Disease management in pediatric lupus: could it pose a burden?

Aims: To identify disease management-related activities that could pose a burden to patients with systemic lupus erythematosus (SLE) and their families. **Methods:** The rheumatology charts of 20 pediatric patients diagnosed with SLE were retrospectively reviewed. One patient evolved into a connective tissue disease picture and was thus excluded from the analysis. The charts were examined to identify the following disease management activities that are required of patients and families during the first 2.5 years after diagnosis: medications used, pediatric rheumatology clinic appointments, laboratory tests, and out- and in-patient diagnostic tests completed. **Results:** Nineteen children had a median age of 14 years (range: 9–17 years). An average of seven medications per interval was used in the first two intervals and did not vary significantly in the third, fourth and fifth intervals. The most common immunomodulating agent prescribed was hydrocholorquine. Mycophenolate mofetil use increased after the first interval. An average of five pediatric rheumatology clinic appointment visits were documented during the first 6-month interval. The average number of appointments decreased over time. The median number of unique days on which laboratory tests were obtained during the first interval was eight and decreased during the time examined. The median number of diagnostic tests fluctuated from zero to two per interval. The median number of unique days on which patients had to go in for tests varied between zero and one during the study. **Conclusion:** Children with SLE are required to take several medications on a daily basis and undergo multiple appointments and testing. Larger prospective studies are needed to further conceptualize the burden of SLE, and describe how burdens relate to clinic appointment and medication adherence. Understanding these issues will aid the development of comprehensive, family-centered treatment that will ultimately optimize health outcomes for these patients.

KEYWORDS: burden ■ pediatric ■ SLE management ■ systemic lupus erythematosus

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Background

Pediatric systemic lupus erythematosus (SLE) is a chronic, fluctuating disease associated with significant organ damage and impaired health-related quality of life [1]. The complex medical treatment needed to manage SLE is time consuming and often requires multiple medications, frequent laboratory monitoring and numerous subspecialty appointments. There is a paucity of information concerning the burden these disease management-related activities could pose to patients and their families. A retrospective chart review was conducted to gain preliminary insight into the activities required for SLE management, and to identify directions for future study through recognition of the possible burdens these activities could present to these young patients and families.

Methods

The rheumatology charts of 20 pediatric patients diagnosed with SLE from 2000 to 2008 were retrospectively reviewed. All patients were treated at the University of Medicine and Dentistry of New Jersey (UMDNJ)–Robert Wood Johnson Medical School in New Brunswick (NJ, USA). The charts were examined to identify the following disease management activities that are required of patients and families: medications used, pediatric rheumatology clinic appointments, laboratory tests and out- and in-patient diagnostic tests completed. Specific demographic information was also collected, including age at diagnosis, ethnicity, gender, primary language, immigration status and immediate family relationships. No charts were eliminated owing to missing data; however, one patient evolved into a connective tissue disease picture, and was thus excluded from the analysis.

The authors initially examined the first 4 years of diagnosis, but later limited their review to 2.5 years owing to missing data and transition to adult rheumatology. The first 2.5 years after SLE diagnosis were divided into five 6-month intervals. Intervals one through five represent the following time points: 0–6, 6–12, 12–18, 18–24 and 24–30 months. Charts with insufficient follow-up data were excluded from a study interval.

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Procedure

Institutional Review Board approval was obtained through UMDNJ. Subjects were selected based on a diagnosis of SLE made by a pediatric rheumatologist. The charts were reviewed by a medical student and a pediatric resident not involved in the diagnosis or treatment of the patients. All variables were first recorded on a data sheet, and later entered into a database for analysis.

Disease management-related activities examined

Medication usage

The total number of medications prescribed per patient was recorded, with emphasis on oral corticosteroids and immunomodulators. Immunomodulators examined included cyclophosphamide, rituximab, hydroxychloroquine, tacrolimus, azathioprine, methotrexate and mycophenolate mofetil. Nonsteroidal anti-inflammatory drugs were excluded as a category because many patients take these medications on an as-needed basis. Medications that were discontinued during the interval were still counted in the total number of medications taken per 6-month period. The percentage of patients who used each immunomodulator per interval was determined by combining the number of patients who currently used and those who discontinued use of a given medication.

Clinic, laboratory blood & diagnostic tests & appointments

The average number of appointments attended for rheumatology clinic, outpatient/inpatient laboratory diagnostic tests was reviewed. Appointments for pediatric rheumatology were identified from the UMDNJ's computerized database and in some cases supplemented by chart review. Diagnostic tests included non-blood diagnostic procedures, including pulmonary function tests, echocardiograms, imaging studies and organ biopsies.

Data analysis

Using the SPSS statistical package (SPSS Inc., IL, USA, version 16) for Microsoft Windows® (Microsoft Corp. WA, USA) initial descriptive analysis was performed on all variables. Categories were examined for mean, median, standard deviation and range. The small sample size did not support the rigor of parametric testing for correlation or regression analysis.

Results

Demographic information

Out of the 20 patients, 11 had either intermittent lack of insurance or inadequate insurance, and nine had insurance for the period studied. Out of 20 patients, one patient evolved into connective tissue disease and was excluded from analysis. The median patient age at first visit for the 19 patients was 14 years (range: 9–17 years). Thirteen patients were female and 14 children were nonwhite. Seven children spoke a language other than English (Spanish = 6; Urdu = 1), but all these children were English speaking. Ten children lived in a home with both parents. There was an average of two siblings per patient. Three children were undocumented immigrants.

Table 1. Medication usage.

Medication use†	I1	I2	I3	I4	I5
Total medications (mean ± SD [n])	7 ± 4 (19)	7 ± 4 (18)	8 ± 4 (17)	6 ± 3 (15)	6 ± 3 (13)
Oral corticosteroid‡ (n [%])	17 out of 19 (90)	16 out of 18 (89)	15 out of 17 (88)	13 out of 14 (93)	13 out of 13 (100)
Cyclophosphamide‡ (n [%])	4 out of 19 (21)	5 out of 18 (28)	6 out of 17 (35)	5 out of 15 (33)	4 out of 14 (29)
Rituximab‡ (n [%])	0	0	1 out of 17 (6%)	1 out of 15 (7%)	1 out of 14 (7%)
Hydroxy-chloroquine‡ (n [%])	14 out of 19 (74)	13 out of 18 (72)	14 out of 17 (83)	13 out of 15 (87)	12 out of 14 (86)
Tacrolimus‡ (n [%])	0	0	1 out of 17 (6)	1 out of 15 (7)	2 out of 14 (14)
Cyclosporine (n [%])	1 out of 19 (5)	1 out of 18 (6)	1 out of 17 (6)	1 out of 15 (7)	0
Azathioprine‡ (n [%])	1 out of 19 (5)	2 out of 18 (11)	2 out of 17 (12)	3 out of 15 (20)	3 out of 14 (21)
Methotrexate‡ (n [%])	3 out of 19 (16)	3 out of 18 (17)	2 out of 17 (12)	3 out of 15 (20)	3 out of 14 (21)
Mycophenolate mofetil‡ (n [%])	1 out of 19 (5)	7 out of 18 (39)	7 out of 17 (41)	8 out of 15 (53)	7 out of 14 (50)
Thalidomide (n [%])	1 out of 19 (5)	1 out of 18 (6)	1 out of 17 (6)	0	0

I1–I5 represents the five 6-month intervals examined.
†Thalidomide was used by one patient (5%) during the first 18 months of diagnosis.
‡Indicates the number of patients who were currently using or had discontinued use of the medication previously.
I: Interval.

Table 2. Clinic, laboratory and diagnostic test appointments and attendance.

	Number of visits, mean ± SD (n)					Tests, median (range, n)				
	I1	*I2*	*I3*	*I4*	*I5*	*I1*	*I2*	*I3*	*I4*	*I5*
Rheumatology	5 ± 3.0 (19)	3 ± 1.7 (18)	3 ± 2.0 (18)	2 ± 2.0 (17)	2 ± 2.0 (16)					
Laboratory test days[†]						8 (2–16, 17)	4 (0–11, 15)	3 (0–19, 16)	3 (0–10, 14)	2 (0–8, 15)
Diagnostic (number of tests)[‡]						2 (0–9, 16)	0 (0–14, 13)	1.5 (0–5, 14)	0 (0–8, 13)	0 (0–4, 15)
Unique diagnostic test days[§]						1 (0–6, 15)	0 (0–11, 13)	1 (0–4, 14)	0 (0–4, 13)	0 (0–4, 12)

I1–I5 represent the five 6-month intervals examined.
[†]Unique days laboratory tests were obtained.
[‡]Diagnostic tests consist of all procedures other than blood tests, including pulmonary function tests, echocardiograms, radiology studies and organ biopsies.
[§]Unique days diagnostic nonlaboratory tests were obtained.
I: Interval; SD: Standard deviation.

Medication usage

An average of seven medications per interval was used in the first two intervals and did not vary significantly in the third, fourth and fifth intervals. The most common immunomodulating agent prescribed was hydrocholorquine. Mycophenolate mofetil use increased after the first interval. Detailed medication usage is summarized in Table 1.

Clinic, laboratory & diagnostic test appointments & attendance

An average of five pediatric rheumatology clinic appointment visits were documented during the first 6-month interval. The average number of appointments decreased over time. Patients saw several subspecialists, but these subspecialist appointments were not all within the authors' institution and, therefore, there is not an exact number per visit. Based on chart records, patients had appointments with the following specialties: cardiology, dermatology, ophthalmology, neurology, nephrology, endocrine, gastroenterology and pulmonary. The median number of unique days on which laboratory tests were obtained during the first interval was eight and decreased during the time examined. The median number of diagnostic tests fluctuated from zero to two per interval. The median number of unique days on which patients had to go in for tests varied between zero and one during the study.

Discussion

This retrospective chart review examined SLE disease management-related activities that may present a considerable burden to patients and caregivers during the first 2.5 years of treatment. The financial burdens presented by SLE [2], as well as the impact of disease-related variables on organ damage [3], have been previously explored. However, the extent of medication use and frequency of clinic appointments described in this study may contribute to our knowledge about the additional burdens that families must endure to facilitate proper SLE diagnosis and management for their children.

The numerous laboratory tests and clinic appointments required of patients probably pose a significant burden. Within the first 6 months of treatment at the authors' center, the charts reflected a median of 8 days during which children underwent laboratory tests, and an average of five pediatric rheumatology appointments per patient (Table 2). This represents a significant amount of time in which the patients and their families made accommodations for

travel, arranged alternate childcare for other siblings, missed work and missed school. The time burden is probably greater than examined, as this analysis did not account for visits to subspecialists or days spent at home secondary to SLE flare.

The ethnic and socioeconomic differences of this population could also contribute to disease burden. Others have shown that children with a primary language other than English have statistically significant differences in chronic disease management and health knowledge when compared with minority children with primary English fluency [4]. In the patients, the lack of insurance in a sizeable number of patients may also influence adherence. Although the limited size of the patient sample does not allow for statistical analysis of demographic factors, the relationship between disease burdens, language and ethnicity has important implications for healthcare practice and requires future study.

This study was limited by the retrospective design and small sample size. Data collection was restricted to the chart review and the date of diagnosis did not always correspond with the earliest available medical records. The authors' charts were only from the pediatric rheumatology department, and may have missed laboratory and/or diagnostic testing completed while the patients were hospitalized or at an outside institution. When available, we also included inpatient laboratory and diagnostic tests in our calculation. However, getting essential tests done while hospitalized is different from getting tests done as an outpatient; in both cases the burden imposed is slightly different. Additionally, the frequency and number of laboratory tests and investigations depend on SLE severity, organ system involvement and disease activity at that time. Different patients may require testing done at different intervals. Since SLE is multisystemic, it is often difficult to compare even stable patients. Both chart review

Executive summary

Background

- Childhood-onset systemic lupus erythematosus (SLE) is a chronic, unpredictable disease that can lead to organ damage and poor quality of life.
- Treatment for children with SLE requires complex management comprising of multiple medications, diagnostic testing, frequent laboratory monitoring and numerous subspecialty appointments.
- There is a paucity of information concerning the burden these disease management-related activities could pose to patients and their families.

Methods

- The rheumatology charts of 20 pediatric patients diagnosed with SLE from 2000 to 2008 were retrospectively reviewed. One patient evolved into a connective tissue disease picture and was thus excluded from the analysis.
- We limited our review to the first 2.5 years after SLE diagnosis and divided them into five 6-month intervals. Intervals one through five represent the following time points: 0–6, 6–12, 12–18, 18–24 and 24–30 months.

Results

- Our subjects were predominantly nonwhite teenage girls.
- An average of seven medications per interval were used in the first two intervals and did not vary significantly in the third, fourth and fifth intervals.
- The most common immunomodulating agent prescribed was hydroxycholorquine. Mycophenolate mofetil use increased after first interval.
- An average of five pediatric rheumatology clinic appointment visits were documented during the first 6-month interval. The average number of appointments decreased over time.
- The median number of unique days on which laboratory tests were obtained during the first interval was eight and decreased during the time examined.
- The median number of diagnostic tests fluctuated from zero to two per interval.
- The median number of unique days on which patients had to go in for tests varied between zero and one during the study.

Discussion & conclusion

- This retrospective chart review examined SLE disease management-related activities that may present a considerable burden to patients and caregivers during the first 2.5 years of treatment.
- In our study, we found that patients needed to take several medications on a daily basis and undergo multiple appointments and testing.
- Larger prospective studies are needed to further conceptualize the burden of SLE, and describe how burdens relate to clinic appointment attendance. Understanding these issues will aid the development of comprehensive, family centered treatment that will ultimately optimize health outcomes for these patients.

and electronic appointment attendance data had to be used to determine visits per interval, and that could lead to some inaccuracies. Depending upon the severity of disease some patients need to be seen more often than others and there is no standard by which we can compare these appointments. Lastly, owing to problems with retrospective data and lack of complete records the authors were unable to calculate missed appointments.

Medication adherence and other adherence-related variables were not consistently reported in the chart and could not be analyzed. Since this is a retrospective study, there are no formal assessments of disease activity and damage. The limited sample size prevented the use of parametric statistics for correlation coefficients and statistical significance. Additionally, inter-rater agreement was not calculated between the variables coded and entered by the resident and medical student. The limited time interval from 2008 to 2010 did not allow the authors to explore if other evolving connective tissue diseases or comorbidities contributed to the increased burden seen in individual patients. Despite these shortcomings, the depth of information examined gives us some insight into the profound impact of pediatric SLE on both patients and caregivers.

Conclusion

This pilot study is the first known to discuss how SLE disease management-related activates could present burden to patients and families. In our study, we found that patients needed to take several medications on a daily basis, and undergo multiple appointments and testing. Larger prospective studies are needed to further conceptualize the burden of SLE and describe how burdens relate to clinic appointment attendance. Understanding these issues will aid the development of comprehensive, family centered treatment that will ultimately optimize health outcomes for these patients.

Financial & competing interests disclosure

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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