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Limited Management of Systemic Erythematosus Lupus in Madagascar

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Abstract: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that involves multiple organs and has alternating periods of flare-ups and quiescence. SLE requires multiple paraclinical and therapeutic investigations that are not accessible by Malagasy patients. We aim to assess the monthly direct cost in SLE referring to international recommendations. The cost of paraclinical exams and treatment expenses were estimated as a percentage of the MMMS (Malagasy Minimum Monthly Salary). According to international recommendations, the cost of first-line paraclinical exams for SLE diagnosis was 274,2% of the MMMS. The costs of diagnostic tests were 110,9% and 923,4% of the MMMS to research renal and neurological damage, respectively. The monthly cost of pharmacological therapies ranged from 132,2% to 205,9% of the MMMS, depending on the severity of SLE. Clinical examination and affordable paraclinical exams were fundamental in our practice to manage systemic lupus erythematosus lupus. Appropriate recommendations for emergent countries should be come up.

Keywords: Systemic Lupus Erythematosus, Cost, International Recommendations

1. Introduction

Systemic lupus erythematosus (SLE) is a complex disease with variable presentations. Prevalence rates was 11 per 10 000 persons in Madagascar. SLE has alternating periods of flare-ups and quiescence [1]. Furthermore, SLE requires multiple paraclinical and therapeutic investigations. SLE is a chronic disorder, and the condition of patients with SLE may worsen if major organs are affected [2]. Over the last three decades, however, the diagnosis and management of SLE have improved; the 10-year survival rate has recently been estimated at about 90% [3]. This means that patients with SLE are living longer, and the burden of the disease at both the personal and societal levels is expected to increase [4].

Different therapeutic classes are used, alone or in combination in SLE: anti-malarial, non steroidal anti-inflammatory, corticosteroids, immunosuppressive agents and biotherapy [5, 6]. Data of direct cost in SLE are not available in Madagascar. Developed countries issue recommendations regarding SLE aren't constantly appropriate for emergent countries [1, 5]. We suggest some remarks concerning the management of SLE in Madagascar, taking account of scientific data, medical ethics, equality and equity. We assessed the monthly direct cost in SLE if we were follow international recommendations for the management of SLE.

2. Methodology

We estimated the cost of paraclinical exams and treatment

which are available in Madagascar, according to SLE damage. Then, we have estimated these costs as a percentage of the MMMS (Malagasy minimum monthly salary: 144 000Ar = USD 43). The cost of investigations for differential diagnosis was not evaluated.

3. Results

The cost of first-line paraclinical exams for SLE diagnosis was 274,2% of the MMMS. Table 1 shows the details of first-line paraclinical exams. Other paraclinical exams such as antibodies of soluble nuclear antigens, antiphospholipid antibodies, anti U1RNP and cryoglobulinemia are very rarely done in first time; the cost of these paraclinical exams was 229% of the MMMS (Table 2).

The costs of diagnostic tests were 110,9% and 923,4% of the MMMS to research renal and neurological damage, respectively. The cost of CT exam (head or abdominal CT, CT angiography) ranged from 173,6% to 347,2% of the MMMS. Head MRI was exceptionally made by Malagasy patients because its costs was 694,4% of the MMMS. Table 3 shows the details of paraclinical exams to research visceral damage.

The monthly cost of pharmacological therapies ranged from 132,2% to 205,9% of the MMMS, depending on the severity of SLE (Table 4). For patients with renal damage, the monthly cost of pharmacological therapies was 239% of the MMMS if we follow international recommendations. Du fait de la non disponibilité du MMF et de l'Azathioprine à Madagascar, the monthly cost of our own treatment regimen was 171% of the MMMS

Table 1. *Cost of first-line paraclinical exams.*

Designation	Cost/MMMS (%)
Blood count + ESR+ CRP	14,5
Creatininemia + Natremia + Kalemia	10,4
Serum protein electrophoresis	34,7
Fibrinogen	7
Proteinuria	3,4
HLM base	7
Antinuclear antibody	34,7
Anti-dsDNA antibodies	55,5
Complementemia	100
Thorax X-ray	7

Table 2. *Cost of second paraclinical exams.*

Designation	Cost/MMMS (%)
Antibodies of Soluble Nuclear Antigens	69,4
Antiphospholipid antibodies	69,4
Anti U1RNP	55,5
Cryoglobulinemia	34,7

Table 3. *Costs of paraclinical exams to research visceral damage.*

Designation	Cost/MMMS (%)
Renal damage	
Urine sediment	10,4
Proteinuria	3,4
Renal ultrasound	27,7
Renal biopsy	69,4
Neuropsychiatric damage	
EEG	41,6
Head CT	173,6
Head MRI	694,4
CSF analysis	13,8
Cardiac damage	
ECG	7
Doppler echocardiography	69,4
Respiratory damage	
PFTs/ DLCO	27,7
CT angiography	347,2
Digestive damage	
ALAT, ASAT, GGT, PAL	11,1
Abdominal ultrasound	27,7
Abdominal CT	173,6
Hematological damage	
Bone marrow	7
Hemostasis tests	9,7

PFTs: Pulmonary function tests
DLCO: Diffusion capacity for carbon monoxide

Table 4. *Treatment expenses.*

Designation	Usual dose	Monthly cost/MMMS (%)
Prednisone 20mg	50mg/j	39
Methylprednisolone inj 120 mg	500mg/j for 3days	39
Hydroxychloroquine	400mg/j	37,5
Cyclophosphamide	500mg/month	27,7
Methotrexate	10mg/week	7
Azathioprine	Not available	
Mycophenolate Mofetil	Not available	
Potassium	600mg/j	14
Calcium/Vitamin D	1000/800UI	14
Sunscreen		27,7

4. Discussion

Several international studies published in the past two decades have explored the impact of SLE on the health care system and society. In particular, cost-of-illness studies have attempted to estimate a cost for SLE management in North America, Europe and Hong-Kong [7, 8]. Despite high interest in SLE research, there is a lack of data on the cost of care of SLE especially in developing countries like Madagascar.

The SLICC criteria for SLE classification requires fulfillment of at least four criteria, with at least one clinical criterion and at least one laboratory criterion or biopsy-proven lupus nephritis with positive ANA or anti-DNA [9]. However, due to high cost of immunological examination, respectively, fifty four percent and 43% of SLE patients have been able to do AAN and anti-dsDNA antibodies according to a study enrolled in Department of Dermatology, University Hospital Joseph Raseta, Antananarivo, Madagascar. None of SLE patients with abnormal urinary sediment had kidney biopsy [10]. In our daily practice, we retain the diagnosis of SLE through physical and biological signs (accessible by our patients), with high specificity for this disease (Table 5).

Table 5. *Specificity and sensibility of each criterion for SLE [9].*

Criterion	Specificity (%)	Sensibility (%)
Malar rash/photosensitive rash/acute cutaneous lupus	80,1	65,2
Discoid rash	93,6	19,7
Oral ulcers	92,1	44,2
Nonscarring alopecia	95,7	31,9
Serositis	97,2	35,2
Arhtritis	43,6	79
Renal damage	96,4	32,9
Neurological damage	99,0	5,5
Hemolytic anemia	99,5	7,1
Leukopenia	94,8	46,4
Lymphopenia < 1500/mm3	81,6	49,0
Lymphopenia < 1000/mm3	94,7	17,0
Thrombocytopenia	98	13,5

To assess disease activity, the different scores such as SLEDAI, SLAM, ECLAM, BILAG [11] are not used in Madagascar due to the high cost of immunological tests. We value clinical signs and ESR to monitor SLE in routine practice. SLE is a chronic autoimmune disease which require long-term management and lifetime follow-up. Furthermore, during disease flares, the drug is very expensive. Background treatment and avoidance of predisposing factors help our patient to limit disease flares.

As recommended by the Task Force Panel of ACR recommendation 2012, all patients with clinical evidence of active lupus nephritis, previously untreated, should undergo renal biopsy (unless strongly contraindicated) so that glomerular disease can be classified by current ISN/RPS classification. In addition, disease can be evaluated for activity and chronicity and for tunular and vascular changes. However, the availability of renal biopsy is limited in Madagascar due to the lack of technical facilities. After the elimination of other cause of urinary sediment abnormalities and / or renal failure, the diagnosis of lupus nephritis was made. As recommended by the Task Force Panel of ACR recommendation 2012, the treatment is based in large part on the classification of type of lupus nephritis by these ISN/RPS criteria. For induction therapy, glucocorticoid (GC) IV for 3 days was combined with Mofetil Mycophenolate (MMF) or cyclophosphamide (CYC), followed by maintenance with MMF or Azathioprine with or not oral corticosteroid [12]. However, MMF and Azathioprine are not available in Madagascar. We adopt the following treatment regimen: monthly administration of CYC IV and GC IV followed by oral corticosteroids for the induction therapy (during 6 months) and once every 3 months for maintenance during 2 years.

Several studies showed that medical direct cost increases with the severity of SLE. SLE patients with flares, renal [13, 14], neuropsychiatric [15] or pulmonary damage incurred higher direct costs. Madagascar minimum wage can't cover the treatment of SLE. All wages contributes to family monthly expenses, medical care take the last place. While we did not assess the indirect cost of SLE, it obviously would have an impact on the economy. The occurrence of disease flares increases the amount of absenteeism, which reduce the production yield.

The development of "Club Malagasy lupus" could help patients with SLE disease. Twinning with others associations could facilitate importation of drugs which are unavailable in Madagascar.

5. Conclusion

Appropriate recommendations for emergent countries should come up and studies focused on the cost/effectiveness should be carried out in developing countries like Madagascar. The improvement of initial and continuing medical education, emphasizing the interest and fundamental role of clinical examination and appropriate use of paraclinical exams should be enhanced.

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