Lupus nephritis: a nursing perspective

Sanma Jose

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Abstract

Lupus nephritis is a common complication of systemic lupus erythematosus (SLE), an autoimmune disease that targets organs such as the kidney. It affects more than 60% of lupus patients and is associated with significant morbidity and mortality. The clinical manifestation of the disease is unpredictable, ranging from no symptoms to serious proteinuria progressing to acute renal failure. Understanding the disease and its progress is vital for nurses to provide optimal care and education to the patient. This paper will discuss the mechanisms of disease and its clinical manifestations, classifications, diagnosis and management.

Keywords
Lupus nephritis, SLE, Kidney disease.

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by auto-antibody production and immune complex development in target organs such as the kidney, with resultant local inflammation leading to organ/tissue damage (Nowling & Gilkeson, 2011). Nephritis is a common complication of SLE affecting more than 60% of lupus patients, and is associated with significant morbidity and mortality (Chen & Fine, 2013; Wang, et al., 2012).

The prevalence of SLE is nine times greater in women than men. The incidence of SLE is two- to eightfold higher in non-European populations, predominantly those of African ancestry (Borchers, et al., 2012). In addition, 10–15% of people with lupus nephritis progress to chronic kidney disease (CKD) stage 5, needing renal replacement therapy and the five-year survival rate of nephritis patients is approximately 82%, whereas five-year survival rate for those without nephritis is 92% (Reyes-Thomas, et al., 2011). Lupus nephritis impacts the clinical outcome of SLE both directly, in the form of target organ damage, and indirectly, through adverse effects of therapy (Uchida & Nitta, 2012; Chen & Fine, 2013). Early treatment is beneficial in the prognosis of this disease, and it has been shown that late diagnosis of lupus nephritis is related to a higher frequency of renal insufficiency (Reyes-Thomas, et al., 2011).

Pathophysiology

Systemic lupus erythematosus is a chronic autoimmune disorder characterised by the production of auto-antibodies directed against nuclear and cytoplasmic antigens, affecting several organs such as the kidneys, joints, nervous system and haematopoietic organs (Fortuna & Brennan, 2013). Within the nephron, the glomerulus is the portion most frequently affected by lupus. Additionally, the renal interstitium and tubules, as well as the vasculature may also be affected (Mok, 2012; Alsuwaida, 2013). However, SLE is characterised by unknown aetiology and a multifactorial pathophysiology (Fortuna & Brennan, 2013).

Active lupus nephritis is an inflammatory response to immune complexes in the kidneys (Rovin & Parikh, 2014). The
mediators of inflammation (including complement, infiltrating leucocytes and cytokines), injure renal parenchyma and its networks. Inflammatory kidney injury results in the local release of kidney antigens via apoptosis and necrosis (Rovin & Parikh, 2014). These antigens, in combination with antigen-presenting dendritic cells, T cells and B cells are conditioned by intrarenal interferon-a (IFN-a) and other cytokines, which are likely to result in intrarenal creation of kidney-specific autoantibodies. This organ-specific autoimmunity may perpetuate kidney inflammation and cause future lupus nephritis flares. Therefore, treatment should focus on reducing inflammation of lupus nephritis and addressing organ-specific autoimmunity to prevent reactivation of lupus nephritis (Rovin & Parikh, 2014).

Classical of lupus nephritis

The current pathological classification criteria of the International Society of Nephrology/Renal Pathology Society (ISN/RPS) for lupus nephritis is based on severity of glomerular injury as determined by renal biopsy (Table 1) (Molino, et al., 2009; Weening, et al., 2004). Hence, the histopathological injury is divided into six classes based on the extent of morphologic lesions, severity, activity, and chronicity (Hanrotel-Saliou, et al., 2011).

• Class I: Minimal mesangial lupus nephritis
This is the mildest form of lupus nephritis and is characterised as normal glomeruli by light microscopy, but immune complex deposition are evident on immunofluorescence microscopy. Class I patients may not suffer from any renal signs and symptoms (Giannakakis & Faraggiana, 2011; Hanrotel-Saliou, et al., 2011).

• Class II: Mesangial proliferative lupus nephritis
This is defined by pure mesangial hypercellularity and immune complexes deposition by immunofluorescence microscopy. A few subendothelial deposits are visible by immunofluorescence, but not light microscopy (Giannakakis & Faraggiana, 2011). Class II patients may suffer from mild proteinuria, microscopic haematuria, and a favourable prognosis is more likely (Hanrotel-Saliou, et al., 2011).

• Class III: Focal lupus nephritis
This is defined by glomerular involvement in less than 50% of the glomeruli, whether it is segmental (part of the glomerulus) or global (the whole glomerulus). Class III also characterises between active — focal proliferative; chronic inactive — focal sclerosing; active and chronic lesions — focal proliferative and sclerosing lupus nephritis (Giannakakis & Faraggiana, 2011). Clinical manifestations are haematuria, proteinuria, a decreased glomerular filtration rate (GFR), nephrotic syndrome and occasionally hypertension (Hanrotel-Saliou, et al., 2011).

• Class IV: Diffuse lupus nephritis
In Class IV, lesions in the capillaries are similar to those in Class III, but involve more than 50% of glomeruli. It should be specified if the lesions are global (Class IV-G) or segmental (Class IV-S) and if there are active (A) or chronic (C) lesions or both (A/C) (Giannakakis & Faraggiana, 2011). The severity of symptoms is increased at this stage with severe haematuria and proteinuria in almost all patients, nephrotic syndrome, hypertension, and reduced GFR (Hanrotel-Saliou, et al., 2011). Acute kidney injury may develop in 16% of the patients (Hanrotel-Saliou, et al., 2011).

• Class V: Membranous lupus nephritis
This is defined as the deposition of subepithelial deposits, such as those seen in idiopathic membranous nephropathy. This can be associated with Class III or IV if intracapillary lesions

Appendix:

Table 1: Abbreviated International Society of Nephrology/Renal Pathology Society (ISN/RPS) Classification of lupus nephritis (2003)

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Minimal mesangial lupus nephritis</td>
</tr>
<tr>
<td>II</td>
<td>Mesangial proliferative lupus nephritis</td>
</tr>
<tr>
<td>III</td>
<td>Focal lupus nephritis a</td>
</tr>
<tr>
<td>IV</td>
<td>Diffuse segmental (IV-S) or global (IV-G) lupus nephritis b</td>
</tr>
<tr>
<td>V</td>
<td>Membranous lupus nephritis c</td>
</tr>
<tr>
<td>VI</td>
<td>Advanced sclerosing lupus nephritis</td>
</tr>
</tbody>
</table>

Indicate and grade (mild, moderate, severe) tubular atrophy, interstitial inflammation and fibrosis, severity of arteriosclerosis and other vascular lesions

a Indicate the proportion of glomeruli with active and sclerotic lesions

b Indicate the proportion of glomeruli with fibrinoid necrosis and cellular crescents

c Class V may occur in combination with class III or IV, in which case both will be diagnosed.

(Weening, et al., 2004)
are present along with subendothelial deposits in more than 50% of the glomeruli (Giannakakis & Faraggiana, 2011). Clinical manifestations are haematuria, proteinuria, hypertension, normal or slightly elevated plasma creatinine, nephrotic syndrome and renal failure is uncommon in Class V (Hanrotel-Saliou, et al., 2011).

• Class VI: Advanced sclerosing lupus nephritis

This refers to those rare cases in which at least 90% of the glomeruli show advanced global sclerosis without any residual activity (Giannakakis & Faraggiana, 2011; Molino, et al., 2009). Symptoms reflect a deterioration of those listed in Class IV and V.

Diagnosis

In diagnosing lupus nephritis, patients with SLE may be presumed to have nephritis on presentation with evident deteriorating renal function (Zubair & Frieri, 2013). It is necessary for patients with SLE to be routinely tested in order to identify any early signs of renal impairment such as reduced estimated glomerular filtration rate (eGFR), elevated serum creatinine, decreased serum albumin and elevated urine protein:creatinine ratio. Significant laboratory tests should be performed such as urea and creatinine levels; urinalysis for protein/ cell casts, and 24-hour urine collection and a morning void protein:creatinine ratio test to check for creatinine and protein concentration/excretion (Zubair & Frieri, 2013; Reyes-Thomas, et al., 2011). Hence, the primary management of SLE focuses on identifying any signs of worsening disease by monitoring anti-double-stranded DNA, creatinine clearance, complement levels, and erythrocyte sedimentation rate (ESR) or C-reactive protein (Zubair & Frieri, 2013; Borchers, et al., 2012).

Active lupus nephritis is considered as a 30% decrease in creatinine clearance, proteinuria >1000 mg/day patients, new onset of clinical symptoms or multiple episodes of nephritis, which is confirmed by renal biopsy (Hsieh, et al., 2012; Zubair & Frieri, 2013). With various histopathological findings conceivable in SLE patients, a biopsy will determine not only the diagnosis and prognosis, but will also guide management of this disease (Borchers, et al., 2012; Bhil, et al., 2006).

A retrospective study of 21 SLE patients with low levels of proteinuria (<1000 mg/day) who underwent renal biopsy showed that proliferative lupus nephritis was present in 57% of patients (Mok, 2012). Hence, the clinical presentation does not always correlate with the type and severity of renal biopsy histology (Hsieh, et al., 2012; Zubair & Frieri, 2013). However, in considering invasive renal biopsy, medical staff members weigh the risks of the biopsy procedure against the need for definite diagnosis, which may or may not result in inevitable renal disease (Bhil, et al., 2006).

Aims and goals of therapy and effect on the patient

Immunosuppressive treatments

According to American College of Rheumatology and Kidney Disease Improving Global Outcomes (KDIGO) guidelines, current treatment of lupus nephritis is based on two phases, initially an induction phase followed by maintenance phase. The inductive therapy induces remission in patients using rigorous immunosuppressive treatments, which often is a combination of medium to high doses of glucocorticoids and a cytotoxic drug for an introductory period of time (3–12 months) (Zubair & Frieri, 2013). Cyclophosphamide (CYC) is a synthetic antineoplastic drug which is effective and reliable in the induction phase. A randomised controlled trial at the National Institute of Health (NIH) provides strong evidence for the efficacy of intravenous (IV) CYC in this phase. Treatment with IV CYC with corticosteroid has been shown to be more effective and prevent more relapses than an IV CYC alone (Uchida & Nitta, 2012). During the induction phase, the response of the patient (both in regard to biochemistry and serological testing as well as symptoms) is monitored and the treatment is modified as necessary (Zubair & Frieri, 2013).

Other agents used in induction therapy include mycophenolate mofetil (MMF) which is a selective lymphocyte immunosuppressive agent; Azathioprine (AZA), an immunosuppressive antimetabolite, which is used to maintain remission and serves an important role as a corticosteroid sparing medication; and Rituximab, which is a B-cell depleting drug that has been shown to be effective in both proliferative and membranous lupus nephropathy (Gunnarsson & Jonsdottir, 2013; Punaro, 2013; Zubair & Frieri, 2013). Studies show that adverse events including infection were reported in patients while on therapy (Uchida & Nitta, 2012). The drugs are given intravenously during this phase and may cause nausea, vomiting, and diarrhoea. Pregnancy precautions should be instigated as MMF is teratogenic (causes embryo malformation), while AZA is considered to be relatively low risk of causing foetal abnormalities (Brochers, et al., 2012). Rituximab is ideally administered using cytotoxic precautions; however, this is reliant on specific hospital policies.

The second part of treatment, the maintenance phase, maintains the response towards pharmacological agents long term, by employing safer immunosuppressants for a 5- to 10-year period. The purpose of this therapy is to prevent disease progression and to have the least amount of chronic, irreversible renal scarring (Zubair & Frieri, 2013). Drugs such as MMF and AZA are effective in consolidating remission and preventing relapse. AZA is mainly a second choice when patients develop intolerance or contraindications to MMF.
Additional treatments for autoimmune diseases such as plasmapheresis may be considered; however, data from prospective controlled trials do not report any benefit of the use of plasmapheresis as efficacious treatment for lupus nephritis (Punaro, 2013; Uchida & Nitta, 2012). Efficacy of plasma exchange appears to be limited to the treatment of lupus patients with concurrent thrombotic thrombocytopenic purpura or catastrophic anti-phospholipid antibody syndrome (Punaro, 2013).

**Prevention of kidney disease for SLE patients**

1) **Anti-hypertensive:** Patients with Class I and II lupus nephritis normally have good prognoses and very rarely require aggressive treatment for their renal disease. However, optimal blood pressure (BP) control with angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) is necessary (Borchers, et al., 2012). Both these groups of drugs reduce intraglomerular pressure, lower systemic arterial BP, reduce proteinuria and, thus, delay the disease progression. A recent multi-ethnic US cohort study proved that the rate of renal involvement-free survival at 10 years is higher for patients treated with ACE inhibitors than those treated with non-ACE inhibitor group (Uchida & Nita, 2012; Griffin & Lightstone, 2013). Therefore, nursing staff should educate renal patients, particularly those with lupus nephritis on the importance of these medications (ACE-inhibitors or ARBs) and monitor their vital signs, especially BP with a goal of <125/75 mmHg in all patients with proteinuria (Griffin & Lightstone, 2013).

2) **Statins:** Analysis of large trials and meta-analysis suggests that dyslipidaemia aggravates the progressive decline of renal function in patients with CKD (Griffin & Lightstone, 2013). Evidence in the literature indicates that use of statins can reduce (plaque) inflammation, vascular stiffness and endothelial dysfunction. However, there are conflicts in the evidence regarding the merits of statins in CKD (Griffin & Lightstone, 2013; Chong, et al., 2011). The Study of Heart and Renal Protection trial about the use of statin therapy did not show any decrease in progression of renal failure but shows significant cardiovascular advantages (Griffin & Lightstone, 2013). Therefore, statin treatment should be given with the aim of reducing cardiovascular risk in accordance with the guidelines (Griffin & Lightstone, 2013; Chong, et al., 2011). Low cholesterol dietary intake and adequate exercise is also necessary in the treatment of hyperlipidaemia. This is relevant for all those with renal insufficiency, particularly those at increased risk due to SLE. If deterioration is inevitable or renal replacement therapy is required, patients will be educated on an individual basis. This article is based on prevention and early stages of lupus nephritis.

**Clinical manifestations and nursing interventions**

The presentation of SLE varies broadly, and therefore patients differ considerably with regard to their clinical and serological manifestations (Ginzler, et al., 2010). The clinical presentation of renal disease in SLE is unpredictable, ranging from no symptoms, “silent” lupus nephritis (trace proteinuria, active urinary sediments (microscopic haematuria, gross haematuria, cellular casts) and hyperlipidaemia) to more serious proteinuria (nephrotic syndrome) (Mok, 2012). Some patients may also develop unexplained non-specific symptoms, such as fever, fatigue, arthralgia, myalgia and weight loss, leading to acute nephritic syndrome with rapid progression to acute kidney injury (Fortuna & Brennan, 2013; Griffin & Lightstone, 2013). Rarely, patients may present with CKD, anaemia and hypertension as the initial signs (Mosca, et al., 2010; Mok, 2012). Regular monitoring of weight, blood tests which include urea and electrolytes, serum creatinine, full blood count and regular BP monitoring are the key nursing considerations. Nursing staff should perform 24-hour urine collection for creatinine clearance and protein excretion, and also urinalysis to identify haematuria, proteinuria and cellular casts (Griffin & Lightstone, 2013).

Patients undergoing kidney biopsy should be informed and made aware of the risks of the procedure as they have an additional risk of bleeding due to concurrent use of corticosteroids or platelet abnormalities (Bihl, et al., 2006). It is important any clotting dysfunction is identified and rectified prior to biopsy. This may require converting the patient from warfarin to short-acting heparin during this time. Aspirin and other non-steroidal anti-inflammatory drugs must be withheld prior to the procedure (Bihl, et al., 2006). Regardless of the risks, all patients having invasive procedures should be closely monitored for bleeding, internally by microscopic and macroscopic urine reviews, externally by monitoring for the presence of haematoma, and identifying alterations in baseline observations.

Comprehensive and timely nursing care will support patient management during all stages of renal dysfunction and assist in reviewing effectiveness (Punaro, 2013). Due to the extensive and complex nature of kidney disease and resultant multidisciplinary management plan, clear and effective communication is necessary between all members of staff. Extensive nursing management and rationales for care of the lupus nephritis patient is covered in Table 2.
Multidisciplinary team support

The nurses’ role as part of the team involves referring the patients to allied health professionals for continual review and education as discussed below:

1) Diet and nutrition: Patient should be on a low-salt diet as high-sodium intake increases albumin excretion and also amplifies the proteinuric effect of hypertension. A reduced-salt diet enhances the protective effects of ACE inhibition in patients with proteinuria (Griffin & Lightstone, 2013; Judd & Calhoun, 2015). Therefore, educating patients with renal disease on a low-salt diet is necessary to attain control over BP. Referral to the dietician is beneficial in individualising treatment and lifestyle adjustments (Judd & Calhoun, 2015).

2) Exercise: Patients suffering from lupus nephritis are at risk of obesity due to the use of steroids and decreased exercise tolerance due to lupus symptoms such as fatigue, arthralgia, and myalgia (Griffin & Lightstone, 2013). Obesity is causally linked to hyperinsulinemia, hypertension, and diabetes mellitus. Patients should be educated and encouraged to exercise and lose weight as evidence shows that exercise improves insulin sensitivity and leads to weight loss (Navaneethan, et al., 2009; Griffith & Lightstone, 2013). To achieve the target goal of weight loss, it is essential for patients to receive the ongoing support given by an exercise physiologist or physiotherapist and good dietary advice (Navaneethan, et al., 2009; Griffith & Lightstone, 2013).

3) Psychological support: Due to the possible rapid deterioration of the disease, patients with lupus nephritis are recommended to undergo lifestyle and dietary restrictions to manage their illness. These restrictions for all patients with kidney disease significantly impact on the social functioning of the patients, leading to anxiety and depression, preventing ability to cope, and adjustment (Finnegan-John & Thomas, 2012). Due to the impact an erratic and extensive disease has upon the patient’s lifestyle and health status, referral to social workers and psychologists is essential to provide counselling, ongoing review, support and education.

Prognosis

Lupus nephritis is the most common and severe complication of SLE and without consistent monitoring and possible renal replacement therapy, death is a possibility (Zubair & Frieri, 2013). Even though there are currently a variety of different treatment options available, only 50% of patients respond to these treatments and most of the treatments have consequences, which make them ill-suited for long-term use (Nowling & Gilkeson, 2011). However, there are many novel treatment options that are currently in the process of development and review, which may have the ability to limit the

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**Table 2**

<table>
<thead>
<tr>
<th>Nursing action</th>
<th>Rationale</th>
</tr>
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<tbody>
<tr>
<td>Monitor blood glucose level (BGL) and action</td>
<td>Steroids can affect insulin production, leading to high BGL</td>
</tr>
<tr>
<td>weight gain and report variations</td>
<td>Steroids can cause redistribution of adipose tissue, which could result in Cushingoid features</td>
</tr>
<tr>
<td>Observe patient for adverse effects due to increased steroid treatment</td>
<td>Steroids cause mood changes, psychiatric symptoms, hypertension, diabetes mellitus, depression, osteoporosis, hyperlipidaemia and growth retardation in children</td>
</tr>
<tr>
<td>Monitor serum electrolyte levels as directed</td>
<td>Reflects change in renal function</td>
</tr>
<tr>
<td>Educate patients regarding strategies to prevent infection</td>
<td>Patients are at increased risk of infection secondary to immunosuppressive medications</td>
</tr>
<tr>
<td>Monitor vital signs (heart rate, BP, respiratory rate and oxygen saturations) and report abnormalities</td>
<td>To monitor changes in clinical condition</td>
</tr>
<tr>
<td>Monitor fluid balance chart/urine output</td>
<td>To assess the impact on renal function</td>
</tr>
<tr>
<td>Monitor for fluid overload and symptoms</td>
<td>Due to side effect of SLE such as shortness of breath, pitting oedema, hypertension, and decreased urine output</td>
</tr>
<tr>
<td>Attend urinalysis</td>
<td>To monitor renal dysfunction including proteinuria (expected range of proteinuria is &lt;0.5 g/24 hours, with normal/near normal renal function), haematuria, colour and specific gravity</td>
</tr>
<tr>
<td>Utilise cytotoxic precautions</td>
<td>For staff safety during cytotoxic medication administration and patient care</td>
</tr>
<tr>
<td>Avoid nephrotoxic medications</td>
<td>To prevent further kidney damage</td>
</tr>
<tr>
<td>Provide medication education</td>
<td>To increase patient understanding, prevent side effects and monitor efficacy of treatment</td>
</tr>
</tbody>
</table>

(Liu, et al., 2013; Ross & Cetas, 2012; Griffin & Lightstone, 2013; Bertsias, et al., 2012)
progress of this devastating disease (Chen & Fine, 2013; Zubair & Frieri, 2013).

Conclusion
Immune complex accumulation in the kidney is the feature of lupus nephritis and triggers a sequence of events that result in kidney inflammation and injury. Corticosteroids and cytotoxic agents are the mainstay treatment for lupus nephritis, but are associated with significant morbidity and sub-optimal outcomes. Early diagnosis and treatment are necessary for favourable treatment results and nurses play a key role in their clinical care. Understanding the disease and the impact is vital for nurses in order to support patients and their families during the disease process.

References