



Complete Summary

GUIDELINE TITLE

Focal segmental glomerulosclerosis: treatment with steroids.

BIBLIOGRAPHIC SOURCE(S)

Thomas M. Focal segmental glomerulosclerosis: treatment with steroids. Nephrology 2006 Apr;11(S1):S182-4.

Thomas M. Focal segmental glomerulosclerosis: treatment with steroids. Westmead NSW (Australia): CARI - Caring for Australasians with Renal Impairment; 2005 Sep. 7 p. [17 references]

GUIDELINE STATUS

This is the current release of the guideline.

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SCOPE

DISEASE/CONDITION(S)

Idiopathic focal segmental glomerulosclerosis

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine

Nephrology
Pediatrics

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the available clinical evidence pertaining to the impact of steroid therapy on renal functional decline in patients with idiopathic focal segmental glomerulosclerosis

TARGET POPULATION

Adults and children with idiopathic focal segmental glomerulosclerosis

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment

Steroid therapy

MAJOR OUTCOMES CONSIDERED

- Proteinuria
- Renal function
- Response rate
- Clinical remission rate

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Databases searched: MeSH terms and text words for focal segmental glomerulosclerosis were combined with MeSH terms and text words for steroid therapy. This search was carried out in Medline (1966 to September Week 2, 2004). The Cochrane Renal Group Trials Register was also searched for trials in focal segmental glomerulosclerosis not indexed in Medline.

Date of searches: 17 September 2004.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level I: Evidence obtained from a systematic review of all relevant randomized controlled trials (RCTs)

Level II: Evidence obtained from at least one properly designed RCT

Level III: Evidence obtained from well-designed pseudo-randomized controlled trials (alternate allocation or some other method); comparative studies with concurrent controls and allocation not randomized, cohort studies, case-control studies, interrupted time series with a control group; comparative studies with historical control, two or more single arm studies, interrupted time series without a parallel control group

Level IV: Evidence obtained from case series, either post-test or pretest/post-test

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Recommendations of Others. Recommendations regarding treatment of focal segmental glomerulosclerosis with steroids from the following groups were discussed: Kidney Disease Outcomes Quality Initiative, UK Renal Association, Canadian Society of Nephrology, European Best Practice Guidelines, and International Guidelines.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the levels of evidence (I–IV) can be found at the end of the "Major Recommendations" field.

Guidelines

While remission may be induced in patients receiving steroids, there have been no level I or II studies confirming the efficacy of this intervention in the preservation of renal function in adults with primary focal segmental glomerulosclerosis (FSGS).

Suggestions for Clinical Care

(Suggestions are based on Level III and IV evidence)

- It is uncommon for patients with normal renal function and non-nephrotic proteinuria to progress to renal impairment. Consequently, steroid therapy in these patients is currently unjustified. Nonetheless, supportive therapy including aggressive control of blood pressure and dyslipidemia and blockade of the renin angiotensin system would seem prudent. In addition, long-term follow-up is still required to monitor for the development of adverse indicators including nephrotic range proteinuria and hypertension that could presage a more progressive course. (Level IV evidence)
- Some studies have shown that, independent of the degree of proteinuria, patients with renal dysfunction and/or interstitial fibrosis have a significantly decreased renal survival. (Level III evidence) This has led some to consider a trial of steroids in FSGS with renal impairment and non-nephrotic proteinuria in an attempt to induce remission. However, there are currently no studies to support this practice. In addition, nephrotic patients with renal dysfunction or interstitial fibrosis tend to be less responsive to therapy. At least some of these patients have secondary FSGS (see guideline titled "FSGS: cytotoxic therapy").
- Because of the desire to induce remission in patients with FSGS and nephrotic range proteinuria, it has been suggested that a 6-month trial of steroid therapy may be useful. Certainly, a prolonged course of steroids (using

- prednisone doses of 0.5–2 mg / kg / day) can induce remission in between 30% to 60% of patients. However, this intervention has not been tested in any randomized controlled trial (RCT), making the accurate interpretation of the utility of steroid therapy problematic. Moreover, many series of patients with nephrotic syndrome have included an unknown number of patients with steroid-reversible nephropathy apart from FSGS, including minimal change disease.
- The Regional Glomerulonephritis Registry Study prospectively followed 95 adult and paediatric patients with biopsy proven FSGS, for a mean of 61 months from the time of biopsy. The probability of remission with a long duration of therapy with corticosteroids (with or without cytotoxic drugs) was similar in adults (39%) and children (44%) with FSGS.
 - Another study also found remission could be induced with steroid therapy in older patients (more than 60 years of age) with FSGS. In this study, 4 of the 9 patients (44%) who received treatment with prednisone achieved complete remission for a median duration of treatment of 6 months, alone or combined with cytotoxic therapy. There were no relapses in those patients who achieved remission and none progressed to renal failure. No untreated patients had a remission and 9 of the 14 untreated or non-responders progressed. Ninety-six per cent of the patients who had a complete remission had preservation of renal function, whereas the probability of end-stage kidney disease (ESKD) was 45% in those who had not responded or who were not treated. Treatment with steroids may be effective in preserving filtration function in children with FSGS with heavy proteinuria (>3 g/day). (Level II evidence)
 - At least 7% of the children enrolled in the International Study of Kidney Diseases have FSGS (ISKDC). In this study, children were given daily corticosteroids in a dose of 60 mg/d/m²; (up to 80 mg/d) for 4 weeks followed by 40 mg/d/m² given on three consecutive days out of seven for 4 weeks and then tapered off over 4 more weeks. Many children developed remission, although many others had remission without a diagnosis of FSGS ever being made. Conclusions about the efficacy of comparative steroids in FSGS are difficult to make in the context of this study. Nonetheless, this regimen has become the standard treatment for childhood nephritic syndrome.
 - Another study reported a 50% response rate in a study of 16 adult patients with nephrotic syndrome and FSGS. Treatment consisted of 60 mg/day of prednisone for at least 1 month. Responses occurred by an average of 3.75 months (range: 1–10 months), and complete remission occurred at 5.75–6.75 months in the three patients who had complete remission.
 - Another study retrospectively reviewed the management of 59 patients with FSGS and nephrotic syndrome treated with corticosteroids and/or immunosuppressive drugs. Twenty-seven patients were initially treated with corticosteroids alone for 9.3 months; 19 patients received corticosteroids and immunosuppressive agents associated or every other month for 5.5 months; 13 patients received either azathioprine or cyclophosphamide alone for 25 months. At follow-up, 60% of patients had experienced complete or partial remission, most commonly after at least 8 weeks of treatment.
 - Another study followed 38 adult cases with biopsy-proven FSGS and nephrotic syndrome treated with prednisolone; 58% showed response (31% complete remission and 27% partial remission).
 - Another study reported a retrospective assessment of 60 patients with nephrotic syndrome and FSGS. Thirty patients received prednisone, at a total

- dose of more than 60 mg/day for a minimum of 2 months, followed by a tapering schedule over 5–6 months. Fifteen patients (50%) achieved a remission by 3.7 months (10 complete remission and 5 partial remissions), with all patients responding within 9 months. Remission was more common in patients who received a dose of 60 mg/day or more of prednisone for a longer period of time.
- Another study reviewed 32 patients with nephrotic syndrome due to FSGS treated with steroids alone. Forty-four per cent had complete remission, 12% partial remission and 44% no response.
 - Another study reviewed 80 nephrotic adults with FSGS and plasma creatinine lower than 3 mg/dL. Patients were given corticosteroids (53 patients) or immunosuppressive agents (27 patients) for a median of 16 and 75 weeks, respectively. Forty-two patients responded with complete remission (29 patients, 36%) or partial remission (13 patients, 16%). Twenty-six patients who did not respond were treated again. Two patients obtained complete remission and 13 a partial remission. Overall, 70% of nephrotic adults with FSGS obtained complete or partial remission and maintained stable renal function for about 10 years when given a prolonged therapy with corticosteroids or immunosuppressive drugs. Patients with collapsing glomerulopathy, a more rapidly progressive form of FSGS, were less responsive to steroids, if at all.
 - Another study reviewed their experience with 43 patients with collapsing FSGS and found that none of the 26 patients benefited from treatment with prednisone alone.

Some studies have suggested that patients with a glomerular tip lesion associated with FSGS may be more likely to respond to steroid therapy, than those with typical sclerosis or collapsing glomerulopathy. However, other studies have shown that steroid responsiveness, rather than histology, predicts good prognosis.

Overall, in those patients who do not receive steroid treatment or do not respond, the rates of progression to ESKD appear to be similar. Despite the of RCTs of corticosteroids in FSGS, it seems clear that following a prolonged course of corticosteroids some patients achieve and sustain a remission of proteinuria, that at the very least, has useful prognostic utility, whether or not it contributes to improved renal functional outcomes.

What Dose Should Be Used?

Most clinical studies have used prednisone doses of between 0.5 and 2 mg/kg/day to produce clinical remission. There is some evidence that doses of greater than 60 mg/day are more likely to induce remission than lower doses. In addition, alternate-day therapy (e.g., doses greater than or equal to 120 mg every second day) may be equally efficacious in FSGS and minimize toxicity. (Level III evidence)

What is the Optimal Duration of Treatment?

Prolonged therapy (of at least 6 months) appears to be important both to sustain remission as well as to induce it. (Level III evidence)

How to Define Steroid-Responsiveness?

Most steroid-responsive patients show some reduction in protein excretion within the first few months of therapy. The median time to clinical remission, when it occurs, is usually 3 to 4 months and most within 6 months of starting steroid therapy. It is therefore prudent that treatment should continue for at least 6 months before declaring the patient steroid-resistant. Although some patients will have remissions after this time, others have suggested that a lack of any decline in protein excretion at 8 weeks in children and 12 weeks in adults is generally indicative of steroid resistance. (Level IV evidence, anecdotal).

Definitions:

Levels of Evidence

Level I: Evidence obtained from a systematic review of all relevant randomized controlled trials (RCTs)

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Level III: Evidence obtained from well-designed pseudo-randomized controlled trials (alternate allocation or some other method); comparative studies with concurrent controls and allocation not randomized, cohort studies, case-control studies, interrupted time series with a control group; comparative studies with historical control, two or more single arm studies, interrupted time series without a parallel control group

Level IV: Evidence obtained from case series, either post-test or pretest/post-test

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of steroids in the management of patients with focal segmental glomerulosclerosis

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Apr

GUIDELINE DEVELOPER(S)

Caring for Australasians with Renal Impairment - Disease Specific Society

SOURCE(S) OF FUNDING

Industry-sponsored funding administered through Kidney Health Australia

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Author: Merlin Thomas

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All guideline writers are required to fill out a declaration of conflict of interest.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Caring for Australasians with Renal Impairment Web site](#).

Print copies: Available from Caring for Australasians with Renal Impairment, Locked Bag 4001, Centre for Kidney Research, Westmead NSW, Australia 2145

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- The CARI guidelines. A guide for writers. Caring for Australasians with Renal Impairment. 2006 May. 6 p.

Electronic copies: Available from the [Caring for Australasians with Renal Impairment \(CARI\) Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

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