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No Difference in Health Related Quality of Life Between Therapeutic Options for Type 1 Gaucher Disease

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NO DIFFERENCE IN HEALTH RELATED QUALITY OF LIFE BETWEEN THERAPEUTIC OPTIONS FOR TYPE 1 GAUCHER DISEASE

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NO DIFFERENCE IN HEALTH RELATED QUALITY OF LIFE BETWEEN THERAPEUTIC OPTIONS FOR TYPE 1 GAUCHER DISEASE

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Type 1 Gaucher disease (GD) is the most common lysosomal storage disorder. Previously, treatment for GD was limited to intravenous enzyme replacement therapy (ERT). ERT reduces symptoms and increases health-related quality of life (HRQoL) in people with this condition. In 2014, oral substrate reduction therapy (SRT) was approved for type 1 GD treatment. Although both therapies alleviate disease symptoms, effects of SRT on HRQoL and preferences for therapy are not well established. Electronic surveys were administered to adults with type 1 GD. HRQoL was scored with the Short Form-36 Version 2® Health Survey and descriptive statistics were used to evaluate additional survey items. No differences in physical HRQoL ($p = 0.756$) or mental HRQoL ($p = 0.650$) were observed between SRT and ERT users. SRT users most often perceived their health to be similar to when they used ERT. Additionally, SRT users expressed convenience and non-invasiveness as reasons for choosing SRT, while many ERT users cited potential side effects and satisfaction with ERT as reasons for declining SRT. There appears to be no difference in HRQoL between ERT and SRT users and no perceived change in HRQoL for SRT users that previously used ERT. Participant responses illustrate that one particular treatment may not be ideal for all patients with type 1 GD depending on perceived convenience, invasiveness, or side effects. This evidence suggests that individuals with type 1 GD be adequately counseled about the risks and benefits of both therapy options now that SRT is clinically available.

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INTRODUCTION

Lysosomal storage diseases (LSDs) are a group of genetic disorders that affect the ability of lysosomes to break down waste inside of various cells of the body. There are approximately 50 different types of LSDs that are clinically recognized and the most common of these is Gaucher Disease (GD) [Grabowski, 1993]. GD involves a deficiency of the enzyme glucocerebrosidase and, as a result, impedes the ability of lysosomes to break down a glycosphingolipid called glucosylceramide that can accumulate within the cells of organs such as the spleen, liver, kidneys, brain, lungs, and bone marrow [Beutler, 1991].

GD is most common in Ashkenazi Jewish populations and, depending on the mutation and phenotypic classification, individuals with GD can be broken down into three different types [Azuri et al, 1998; Koprivica et al, 2000]. Type 1 GD is the most common form of the disease and is often referred to as non-neuropathic due to the fact that there are no neurological symptoms of the disease in these patients. Types 2 and 3 are considered acute and chronic neuropathic forms of the disease, respectively, and can result in neurologic symptoms such as seizures or movement disorders [Beutler, 1991; Grabowski, 1993]. Symptoms that can be present in all three types of GD include hepatosplenomegaly, anemia, bone and joint pain, and lung disease [Beutler, 1991].

While there is no cure for GD, enzyme replacement therapies (ERTs) were introduced to the medical community in 1991 as a treatment for non-neurologic symptoms of GD. Therefore, these courses of treatment have been most effective for treatment in patients with type 1 GD [Kay et al, 1991; Verderese et al, 1993]. ERT must be given through infusion biweekly over the course of several hours and many individuals use central venous access devices (CVADs) for therapy administration. In August, 2014, a new treatment referred to as substrate reduction

therapy (SRT) was approved by the Food and Drug Administration (FDA) for patients with type 1 GD [Futerman et al, 2004]. This type of therapy is delivered orally once or twice daily depending on patient metabolizer status and has been proven to be as effective as ERT in treatment of physical symptoms of the disease throughout its clinical trial [Kamath et al, 2014; Lukina et al, 2014; Poole, 2014; Mistry et al, 2015].

Although SRT is effective at treating physical manifestations of type 1 GD, little is known regarding the influence this novel therapy could have on the health related quality of life (HRQoL) of individuals with this genetic condition. In the past, HRQoL has been used to collect information about the physical and psychosocial effects of chronic disease on patients' lives. Patients with chronic conditions such as fibromyalgia, chronic obstructive pulmonary disease (COPD), and acquired immunodeficiency syndrome (AIDS) have lower HRQoL than members of the general population across several different categories including physical and mental quality of life [Schlenk et al, 1998]. While studies of chronic genetic disorders have historically focused on identification and treatment of manifestations, learning about HRQoL for patients with certain genetic conditions may allow health care providers, such as medical geneticists and genetic counselors, to better understand the disease burden of these individuals and the impact that their disease has on everyday life [Sprangers & Aaronson, 1992]. Previous studies have shown that patients with type 1 GD, as well as other LSDs such as Fabry disease and Pompe disease, have a decreased HRQoL when compared with United States population norms [Damiano et al, 1998; Hayes et al, 1998; Masek et al, 1999; Gold et al, 2002; Giraldo et al, 2005; Kanters et al, 2011; Bouwman et al, 2011]. Furthermore, ERT has been shown to improve HRQoL in patients with type 1 GD [Damiano et al, 1998; Masek et al, 1999; Weinreb et al, 2007].

Due to the recent availability of SRT for patients with type 1 GD, no study to date has captured the perception of disease burden and HRQoL in patients that are specifically utilizing SRT for treatment. Because SRT is an oral therapy, it may impact patients differently, while still providing the same symptom relief for GD. As a result, HRQoL in patients with type 1 GD using SRT may be different than what is reported in the literature for patients using ERT. Additionally, patients who used ERT in the past but who are currently using SRT may report a self-perceived increase in some aspects of quality of life. In this study, we sought to investigate whether or not patients using SRT to treat non-neuropathic GD have similar or better HRQoL and perception of disease burden than those patients using ERT. This information could be instrumental in educating healthcare providers and patients about the full range of risks and benefits of these courses of treatments outside of treating the physical manifestations of the disease.

MATERIALS AND METHODS

Participants and Data Collection

A link to a study questionnaire was posted in online group forums consisting of patients with type 1 GD and their family members, including the Yahoo! Gaucher Disease group (https://groups.yahoo.com/neo/groups/gaucherdisease/info), the National Gaucher Foundation (NGF) website (http://www.gaucherdisease.org/), and the National Gaucher Foundation of Canada (NGF Canada) listserv. Additionally, letters describing the study purpose were sent electronically to physicians at GD treatment centers, as well as to genetic counselors that belong to the Metabolic Special Interest Group within the National Society of Genetic Counselors. These healthcare providers were provided with study access information so that their interested patients could participate in this research. Electronic advertisements were sent every three weeks to the online groups and healthcare providers during a collection period ranging from October

12th, 2015 to January 7th, 2016. To be eligible to participate in this study, individuals had to be 18 years of age or older and have a self-reported diagnosis of type 1 GD. Participants were informed prior to beginning the survey that two dollars would be donated to the NGF for each complete survey that was submitted. Participants were also asked to identify if they had participated in this study previously so that responses would not be duplicated. The total number of individuals with type 1 GD that this survey reached is unknown due to a paucity of data on the number of patients approached by the healthcare providers and the degree of overlap between patient populations and support groups; therefore, a response rate could not be reliably determined. Research data was collected through REDCap™, a secure electronic survey portal. Informed consent was obtained as a precursor for individuals to begin the survey. This study received institutional review board exemption from the University of Texas Health Science Center (IRB #HSC-MS-15-0388).

Assessment Tools

The study questionnaire was comprised of different sections to assess disease history, treatment history, HRQoL, and demographics. The questionnaire consisted of mostly forced choice options with some open-ended questions. None of the items were deemed mandatory in the questionnaire. The survey was structured with gateway questions so that only applicable questions would be presented to the participant based on their answers to previous questions. The portion of the survey measuring HRQoL was executed using the validated tool Short Form-36 Version 2® (SF-36v2®) Health Survey from OPTUM QualityMetric, Inc. [Jenkinson et al, 1999]. The SF-36v2® Health Survey questionnaire consists of 36 items forming eight scales measuring physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotion, and mental health. Scores from each of these eight scales compose total physical

component scores (PCS) and total mental component scores (MCS) ranging from 0 - 100 using QualityMetric Health Outcomes™ Scoring Software 4.5. A score of 50 indicates an average HRQoL score and higher scores on these scales indicate higher HRQoL. Age and gender matched norm data from the general United States population in 2009 was used for data comparison [Maruish, 2011]. Individuals currently using SRT that used ERT in the past were also asked questions about how their satisfaction with different aspects of their life compares between now and when they were using ERT as their primary treatment for type 1 GD.

Statistical Analyses

Participant responses to the survey were recorded and forced-choice question answers were entered into STATA®, a statistical software program for data analysis (v. 13. StataCorp LP, College Station, TX). Frequencies (with percentages) were calculated for all data. SF-36v2® PCS and MCS for adults using SRT were compared to United States 2009 population norms using a Wilcoxon signed rank test. PCS and MCS for ERT and SRT treatment groups were compared and analyzed using a Mann-Whitney test. Kruskal-Wallis, Chi-square, and Spearman correlation tests were performed to assess potential influence of demographic data including sex, age, income, education, and marital status on PCS and MCS. Spearman correlation tests were also used to determine if number of symptoms related to type 1 GD or number of other chronic conditions apart from type 1 Gaucher disease statistically influenced the PCS or MCS of participants. Descriptive statistics were used to analyze all other parts of the questionnaire.

RESULTS

Description of Sample

Forty-seven adults with type 1 GD completed the study questionnaire. Our study population consisted of 35 (74%) women, 46 (98%) Caucasians, and 29 (62%) individuals of Ashkenazi Jewish ancestry. Almost all participants (n=41, 87%) lived in the United States at the time that the survey was administered. Other participants (n=6) reported Canadian or Northern European residence. Participant current ages ranged from 18 to 78 years old with approximately one-third of participants falling in each of the following age ranges: 18-40 years, 41-60 years, and 60-78 years. Most participants who responded to additional demographic questions had achieved at least an undergraduate degree (n=34, 72%), were married (n=23, 49%), and had an average total annual household income less than 100,000 dollars per year (n=23, 51%) (Table 1).

Table 1 - Demographic and Background Characteristics of 47 Participants with Type 1 GD

Characteristic	n	%
Mean Age (Range)	49 (18 – 78)	
18-40	15	33
41-60	18	39
61-78	13	28
Chose not to answer	1	
Sex		
Female	35	74
Male	12	26
Ethnicity		
Caucasian	46	98
Hispanic/Latino	1	2
Jewish ancestry		
Yes	29	62
No	18	38
Country of residence		
United States	41	87
Other	6	13
Highest level of education		
Some college or less	13	28
College degree or higher	34	72
Marital status		
Married	23	49
Single, Divorced, or Widowed	24	51
Total annual household income		
Less than $100,000	23	51
$100,000 or greater	22	49
Chose not to answer	2	

Medical and Treatment History

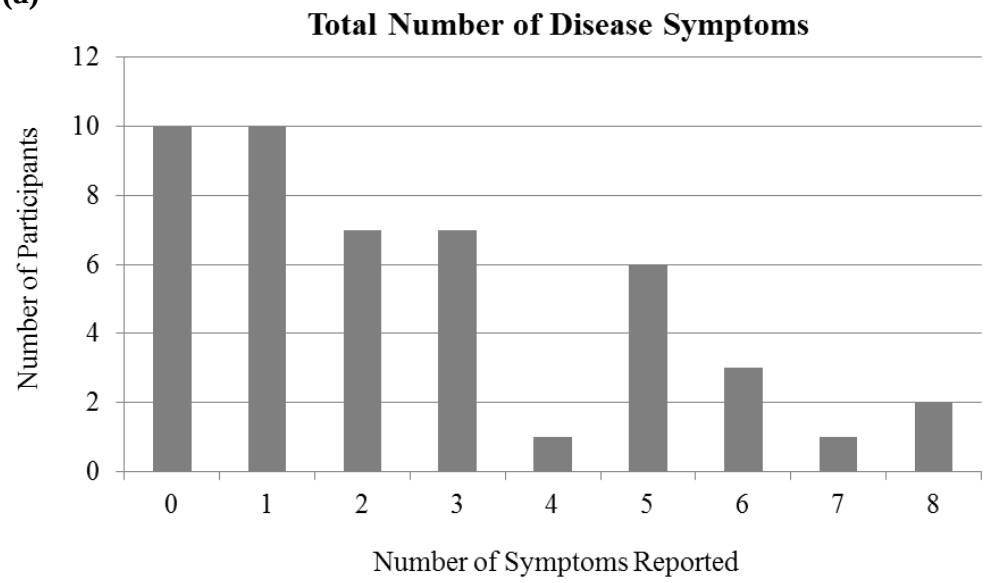
The median age that participants were diagnosed with type 1 GD was 23 years with an interquartile range (IQR) of 5 to 39 years of age and responses ranging from 1 to 59 years of age. Slightly less than two-thirds of participants (n=29, 61%) had one or more chronic conditions in addition to type 1 GD, the most common being hypertension (n=14), back problems (n=12), and arthritis (n=12) (Figure 1a). Most participants (n=38) had one or more current symptom of type 1 GD at the time of the survey, the most frequent being fatigue (n=30), enlarged liver (n=15), and enlarged spleen (n=14) (Figure 1b).

All but one survey participant was receiving some type of therapy as a treatment for type 1 GD at the time of this study (Table 2). The median age that individuals began treatment for type 1 GD was 38 years of age with an IQR of 21 to 50 years old and responses ranging from one to 62 years of age. Thirty-two of the 47 participants (68%) reported currently using ERT via intravenous infusions (Table 2). Twenty-seven of 32 ERT users reported using ERT for more than five years (84%) and none of these participants had been using ERT for less than one year. Twenty-four of the 32 ERT users (72%) reported being offered SRT by a physician in the past.

Fourteen of the 47 total participants (30%) reported currently using SRT (Table 2). Fifty-seven percent of these SRT users (n=8) had been using SRT for less than one year, while the other six had been using SRT for more than one year. Though SRT is only recently clinically available, one participant started SRT as an investigational therapy prior to this therapy and, as such, had been using SRT for more than five years. Additionally, all but one SRT user (n=13, 93%) had used ERT in the past. Twelve of these 13 current SRT users (92%) had used ERT for more than one year before changing treatment methods to SRT.

Figure 1 - Medical History Information of Survey Participants

(a)



(b)

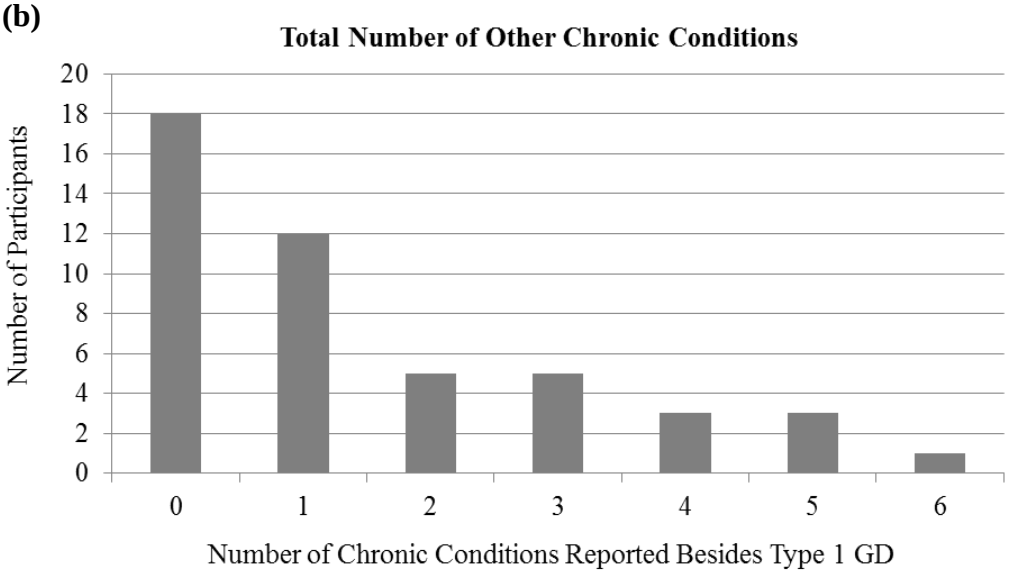


Figure 1 - (a) Frequency chart for different number of symptoms of type 1 GD that were reported by survey participants **(b)** Frequency chart for different number of chronic conditions reported besides type 1 Gaucher disease by participants

Table 2 - Current Treatment Method and Length of Therapy Use

Current Treatment Method	n	%
ERT	32	68
Less than 1 year	0	0
Between 1 and 5 years	4	13
More than 5 years	27	84
Did not indicate length of therapy	1	3
SRT	14	30
Less than 1 year	8	57
Between 1 and 5 years	5	36
More than 5 years	1	7
No current treatment	1	2

Reactions Toward SRT

Individuals currently using ERT that had been offered SRT in the past by a physician (n=24) were asked what reasons contributed to their decision not to use SRT (Table 3). Free responses to this question were parsed and categorized into four themes including potential or experienced side effects of SRT (n=13), satisfaction with ERT (n=8), feeling as though there is not enough research on SRT (n=6), and not having time to do candidate testing for SRT (n=1). Due to the open-ended nature of the response, at times, more than one theme was applicable to an individual participant.

Thirteen individuals currently using SRT were asked what reasons contributed to their decision to use SRT (Table 4). Free responses to this question were categorized into five themes: convenience of SRT (n=7), less invasive than ERT (n=4), reaction to ERT (n=2), continued SRT

after FDA study (n=1), and recommended by a doctor (n=1). Similar to the other open-ended item, more than one theme was occasionally applicable to an individual.

Table 3 - Reasons Cited for Declining SRT

Reason Cited	Frequency	Selected quotes from participants
Side effects of SRT	13	"The possibility of [side effects]…"
Satisfaction with ERT	8	"My physician offered [SRT] as something to think about, but I chose not to consider it because ERT works so well for me."
		"I prefer to have an infusion [every] 14 days than taking tablets every day."
Not enough research on SRT	6	"I feel like [SRT] is being pushed on us, which makes me uneasy…. The drug is too new…."
Have not had SRT candidate testing	1	"[I] have not had time to do extra [metabolizer status] tests."

Table 4 - Reasons Cited for Using SRT

Reason Cited	Frequency	Selected quotes from participants
Convenience	7	"It is very convenient to take [SRT] because I can take pills instead of driving to a facility to take [ERT]."
Less invasive/Hate needles	4	"Less invasive than ERT; less interference with lifestyle."
Reaction to ERT	2	"[I] developed a serious allergic reaction to [ERT] after many years on it without any problems."
Continued after FDA studies	2	"I joined an SRT drug study during the ERT shortage and stayed on SRT after FDA approval."
Doctor recommended	1	"My doctor recommended [SRT]."

HRQoL in ERT and SRT Current Users

When compared to median PCS and MCS for normative 2009 SF-36v2® Health Survey data concerning United States adults which are 53.07 and 52.94, respectively, median PCS and MCS for current SRT users were slightly lower ($p < 0.001$ and $p = 0.014$). The median PCS resulting from the SF-36v2® Health Survey for the 32 current ERT users was 48.16 (IQR of 41.48 to 53.66), while the median PCS was 49.29 (IQR of 39.37 to 55.53) for the 14 current SRT users (Figure 2a). No statistically significant difference in PCS was observed between current ERT and current SRT users ($p = 0.756$). The median MCS for current ERT and current SRT users were 50.68 (IQR of 43.76 to 55.76) and 50.08 (IQR of 42.93 to 54.67), respectively (Figure

2b). Similarly, no significant difference in MCS was discerned between these two treatment groups ($p = 0.650$).

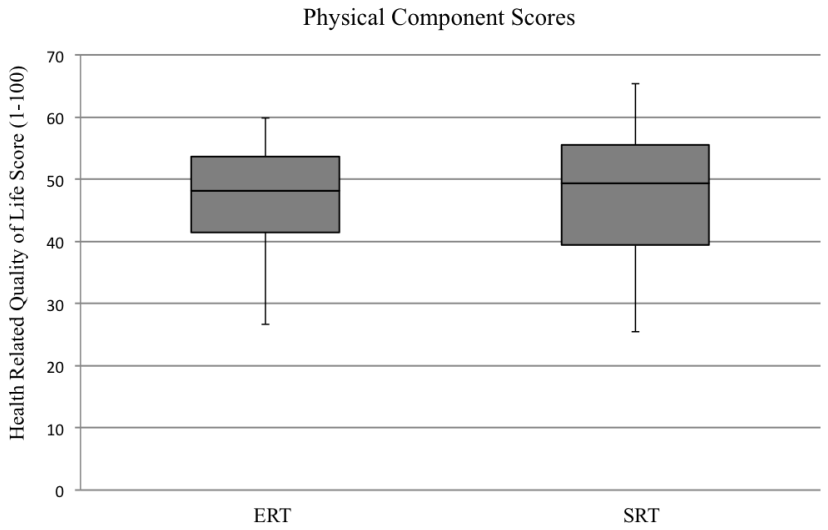
When PCS and MCS for all users were stratified by sex, income, education, marital status and number of other chronic conditions excluding type 1 GD, no statistically significant influence on PCS and MCS for HRQoL was observed. The number of symptoms related to type 1 GD that a participant experienced was statistically associated with a negative influence on PCS ($p < 0.001$) and MCS ($p < 0.001$). Furthermore, while no association of age and PCS was observed ($p = 0.103$), there was a correlation observed concerning increased age and increased MCS ($p = 0.003$).

Perceived Changes in HRQoL in SRT Sample

Twelve current SRT users who reported using ERT in the past responded to items comparing their perceptions of health for both treatments with regard to five health categories: "general health", ability to complete everyday activities or "physical ability", "emotional health", "social interactions", and "satisfaction with life". More than half (n=7) of the current SRT users report no difference in their perception of health while using SRT as compared to ERT with regard to general health, emotional health, social interactions, and satisfaction with life. Two-thirds (n=8) of current SRT users report no perception of difference in health between therapy options with regard to physical ability (Figure 3). Between one and two current SRT users per health category reported having a somewhat better or much better perception of health while using SRT as compared to when using ERT. Two participants reported experiencing much worse health while using SRT than when using ERT for each of these five health categories. These two participants both indicated in free response items that their only reasons for using SRT were that they "hate needles" and that they experienced side effects of SRT.

Figure 2 - Physical and Mental HRQoL Component Scores by Therapy

(a)



(b)

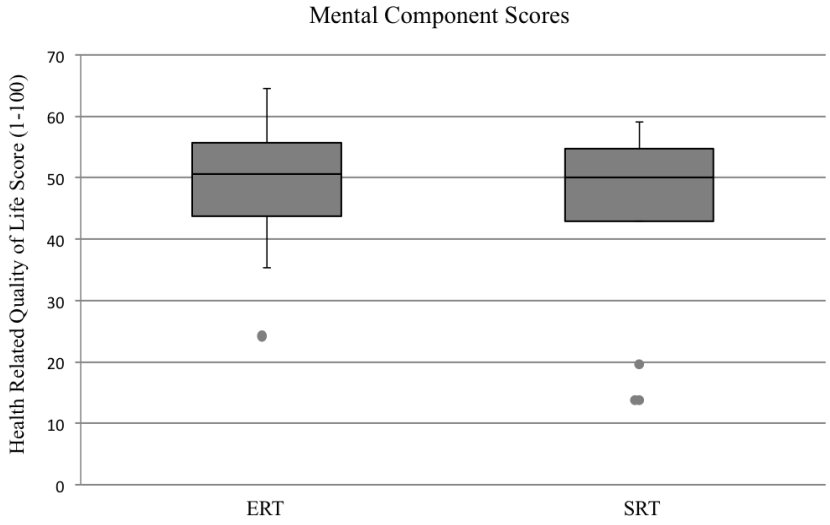


Figure 2 - (a) Boxplot of SF-36v2® Health Survey PCS of current ERT and SRT users by therapy **(b)** Boxplot of SF-36v2® Health Survey MCS of current ERT and SRT users by therapy

Figure 3 - Perceived Changes in HRQoL in SRT Users who Used ERT in Past

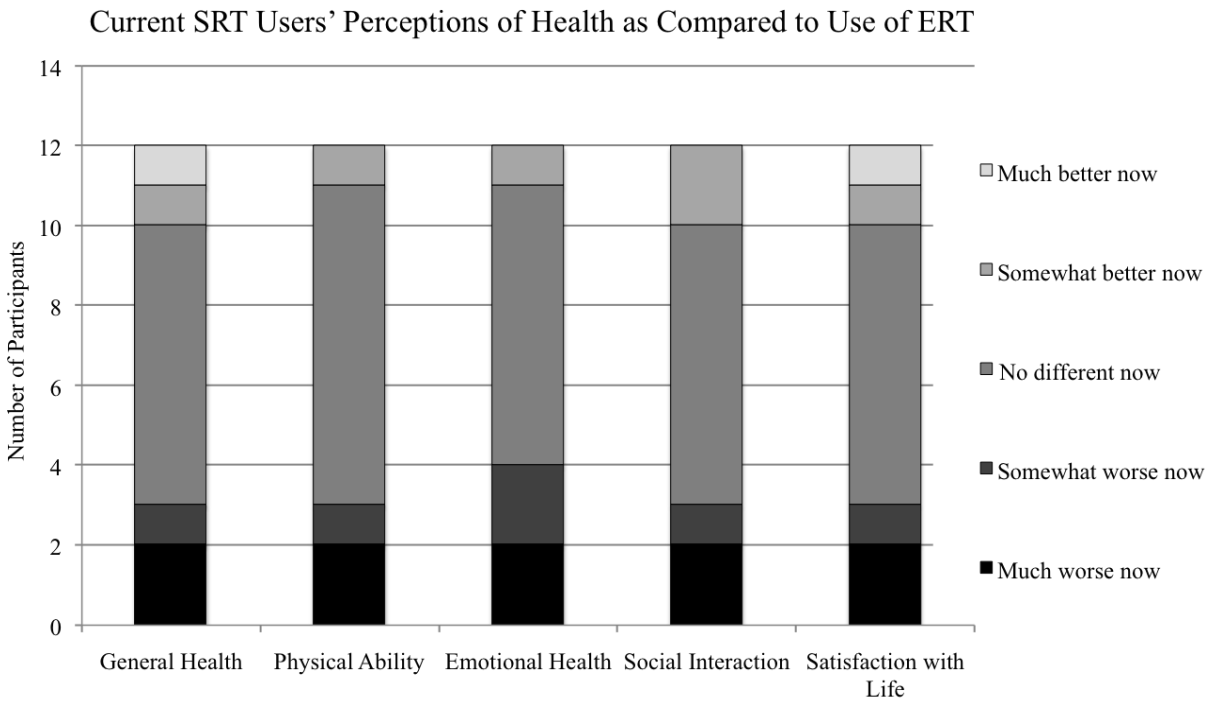


Figure 3 - Stacked column chart of SRT users' perceptions of current health as compared to health during past use of ERT

DISCUSSION

GD is the most common inherited LSD, affecting approximately 1 in every 60,000 to 100,000 people worldwide [Meikle et al, 1999; Poorthuis et al, 1999]. Treatment for type 1 Gaucher disease has traditionally been administered in the form of ERT via biweekly intravenous infusions. However, in August, 2014, an oral SRT was approved by the FDA for clinical treatment of type 1 GD. While evidence in the literature suggests that the use of ERT improves HRQoL for individuals with type 1 GD, no study to date has investigated the HRQoL of those using SRT as a therapy for type 1 GD [Damiano et al, 1998; Masek et al, 1999; Weinreb et al, 2007].

The most common reasons current ERT users declined the use of SRT were potential or experienced side effects and satisfaction with ERT. Previous research of therapy preferences in chronic inherited conditions, such as hemophilia, have shown that risk of side effects are a major factor in patient preferences for a particular therapy [Scalone et al, 2009; Mohamed et al, 2011; Chaugule et al, 2015]. This study shows that the risk of side effects as a marker for therapy preference extends to patients with type 1 GD that considered the switch from ERT to SRT. The idea that individuals who were satisfied with their use of ERT and, perhaps, were comfortable with the routine of their bi-weekly intravenous infusions was not a surprising one, especially considering that greater than 84% of current ERT users had been using ERT for more than five years. However, it was unexpected that two current ERT users perceived having an intravenous infusion of ERT every 14 days as more convenient than taking oral tablets as treatment for type 1 GD. These results are possibly a reflection of patients' preferences for course of treatment. If so, this may be reminiscent of the resistance to new therapies in the context of other medical conditions. An investigation of patient preferences for treatment of chronic hematological

conditions showed that even if new treatments become available, a large percentage of patients feel uncertain about or refuse change in treatment [Renzi et al, 2015]. Additionally, research regarding patients with β-thalassemia found that this population may be resistant to switching from intravenous infusions to oral therapies, perhaps due to conflicted feelings of trying a new therapy when they are satisfied with a current treatment method [Trachtenberg et al, 2014].

The most common reasons current SRT users cited as contributing to their decision to use this therapy were convenience and the less invasive nature of SRT. Due to the difference in the route of administration for ERT and SRT, convenience and less invasiveness were predicted advantages that current SRT users would cite as reasons for using this new therapy for type 1 GD. Other SRT users mentioned continuing SRT after the FDA clinical trial because this therapy was effective or that their doctor recommended this type of therapy. These findings mirror reasons why other patient populations, including those with multiple sclerosis, have switched therapies in the past. A study of individuals receiving treatment for multiple sclerosis in 2014 revealed that the main reasons cited for switching therapies was because a doctor recommended the new treatment or because the patient perceived it as an effective treatment option [Salter et al, 2014].

Median PCS and MCS for individuals using SRT to treat type 1 GD were slightly lower than median PCS and MCS for United States adults who took the SF-36v2® Health Survey in 2009. Previous studies revealed that individuals with type 1 GD have lower HRQoL than average and that people with type 1 GD using ERT have increased HRQoL as compared to those not receiving treatment [Damiano et al, 1998; Masek et al, 1999; Weinreb et al, 2007]. While we did not specifically compare the HRQoL of current SRT users to those with the type 1 GD that are not receiving treatment, it is possible that current SRT users may have decreased HRQoL as

compared to adults without type 1 GD since these individuals still experience a rare and chronic medical condition that necessitates treatment.

No significant difference in PCS or MCS between current ERT and SRT users was observed. The use of SRT was hypothesized to increase HRQoL above that of individuals using ERT to treat type 1 GD since it is considered by many to be a more convenient and less invasive type of therapy. This hypothesis was not confirmed by this data; however, our findings are substantial in the investigation of SRT as a newly approved therapy for type 1 GD. This is due to the demonstration that SRT is, on average, just as effective at maintaining HRQoL in individuals with type 1 GD as ERT. Moreover, current SRT users that used ERT in the past most often reported no difference in their perception of different aspects of health when asked to compare their current health to their health while using ERT. Although self-perceptions of health are subjective to the individual, it was unexpected that the majority of current SRT users would perceive no difference in these categories related to HRQoL with respect to the two treatment options. Of note, two of the 12 respondents for this set of items indicated that each of the five aspects of their health inquired about were "much worse now with SRT" than when they used ERT in the past. These two participants also commented that they experienced side effects related to SRT. While the convenience of SRT may be an attractive component of this treatment method, if individuals with type 1 GD experience side effects related to their therapy, this may not be the ideal treatment regimen for these patients.

The study offers considerable strengths relevant to the interpretation of these findings. Of great importance is that this is the first study to address the potential influence of SRT for type 1 GD on HRQoL, rather than the purely physiological parameters of other research regarding this novel treatment option. This report is also the first to address participants' perceptions of why

individuals have chosen or declined the use of SRT for type 1 GD in comparison to the traditional intravenous infusion of ERT. Additionally, this study was administered electronically and, therefore, had participants from across the United States and other countries. This part of our study design was intentional in order to eliminate the potential sample bias of patients with type 1 GD at a single treatment center.

Despite these strengths, there are also some limitations with regard to the results of this study. The number of participants that were current SRT users is small and greater numbers of current SRT users with type 1 GD would be desired to corroborate these findings in a bigger sample. While a large sample size is ideal, type 1 GD is a rare disease and, since SRT has only been clinically available outside of FDA drug trials since August 2014, there are few members of the GD community currently using SRT. Because SRT is only available to adult patients, there is the possibility for a larger population to better assess the effects of SRT on HRQoL in the future as younger patients with type 1 GD become adults and potentially elect SRT. Another potential bias for this study is that many of the participants were recruited from GD electronic support forums and the National Gaucher Foundation membership. Selecting study participants from electronic information and support communities may introduce a sample bias if the responses of these participants are not comparable to that of the average adult with type 1 GD [Gawlinski et al, 2009]. Our group corrected for this possible bias by extending invitations to participate to patients of medical geneticists and metabolic genetic counselors that have type 1 GD. Despite this, participants were not asked to report how they learned about this study so a reliable response rate from different participant sources cannot be calculated. Lastly, our sample had a large proportion of participants that were Caucasian, well educated, and financially successful. While this may be representative of the type 1 GD population in general as compared to the

average adult in the United States, this sample makeup could also potentially introduce influence on the results of this study.

Another important aspect of this study's analysis is that the SF-36v2® Health Survey was administered at only one point in time to each participant. Therefore, while current SRT users were asked to compare various aspects of their self-perceived health as compared to when using ERT, a more precise comparison regarding the effect of SRT on HRQoL may be obtained in a study that collects HRQoL scores at various points in time for ERT users with type 1 GD that switch to SRT. This proposed methodology would allow for matched statistical comparison for individuals that have used both therapies and also allow for HRQoL comparison depending on how long participants have used a certain therapy for type 1 GD. Finally, there is no way to account for all of the factors that may influence someone's HRQoL. Analysis of sex, income, education, marital status, and number of chronic conditions other than type 1 GD showed no statistically significant association with or influence on HRQoL scores for current ERT or current SRT users. Unsurprisingly, the higher number of symptoms someone experienced as related to type 1 GD was associated with a lower PCS and MCS. Increase in age also showed a slight association with increase in MCS within our sample. This is not a typical observation in the general population but is one that has been seen in individuals with some chronic mental health disorders [Folsom et al, 2009]. Despite these findings, the small sample size limited the use of larger multivariable analytic models adjusting for various factors. Furthermore, it is possible that a factor not accounted for in this survey could influence the PCS and MCS and, therefore, the HRQoL of all participants.

Overall, the results of this study propose that there is no significant difference in HRQoL between current ERT and current SRT users for type 1 GD. This is in addition to previous

literature showing that the efficacy of SRT to treat physical symptoms of type 1 GD is comparable to traditional ERT [Kamath et al, 2014; Lukina et al, 2014; Poole, 2014; Mistry et al, 2015]. Based on this evidence, the effects of SRT on the individual appear to be similar to those of ERT unless patients experience side effects related to therapy that could reduce HRQoL. Furthermore, many patients that use either ERT or SRT cite a variety of reasons, many of which are individualized, for why they may prefer their current treatment to another option. Together, these findings suggest that individuals with type 1 GD should be thoroughly counseled about the risks and benefits of both forms of therapy when beginning treatment or establishing care for this condition.

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