple Sclerosis

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ABSTRACT: ***Background:*** The Canadian Burden of Illness Study Group reported that the quality of life (QoL) of multiple sclerosis (MS) patients falls drastically, early in the disease. With disability progression, the physical functioning scales of the Short Form 36 (SF-36) showed further decreases in QoL. The objective of this study is to describe the QoL of MS patients treated with interferon beta-1b (IFNB-1b) and to compare it to the QoL observed in a group of patients who had not been treated with IFNB-1b. ***Methods:*** Treated patients were prospectively recruited and were seen at their regular visit to the MS clinic. They self-completed the SF-36 questionnaire and their QoL was described and retrospectively compared to that of historical controls. ***Results:*** When IFNB-1b treated patients were compared to historical control patients with the same relapsing forms of MS, the treated patients with an Expanded Disability Status Scale (EDSS) score lower than 3.0 had a significantly better QoL. This was significant for four of the eight SF-36 domains: Physical Function (+22%, p=0.0102), Role-Physical (+100%, p=0.0022), General Health (+27%, p=0.0070) and Social Function (+19%, p=0.0287). The average QoL difference was 8% in the EDSS 3.0-6.0 group and 10% in the EDSS >6 group. ***Conclusion:*** Patients with relapsing forms of MS treated with IFNB-1b have better QoL than patients who are not treated, especially those with an EDSS < 3.0.

RÉSUMÉ: Le traitement par l'interféron bêta-1b améliore la qualité de vie des patients atteints de sclérose en plaques. ***Contexte:*** Le Groupe canadien sur le fardeau de la maladie (Canadian Burden of Illness Study Group) a rapporté que la qualité de vie (QV) des patients atteints de sclérose en plaques (SEP) chute de façon drastique tôt au cours de la maladie. Avec la progression de l'invalidité, les échelles de fonctionnement physique de la Forme courte d'échelle à 36 questions (SF-36) ont montré une diminution plus marquée de la QV. Le but de cette étude était de décrire la QV de patients atteints de SEP traités par l'interféron bêta-1b (IFNB-1b) et de la comparer à la QV d'un groupe de patients n'ayant pas reçu ce traitement. ***Méthodes:*** Les patients traités ont été recrutés prospectivement et ont été vus à leur visite régulière à la clinique de SEP. Ils ont complété un questionnaire auto-administré, le SF-36, et leur QV a été décrite et comparée rétrospectivement à celle de contrôles historiques. ***Résultats:*** Quand les patients traités par le IFNB-1b ont été comparés aux contrôles historiques souffrant des mêmes formes rémittentes de SEP, les patients traités qui avaient un score plus bas que 3.0 à l'échelle d'invalidité EDSS avaient une QV significativement meilleure. Ceci était significatif pour quatre des huit domaines SF-36: fonctionnement physique (+22%, p=0.0102), rôle-physique (+100%, p=0.0022), santé générale (+27%, p=0.0070) et fonction sociale (+19%, p=0.0287). La différence moyenne dans la QV était de 8% dans le groupe ayant un EFSS de 3.0 à 6.0 et de 10% dans le groupe dont le score était >6. ***Conclusion:*** Les patients atteints de formes récurrentes de la SEP qui sont traités par l'IFNB-1b ont une meilleure QV que les patients qui ne sont pas traités, surtout ceux qui ont un EDSS <3.0.

Can. J. Neurol. Sci. 1999; 26: 276-282

Multiple sclerosis (MS) is a common disease of the central nervous system (CNS) and a major cause of neurologic disability in adults. The disease is associated with various transient and permanent neurological symptoms and its course is difficult to predict. Since patients with MS have a normal life expectancy,[1,2] the accumulation of disability over the course of the illness has profound effects on an individual's daily activities.[3] The major factors that contribute to a patient's quality of life (QoL) are the ability to perform daily life activities, the level of well being and of satisfaction with life, and the effect of disease-specific symptoms on these parameters.[4] Clearly many of the symptoms of MS, including increasing disability, may have direct and indirect effects on these parameters. The Canadian Burden of Illness Study Group assessed health-related QoL in patients

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RECEIVED JANUARY 6, 1999. ACCEPTED IN FINAL FORM AUGUST 9, 1999

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attending MS clinics and reported that MS has a profound and early impact on QoL.[5] Patients were categorized in three disability groups according to the Expanded Disability Status Scale (EDSS). QoL was measured with one of the generic instruments most commonly used, the 36-Item Short-Form Health Survey (SF-36).[6,7] The advantage of the SF-36 is that it has broad applications and has been validated in several disorders as well as in the general population, therefore making comparisons possible.[6] Results of the Canadian study indicated that, compared to the general population, QoL scores for patients with mild MS (EDSS < 3.0) were on average 30% lower for all SF-36 scales.[5] The score for role-physical,[6] the SF-36 domain which reflects the physical limitations and their impact on work or other usual activities, was 63% lower than that reported for the general population. With EDSS progression, a statistically significant decrease in QoL was observed in three of the eight domains of the SF-36: physical function, role-physical and social function.[5] The relative stability of the other QoL domains with progression of disability might reflect the adaptation of the patient to the disease or the insensitivity of the SF-36,[5] as suggested in other QoL studies in MS.[8,9]

For many years, MS was a disease for which only symptomatic treatments existed. However, since 1995, four compounds have shown to have beneficial effects on the underlying disease. Interferon beta-1b (IFNB-1b) was the first medication proven to be efficacious in the treatment of relapsing-remitting MS (RRMS). Given subcutaneously at a dose of 8 million international units every other day, IFNB-1b reduces the frequency and severity of clinical exacerbations, as well as MS activity in the brain as assessed by magnetic resonance imaging (MRI).[10,11,12] A trend toward a slower disability progression was also observed.[10,12] These findings have also been seen in other studies with two forms of IFNB-1a and with glatiramer acetate.[13,14,15] Furthermore, a recent European study has shown that IFNB-1b delays sustained neurological deterioration in patients with secondary-progressive MS.[16]

We undertook to study the effect of IFNB-1b on the QoL of MS patients treated for several years, and to compare it to that of historical controls with the same forms of MS.[5] Four Canadian MS clinics enrolled 157 patients in the pivotal IFNB-1b trial initiated in 1987 and extended as an open trial in 1993.[10,12] At the time of the present study, most of these patients were still available for follow-up. The availability and the existence of relevant natural history QoL data in patients with relapsing MS offered Canadian MS clinics a unique opportunity to conduct such a study.

Methods

Objectives

This study was conducted primarily to describe the QoL of patients suffering from relapsing forms of MS treated with interferon beta-1b (Betaseron®, Berlex Canada Inc.) and to compare it to the QoL of patients with the same forms of MS who were never treated with IFNB-1b, and with those who have stopped IFNB-1b treatment. Secondarily, we wanted to evaluate what impact IFNB-1b might have on resource utilization parameters (hospitalizations and time lost due to MS [work time and leisure time]), which had been identified as the main MS cost drivers by the Canadian Burden of Illness Study Group.[17]

Patients

All treated patients had taken part in the pivotal IFNB-1b phase III study (BL-3110).[10] At the time of enrollment into study BL-3110, patients had either clinically definite or laboratory-supported definite MS. They were between the ages of 18 and 50 years, ambulatory with EDSS scores less than 6.0, and had had at least two MS exacerbations in the preceding two years and were all relapsing-remitting MS (RRMS) patients. To enter the present study, they had to have received at least one dose of 8 MIU of IFNB-1b, either during the initial study or its extension. Patients might have evolved to a secondary-progressive form of MS (SPMS). This study was approved by the institutional ethics review boards of the four participating institutions, and all patients gave informed consent. The historical control comparison group was composed of RRMS and SPMS patients who took part into the Burden of Illness Study in Canada [5,17] and who were never treated with IFNB-1b.

Study design

This was a multicenter study involving four MS clinics in three provinces. A total of 117 treated patients (Ontario, Center 1=38; British Columbia, Center 2=32; Quebec, Center 3=29; Quebec, Center 4=18) were prospectively recruited and their QoL was retrospectively compared to that of historical controls. Treated patients were seen during a regular visit at their MS clinic and the following information was collected in a case report form (CRF) designed for the study: demographic data, clinical status since disease onset and resource utilization data for the three months before study entry. Subjects were requested to complete the French or English Canadian version of the SF-36 QoL questionnaire as completely and accurately as possible, reflecting their QoL for the one month before study entry. If the patient could not complete the questionnaire alone, the study coordinator or the caregiver assisted the patient according to the instructions provided with the study protocol. All aspects of the study were carefully monitored by trained representatives of a contract research organization. Study progress was periodically reviewed with the study coordinators.

Statistical methods

Treated patients were categorized into three disability groups according to their EDSS score at entry in this present study: EDSS < 3.0, EDSS 3.0 to 6.0, and EDSS > 6.0. In the case of an exacerbation at the time of assessment, the EDSS score just before the exacerbation was used. Patients who had discontinued treatment (dropouts) were pooled to form a fourth group. Descriptive statistics of these groups were computed for socio-demographic parameters and MS related data. Answers to the SF-36 questionnaire were transformed for each patient into ten scores, ranging from 0 to 100, representing the eight QoL domains of the SF-36 and the physical and mental summary scores, according to the methods described by Ware.[18,19] Higher scores are associated with a better QoL. Descriptive statistics for these scores were computed.

Scores obtained in the three disability groups were compared using a Kruskal-Wallis analysis of variance. The QoL results of IFNB-1b treated patients were then compared to those of a

Table 1: Reasons for Treatment Cessation (dropout patients)

Reason	**Occurrence** [freq.* (%)]
Side Effects	17 (33%)
Patient Preference	14 (27%)
Disease Progression	10 (20%)
Frequent Exacerbations	3 (6%)
Others	7 (14%)

*Patients could provide more than one reason for treatment cessation.

subset of 152 patients from the Canadian Burden of Illness Study Group[5, 17] affected by a relapsing form of MS (historical controls). The Wilcoxon test was used to compare scores in the two study groups.

Finally, hospitalizations and time lost due to MS (work time and leisure time) were computed per current disability category and results were compared to the historical controls using a Student t-test.

Results

Socio-demographic and disease characteristics

One hundred and seventeen patients were enrolled in this study: 80 patients were still taking IFNB-1b treatment and 37 had stopped receiving the medication for different reasons (Table 1). Only 18/135 eligible patients from the original BL-3110 study (22/157 patients never received IFNB-1b and were thus not eligible for the present study) were not found or refused to participate in the present study, leading to a 86.7% retrieval rate. The socio-demographics and disease characteristics for the study patients are presented in Table 2. Those of the historical controls are presented in Table 3.

Treated patients and the historical controls were comparable for age, gender and average EDSS ($p>0.05$). However, time since disease onset (TSDO) was longer in the treated patients than in historical controls. This difference was particularly pronounced in the low disability group ($p=0.0003$). When analyzed at the time of treatment initiation, TSDO in the treated group was similar to that of the historical controls, as were age, gender and average EDSS ($p>0.05$).

Table 2: Socio-Demographic and Disease Characteristics of Patients Treated with IFNB-1b

Variable	**EDSS < 3.0 (n = 30)**	**EDSS 3.0 - 6.0 (n = 32)**	**EDSS > 6.0 (n = 18)**	**Treatment Dropouts (n = 37)**
Age (years) [mean ± SD]	42.0 ± 8.0	42.5 ± 7.6	45.3 ± 7.2	44.4 ± 7.6
Gender [freq. (%)]				
Male	6 (20%)	11 (34%)	6 (33%)	10 (27%)
Female	24 (80%)	21 (66%)	12 (67%)	27 (73%)
Education level [freq.(%)]				
High School Degree and Lower	10 (33%)	14 (45%)	10 (56%)	12 (32%)
Post-Secondary and Higher	20 (67%)	18 (55%)	8 (44%)	25 (68%)
Current Employment Status [freq. (%)]				
Active – full year/time	16 (53%)	11 (33%)	0 (0%)	5 (14%)
Active – other worker	4 (13%)	4 (13%)	1 (6%)	4 (10%)
Unemployed	6 (21%)	13 (41%)	17 (94%)	23 (62%)
Other	4 (13%)	4 (13%)	0 (0%)	5 (14%)
Employment Change due to MS [freq.(%)]	9 (30%)	14 (44%)	14 (78%)	23 (62%)
Time Since MS Onset, IFNB-1b Init. (y)[mean ± SD]	8.3 ± 5.2 p=0.65*	11.7 ± 5.5 p=0.03*	14.6 ± 7.3 p=0.18*	11.3 ± 6.2
Time Since MS Onset, Current (y) [mean ± SD]	13.7 ± 4.6 p=0.0003*	16.8 ± 5.6 p=0.26*	19.5 ± 6.9 p=0.64*	16.4 ± 5.5
Current Form of MS [freq.(%)]				
Relapsing-Remitting MS	29 (97%)	27 (84%)	7 (39%)	19 (51%)
Secondary-Progressive MS	1 (3%)	5 (16%)	11 (61%)	18 (49%)
EDSS Score, Current [mean ± SD]	1.6 ± 0.7	4.2 ± 1.3	7.1 ± 0.7	5.2 ± 2.5
Pts with current exacerbation at time of visit [freq.(%)]	2 (7%)	5 (16%)	0 (0%)	1 (3%)
EDSS Score, at IFNB-1b Initiation [mean ± SD]	1.7 ± 0.9	3.5 ± 1.6	5.6 ± 2.0	3.7 ± 1.8
Duration of IFNB-1b Treatment (y) [mean ± SD]	5.5 ± 2.1	5.1 ± 2.0	4.9 ± 1.9	5.2 ± 2.1
Current Dose of IFNB-1b (MIU) [mean ± SD]	7.6 ± 1.1	7.8 ± 0.7	7.8 ± 0.9	N/A

*Compared with Time Since MS Onset of historical controls.

https://doi.org/10.1017/S031716710000038X Published online by Cambridge University Press

Table 3: Socio-Demographic and Disease Characteristics of Historical Controls

Variable	EDSS < 3.0 (n = 54)	EDSS 3.0 - 6.0 (n = 58)	EDSS > 6.0 (n = 40)
Age (years)			
Mean ± SD	39.3 ± 9.4	44.1 ± 9.8	47.1 ± 12.4
Gender [freq. (%)]			
Male	7 (13%)	19 (33%)	10 (25%)
Female	47 (87%)	39 (67%)	30 (75%)
Education level [freq.(%)]			
High School Degree and Lower	31 (57%)	28 (48%)	21 (53%)
Post-Secondary and Higher	23 (43%)	30 (52%)	19 (47%)
Current Employment Status [freq. (%)]			
Active – full year/time	20 (37%)	18 (31%)	2 (5%)
Active – other worker	11 (20%)	7 (12%)	2 (5%)
Unemployed	17 (32%)	23 (40%)	29 (72%)
Other	6 (11%)	10 (17%)	7 (18%)
Employment Change due to MS [freq.(%)]	22 (41%)	33 (57%)	35 (88%)
Time Since MS Onset (y)			
Mean ± SD	8.7 ± 7.4	14.9 ± 8.7	18.2 ± 10.4
Current Form of MS [freq.(%)]			
Relapsing-Remitting MS	49 (91%)	29 (50%)	1 (3%)
Secondary-Progressive MS	5 (9%)	29 (50%)	39 (97%)
Current EDSS Score			
Mean ± SD	1.8 ± 0.5	4.6 ± 1.2	7.2 ± 0.6
Pts with current exacerbation at time of visit			
Freq.(%)	16 (30%)	11 (19%)	6 (15%)

EDSS scores in relation to TSDO, at treatment initiation and study entry, are presented in Figure 1. At time of treatment initiation, IFNB-1b treated patients had an EDSS versus time since disease onset pattern similar to the historical controls. However, after an average treatment duration of five years, the EDSS versus TSDO pattern was shifted to the right suggesting that patients benefit from a much slower disease progression over the treatment period.

Quality of Life based on current EDSS

The scale structure, reliability and validity of the SF-36 questionnaire were assessed in a previous MS study[5] and the results obtained were all within the published norms expected for a validated QoL instrument. In the present study, the QoL scores for all scales decreased as EDSS scores increased (Table 4). However, the difference in QoL between the three disability levels was only significant in three domains: physical function (p=0.0001), role-physical (p=0.0011) and general health (p=0.0023). The most noticeable decline across the three disability groups occurred in physical functioning where the average score went from 74.5 at mild disability, to 15.1 at severe disability, an 80% decrease. A similar decline is reported in the role-physical scores where the QoL score decreases from 56.7 in the mild stage to 15.3 in the severe stage. The QoL scores of dropout patients, who were distributed over the three disability levels, were similar to those of the moderate disability group.

When compared with the scores of historical controls at similar disability levels, QoL of IFNB-1b treated patients was higher, particularly for patients with an EDSS < 3.0 (Table 4 and Figure 2). The most significant contrasts were observed for role-physical (+100%, p=0.0022), general health (+28%, p=0.0070), physical function (+22%, p=0.0102) and social function (+19%, p=0.0287).

The overall average score difference between treated patients and historical controls was 8% in patients with moderate disability and 10% in patients with severe disability. Except for the physical function in the severe disability group, the changes in the various domains of the SF-36 did not reach statistical significance.

Resource utilization

Very few hospitalizations occurred, in both groups, during the three months before study entry. The number of treated patients hospitalized during this reference period was 2 (7%) in

https://doi.org/10.1017/S031716710000038X Published online by Cambridge University Press

Table 4: SF - 36 Assessment of QoL: Summary Statistics per Current EDSS

	EDSS < 3.0		EDSS 3.0 – 6.0		EDSS > 6.0		p-value*
	IFNB-1b (n = 30)	Controls (n = 53†)	IFNB-1b (n = 32)	Controls (n = 58)	IFNB-1b (n = 18)	Controls (n = 40)	
Physical Function	74.5±21.8	61.1±22.2‡	44.1±20.9	37.4±19.7	15.1±14.4	11.1±22.1‡	0.0001
Role-Physical	56.7±39.9	28.3±38.3‡	27.3±38.8	22.0±33.5	15.3±22.9	12.5±30.5	0.0011
Bodily Pain	69.1±24.4	59.5±26.9	63.8±25.3	59.1±25.8	63.0±30.0	55.3±32.4	0.5575
General Health	68.7±22.4	53.9±23.5‡	53.9±22.0	55.7±21.2	45.6±21.6	46.9±26.5	0.0023
Vitality	49.2±25.6	41.4±19.6	42.5±22.4	38.1±21.1	40.3±17.9	32.9±19.3	0.4231
Social Function	73.5±24.9	61.7±22.4‡	65.8±22.9	59.3±25.1	56.5±29.8	45.2±28.7	0.1138
Role-Emotional	65.6±40.6	60.4±41.9	59.9±40.2	56.3±45.1	50.0±40.1	50.0±47.2	0.3916
Mental Health	66.4±21.8	62.1±19.8	63.4±21.8	62.8±19.3	63.1±18.2	63.1±20.7	0.6972
Summary Scores							
Physical	67.2±22.4	47.8±19.5‡	47.3±19.2	43.5±7.8	34.8±17.5	31.5±19.0	0.0001
Mental	63.7±25.0	57.9±27.9	57.9±20.2	54.1±22.5	52.5±20.8	47.8±21.7	0.2231

Values are means±SD

* comparison of treated patients scores, across the three disability levels, using a Kruskal-Wallis test

† one patient did not answer the questionnaire

‡ $p < 0.05$; comparison between treated patients and controls, within same disability level, from a Wilcoxon test

the low EDSS group, 1 (3%) in the moderate group and 3 (17%) in the severe group, while the average length of stay per hospitalization was 0.73 day in the low EDSS group, 0.16 day in the moderate group, and 1.14 day in the severe disability group. Only one hospitalization occurred because of a condition related to MS.

Since a previous study[17] has shown that MS, even at the early stages of the disease, has a large impact on the employment status of patients, we also examined the effect of IFNB-1b treatment on workdays lost. In treated patients, the average number of workdays lost by active patients over a three-month period amounted to 2.0 in the low EDSS group, and 25.0 in the moderate group. In comparison, average number of workdays lost by historical active patients was 15.6 in the low EDSS group (p=0.29), and 29.9 in the moderate EDSS group (p=0.81). Other time lost in the treated patients group averaged 33.8 days over a three-month period in the mild group, 53.1 in the moderate group, and 65.7 in the severe disability group whereas time lost in the historical controls group was 41.9 days in the mild group (p=0.59), 46.0 in the moderate group (p=0.58) and 67.4 in the severe group (p=0.91).

Discussion

Schwartz et al. reported their results of a short-term Extended Quality-Adjusted Time Without Symptoms and Toxicity (Q-TWIST) analysis in 34 patients treated with IFNB-1b versus 45 controls.[20] Using this methodology, which evaluates the trade-off between the adverse effects of a treatment and delayed disease recurrence, they did not observe any significant differences between the two groups over the first year of treatment.[20]

To our knowledge, the present study is the first report on QoL of MS patients under long-term IFNB-1b treatment. Comparisons were conducted with untreated historical controls obtained from a previous Canadian study.[5] We concede that the use of historical controls is a limitation. However, in the context of long-term QoL evaluation, a classical double-blind, placebo-controlled design would not have been feasible for practical and ethical reasons. The advantage of the current design was that we were able to make our observations in a group of patients treated with IFNB-1b for an average duration of five years under non-study conditions, having probably washed out from the clinical trial effect. Our treated patients were followed by the participating MS clinics as routine patients, no longer exposed to the privileged or protected environment often associated with clinical trials. The study design is believed to be appropriate and valid for several reasons: sources of data were both derived from Canadian populations, patients were all followed by MS clinics with consistent follow-up and monitoring, and QoL was measured with the same instrument. Additionally, socio-demographic and disease characteristics before treatment initiation were not different, and primary QoL data were analyzed using the same methodology with patients similarly stratified by disability level. A longitudinal analysis of QoL was not possible in this study population, since the SF-36 questionnaire was not administered in the pivotal IFNB-1b study.

The relative insensitivity of the SF-36 to QoL changes seen with higher MS disability, especially in the mental domains, have been discussed at length in previous publications.[5,9] However, this study presented an opportunity to test the potential usefulness of the SF-36 instrument in assessing QoL changes resulting from a MS-specific treatment.

As reported for historical controls,[5] and as expected, the QoL in treated patients decreased as the EDSS score increased. The improvement of QoL, demonstrated in patients with low disability receiving IFNB-1b when compared to the untreated population at similar disability level, is an important finding. In spite of the modest sample size, this positive impact achieved statistical significance in patients with mild disease for four

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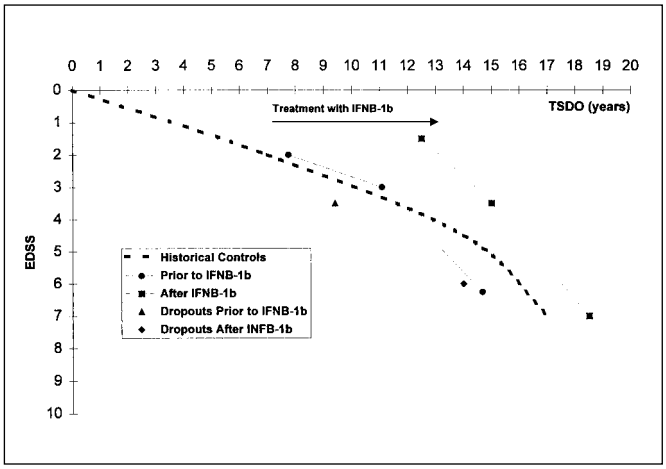

Figure 1: *Expanded Disability Status Scale (EDSS) scores in relation to time since disease onset (TSDO) of historical control patients and IFNB-1b treated patients (prior and after treatment).*

IFNB-1b treated patients were grouped into three disability levels using their EDSS at time of study entry and median EDSS and TSDO were computed at treatment initiation and at study entry. EDSS scores of pooled dropout patients, before and after treatment, are also presented in relation to TSDO.

domains: physical function, role-physical, general health, and social function. In these domains, the increase ranged from 19% for social function, to 100% for role-physical. The eight SF-36 scales form two distinct clusters due to the physical and mental health parameters measured.[6,18] The positive impact of IFNB-1b was most apparent in scales that correlate with the physical component (physical functioning, role-physical) or which have correlations with both physical and mental components (general health and social functioning). Scales which are exclusively associated with the mental component (mental health and role-emotional) showed little improvement in scores after IFNB-1b treatment, even in the mild MS group. In this patient group, IFNB-1b treatment increased the role-emotional score by 8.6%, compared to the historical control, while the increase in the mental health scale was only 6.9%.

The overall improvement of QoL at low disability level was such that IFNB-1b treated patients approached QoL levels reported for an age-matched general US population.[18] Based on this comparison, treated patient scores were on average 82% of those of a normal population, while untreated patient scores were 67% of the published norms.

IFNB-1b treated patients with more disabling MS showed a trend towards higher QoL scores when compared to the historical controls. In patients with moderate disability, seven scales showed higher scores in the IFNB-1b group (average increase: 8%). This pattern was maintained in the high EDSS group (average increase: 10%) with only the physical function scale showing a statistically significant improvement in patients taking IFNB-1b.

This better QoL in treated patients might be explained by the reduction in the number of exacerbations. During the pivotal trial, IFNB-1b treatment showed a reduction of 30% in the frequency and severity of exacerbations[10] and this reduction in the exacerbation rate persisted over five years.[12] In the present trial, a lower relapse rate was also observed in treated patients compared to historical controls. Parkin et al.[21] have shown, in their cost-analysis of interferon beta-1b for multiple sclerosis, that patients in remission had better quality of life scores than patients who recently experienced a relapse. Highly statistical differences were seen between the relapse and remission groups, in favor of the remission group, in scores on the physical function, role-physical, and social function as well as in the change in health item and in the physical health composite score of the MSQoL-54 questionnaire. This further reinforces the thesis that, in our study, the lower relapse rate in treated patients may explain a better QoL despite similar EDSS values.

Another explanation of the better QoL in treated patients might be the reduction in total brain lesion area shown with IFNB-1b treatment. It has been proposed by Pozzilli et al.[22] that cognitive dysfunction correlates with the number of brain lesions in MS patients. Since cognitive dysfunction has been linked to an impact on overall QoL (Rao et al.[23]), we can speculate that IFNB-1b, by reducing the number of brain lesions, improves the QoL of treated patients.

At last, and as mentioned earlier, it is unlikely that a more optimistic outlook of life would explain the higher QoL scores in treated patients as mental scores are only marginally affected.

The present study demonstrates that despite limitations, the SF-36 is sensitive enough to detect QoL changes in treated MS patients. As discussed previously,[5] floor and ceiling effects may make SF-36 scales insensitive to small changes in MS patient QoL. Nonetheless, the instrument is useful for providing a baseline assessment of QoL, particularly in patients with mild disease, the patient population that benefits most from IFNB-1b treatment. However, a disease-specific instrument, that might be more sensitive to QoL changes at higher disability levels, is needed.[9,24]

Resource utilization analysis showed that over the three-month assessment period, mildly disabled patients treated with IFNB-1b experienced less loss of time from work. This

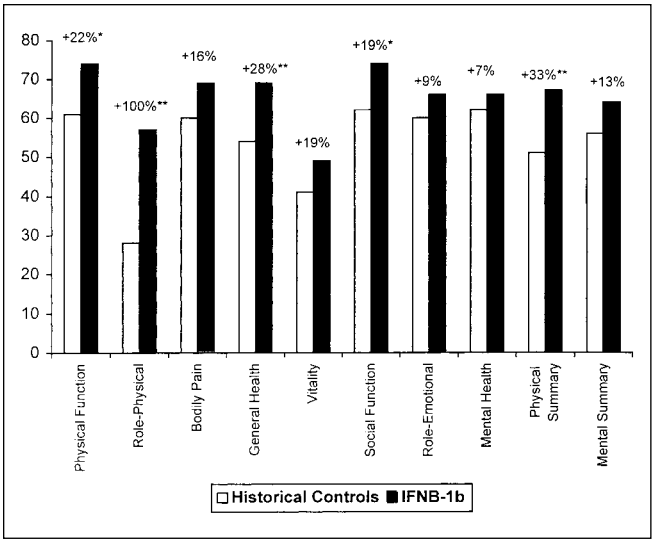

Figure 2: *Quality of life scores of IFNB-1b treated patients and historical control patients in the low disability level group (EDSS < 3.0).*

** $p < 0.05$; ** $p < 0.01$*

https://doi.org/10.1017/S031716710000038X Published online by Cambridge University Press

reduction in number of workdays lost may indicate a more normal lifestyle. Furthermore, while the employment status of the two groups was not statistically different, treated patients tended, at least until they reached an EDSS of 6.0, to be more active and less subject to unemployment than the historical controls.

Conclusions

The results of the present study show that IFNB-1b provides MS patients with an important and durable increase of QoL at lower disability levels when compared to historical control patients. The improvements are particularly apparent in QoL domains impacting on activities of daily living, and indicate that treated patients spend a longer time in a better health state. The decline in QoL seems delayed in IFNB-1b treated patients as patients in the low EDSS group have a better QoL after five years of treatment (mean disease duration of 13.7 years) than untreated patients who have a mean disease duration of 8.7 years.

Preliminary information on the main cost drivers of MS suggest that better and prolonged QoL states are associated with reduced financial consequences and, possibly, easier participation in the society's workforce.

Further research with a QoL instrument more sensitive to changes at high disability levels would be useful to fully understand the treatment effect. As well, a more detailed economic analysis would determine more precisely the changes that IFNB-1b produces on resource utilization.

Acknowledgments:

This study was made possible by a grant from Berlex Canada Inc.

The authors thank the study coordinators: Jane Lesaux (London UH), Janet Wallin and Beatrix Paszner (UBC), Renée Dubois (CHUM) and Marc Lemieux (MNI).

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