Long term effectiveness of intravenous immunoglobulin in Churg-Strauss syndrome

M G Danieli, M Cappelli, G Malcangi, F Logullo, A Salvi, G Danieli

Objective: To study the long term effectiveness of intravenous immunoglobulin and plasmapheresis associated with prednisone and cyclophosphamide in Churg-Strauss syndrome.

Subjects and methods: We studied 18 subjects with new onset Churg-Strauss syndrome. All received the “standard” treatment based on prednisone (1 mg/kg/day for 1 month and then slowly tapered) and cyclophosphamide (2 mg/kg/day for 6 months in severe cases). In nine patients, synchronised cycles with plasmapheresis and intravenous immunoglobulin (2 g/kg) were repeated monthly for 6 months and every other month for a further three cycles. Clinical (disease activity monitored by Birmingham vasculitis activity score (BVAS) and damage index (modified Rankin score)) and functional (C reactive protein, blood eosinophil count, and electromyogram-electroneurogram) parameters were collected during treatment and the 3 year follow up period.

Results: After 12 months, all patients in the treatment group and four (44%) in the control group were in remission. At the end of the 3 year follow up period, we documented significant differences in BVAS (p<0.01), global damage (p<0.02), modified Rankin score (p<0.04), and the daily maintenance prednisone dose (p<0.002) between the two groups. We found a tendency towards lower frequency of relapse and incidence of osteoporosis in the treatment group.

Conclusion: Complete clinical and functional recovery with a long term stable remission and a low incidence of side effects can be achieved by intravenous immunoglobulin associated with plasmapheresis in patients with Churg-Strauss syndrome.

Churg-Strauss syndrome (CSS) is a necrotising vasculitis of medium and small sized vessels. The disease, firstly described in 1951 by the pathologists Churg and Strauss, is characterised by bronchial asthma, eosinophilia, and clinical evidence of systemic vasculitis associated with circulating antibodies to antineutrophil cytoplasmic antigen (ANCA). Corticosteroids and cytotoxic drugs are the cornerstone of therapy, and permit control of disease activity in the great majority of cases. However, half of the patients relapse within 2 years of achieving remission and experience substantial drug dependent morbidity. Moreover, neuropathy is present in about 95% of patients with CSS. Therapeutic approach to the CSS associated neuropathy is still unresolved and resolution of the disability remains a critical issue in this group of patients.

Effectiveness of intravenous immunoglobulin (IVIg) alone or as add on therapy has been evaluated in several types of ANCA associated vasculitis, and in various immune mediated neuropathies, even though its mechanisms remain only partially understood. Only case reports have been published on its use in CSS. Different mechanisms of action have been proposed to explain the beneficial effects of IVIg. The more relevant seem to be linked to an acceleration of the catabolism of the IgG antibodies.

Previous reports suggested that repeated plasmapheresis (PP) is effective against progressive and severe immune mediated diseases. The rationale underlying this approach is that PP removes humoral pathogenic substances from the circulation, and subsequent infusion of an immunosuppressant or an immunomodulatory agent prevents the consequent immune system rebound.

The aim of the present study was to evaluate the benefit and the safety of IVIg synchronised with PP in nine patients with CSS. Data were compared with those obtained with the “standard” treatment based on corticosteroids and cyclophosphamide.

METHODS

Patient selection

Between 1995 and 1999, nine consecutive patients were prospectively enrolled to receive IVIg synchronised with PP (treatment group). Subjects comprised patients who fulfilled the 1990 American College of Rheumatology criteria for Churg-Strauss syndrome. In all cases, the disease was newly diagnosed. Exclusion criteria included serious infections in the previous 6 months, known malignancy, and other concomitant severe or uncontrolled disease. All patients enrolled in this study provided informed consent to the treatment protocol approved by the institutional review board. Patients at risk of pregnancy were advised to use adequate contraception during the study period and for 6 months after the end of the treatment.

Nine patients with new onset disease and similar baseline characteristics (table 1), fulfilling the inclusion criteria of this study, receiving the “standard” treatment (as above) and prospectively followed in our centre, were selected from our institute database of 32 patients with CSS to form a control group. None of the patients in the groups received antileukotriene treatment for asthma.

Abbreviations: ANCA, antineutrophil cytoplasmic antigen; BVAS, Birmingham Vasculitis Activity Score; CSS, Churg-Strauss syndrome; EMG, electromyograph; ENG, electroneurograph; FFS, five factor score; IVIg, intravenous immunoglobulin; PP, plasmapheresis; SNVDI, Systemic Necrotising Vasculitis Damage Index
Clinical and functional assessment

To assess the systemic syndrome fully, we adopted a standardised protocol for clinical and functional evaluation. At each assessment, all of the patients underwent a complete medical history and full physical examination. The neurological assessment comprised the patient’s neurological history, a complete standard neurological examination, and electrodiagnostic studies. The functional state of the patients was clinically evaluated using the modified Rankin score.21

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Peripheral neuropathy was classified clinically as true mononeuritis multiplex, overlapping mononeuritis multiplex, asymmetrical polyneuropathy, and symmetrical sensorimotor polyneuropathy.22

The biochemical analyses included a full blood count (eosinophilia was taken as >10% eosinophils in the total white blood cell count), acute phase reactants (C reactive protein (CRP); normal <60 mg/l), creatinine, liver function tests, urine analysis and sediment, and 24 h urinary protein. Investigation of antibodies directed against ANCA was performed by ELISA for PR3-ANCA and MPO-ANCA antibodies.23

Other tests included pulmonary function; the diffusion capacity of the lung for carbon monoxide expressed as a percentage of the predicted value (TLCO); chest radiography and high resolution computed tomography. Electromyograph-electroneurograph (EMG-ENG) measurements were obtained with a Viking Nicolet II and IV electromyograph according to the standard techniques.24 Other examinations were carried out where clinically indicated.

Disease assessment

The Birmingham Vasculitis Activity Score (BVAS) was selected to evaluate the activity of the disease at study entry and during the follow up period.25 At the onset, according to Guillevin et al.,26 the five factor score (FFS) defined the patients with a poorer outcome. At the last assessment, the Systemic Necrotising Vasculitis Damage Index (SNVDI) was employed to score the severity of vasculitis.27 In one subject in the control group, these vasculitis scores were recalculated because they were not initially performed.

Treatment protocol

At the onset, patients received the “standard” treatment based on prednisone and cyclophosphamide. Prednisone was started at 1 mg/kg/day for 1 month and then tapered to the maintenance dose of 10 mg/day by month 6. Five and four patients in each group whose FFS and/or BVAS values were >1 and/or >20, respectively, or presenting clinical and functional signs of severe disease, received oral cyclophosphamide (2 mg/kg/day in two divided doses, one every 2 weeks).

Table 1 Baseline characteristics in 18 patients with CSS treated with a “standard” prednisone/cyclophosphamide treatment (treatment group) or without (control group) intravenous immunoglobulin synchronised with plasmapheresis. Five and four patients in each group (numbers 1–5 and 10–13), whose FFS values were >1, received oral cyclophosphamide for 6 months (see Methods for details)
adapted to the neutrophil count, together with prednisone) for 6 months.

In nine patients, synchronised therapy (monthly synchronised cycles of PP followed by IVIg infusion) was added to this “standard” treatment. Patients received PP (Cobe Spectra and Baxter CS-3000) 50 ml/kg, with 4% human albumin being the substitution fluid. The apheresis sessions were scheduled on days 1, 3, and 5 to avoid clotting disturbances. IVIg (lg vena N IV<sup>®</sup>; Sclavo, Siena, Italy) 1 g/kg was infused at 5 g/hour on days 6 and 7. In patients with renal or cardiac impairment, the rate of infusion was slower. This treatment was repeated monthly until month 6 and bimonthly for a further three cycles. Thereafter (month 18), patients who had improved received no therapy or a minimum prednisolone dosage to maintain remission (or to control asthma). Only one patient was treated with methotrexate (10 mg/week) as a steroid sparing drug.

In the control group, according to the clinical and/or laboratory response to treatment, patients were given a low dose corticosteroid.

**Endpoints**

The primary endpoints were: (a) the percentage of patients who achieved remission and (b) the global severity of the syndrome at the end of the follow up period. Remission was defined as the resolution of the clinical manifestations of CSS (not considering asthma) and of the eosinophilia, lasting at least 6 months. Minor neurological sequelae of neuritis could persist. The patient was considered to be in treatment free, sustained remission when remission was maintained for at least 18 months after discontinuation of treatment. The global severity of the vasculitis was assessed by the SNV-DI and the modified Rankin scores.

Predefined secondary endpoints were: (a) the number of relapses, defined as new clinical manifestation(s) of CSS after a remission period lasting 6 months or worsening of previous features (not including asthma or eosinophilia); (b) the mean corticosteroid dose necessary to maintain the remission; and (c) the incidence of treatment dependent side effects.

**Follow up**

In all patients, clinical status and laboratory parameters were evaluated and noted prior to the treatment, monthly until month 12 and bimonthly thereafter, or when clinically indicated. EMG-ENG was performed at the baseline and then repeated at months 8 and 12 and subsequently at least once a year. The type and severity of any adverse events were recorded. Osteoporosis was defined as a bone mineral density of more than 2.5 SD from the young adult peak mean.

**Statistical analyses**

Data collected in the clinical charts of the 18 patients were analysed using the NCSS statistical program.<sup>28</sup> Quantitative variables were expressed as median and nonparametric 95% confidence interval (CI). Owing to the small size of the samples, Mann-Whitney U test was used for intergroup comparisons. Comparison between frequencies was performed by Fisher’s exact test. Statistical significance was defined as p<0.05.

**RESULTS**

**Characteristics of the patients**

Table 1 shows the baseline characteristics and presenting features of the 18 patients with CSS. There were no significant differences between the two groups with the respect of the various demographic, clinical and serological features. All of the patients suffered from asthma, requiring continuous therapy.

Multisystemic involvement at the onset of the vasculitis process is detailed in table 1. In particular, when referred to us, five and three patients in the treatment group had involvement of the peripheral nerve manifested respectively as asymmetrical polyneuropathy and mononeuritis multiplex. One patient in this group had isolated right peroneal mononeuritis. The neurological pattern was similar in the control group. There was no difference in the baseline modified Rankin scores between the two groups (median 3; CI 2 to 4 in both groups).

Pretreatment median FFS and BVAS values were not different between the two groups. All patients had elevated CRP values (fig 1), with no intergroup differences. Positivity to MPO-ANCA was detected in four and five patients in the treatment and control group, respectively.

**Clinical course and response to treatment during the first 18 months**

From the start of the IVIg infusions, we documented a clinical and functional improvement that was complete or worthwhile at month 6 (fig 2). At month 12, all of the patients in the treatment group in comparison to four (44%) in the control group were in remission.

As for the neurological involvement, the modified Rankin score improved in all of the patients, except in two cases in month 6 (fig 2). At month 12, all of the patients in the treatment group had a statistically significant difference in the CRP serum levels from those treated with a “standard” prednisone/cyclophosphamide treatment (Mann-Whitney U test). Error bars represent the range.
cyclophosphamide and the other two had not. Clinical of treatment. Of the six relapsed patients, four had received
inversion process. In the control group, two patients with
ted, to a variable degree, a progressive, although slow, re-

Whitney test). Permanent disease associated damage was

U test). In all of the patients

U test). Fig 1 shows a

U test). Fig 1 shows a

Table 2 Outcomes in 18 patients with CSS treated with a “standard” prednisone/cyclophosphamide treatment with (treatment group) or without (control group) intravenous immunoglobulin synchronised with plasmapheresis. The table shows the values at last assessment for SNVDI, BVAS and modified Rankin scores.

<table>
<thead>
<tr>
<th>No/Sex/age (years)</th>
<th>Follow up (months)</th>
<th>Relapse</th>
<th>Outcome</th>
<th>Maintaining drug (mg/day)</th>
<th>SNVDI</th>
<th>BVAS</th>
<th>Modified Rankin score</th>
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<tbody>
<tr>
<td>Treatment group</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/F/55</td>
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<td>SR</td>
<td>No</td>
<td>5</td>
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<td>2</td>
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<tr>
<td>2/M/69</td>
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<td>2</td>
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<td>SR</td>
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<td>Control group</td>
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<td>DFZ (9)</td>
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<td>2</td>
<td>1</td>
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<tr>
<td>13/F/66</td>
<td>32</td>
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<td>R</td>
<td>PRD (10)</td>
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<td>2</td>
</tr>
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<td>66</td>
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<td>No</td>
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<td>6</td>
<td>2</td>
</tr>
<tr>
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<td>Yes</td>
<td>R</td>
<td>Methyl-PDN (8)</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

BVAS, Birmingham Vasculitis Activity Score; SNVDI, Systemic Necrotising Vasculitis Damage Index; R, remission; SR, treatment free sustained remission for at least 18 months after discontinuation of treatment; MTX, methotrexate, 10 mg/week; PRD, prednisone; DFZ, deflazacort; Methyl-PDN, methyl-prednisolone.

the control group, in whom it was stable. EMG-ENG studies, performed at months 8 and 12, documented a sustained improvement in the upper and lower limbs of all patients, except two in the control group.

The elevated pretreatment median BVAS continued to decrease until month 12, being, at that time, 4 (95% CI 4 to 6) and 7 (95% CI 7 to 10) for the treatment and control groups, respectively (p < 0.001, Mann-Whitney U test). Table 2 shows the outcomes of the 18 CSS patients after a median follow up period of 44 and 55 months, in the treatment and control groups, respectively (p = NS). At the last assessment, three patients in the treatment group were considered to be in treatment free sustained remission, the other patients being in treated remission. Median SNVDI values were 4 (95% CI 3 to 5) and 5 (95% CI 4 to 6) in the treatment and control groups, respectively (p < 0.02, Mann-Whitney U test). Permanent disease associated damage was present almost exclusively in the control group and was characterised by fibrosing interstitial lung disease (n = 1), moderate renal insufficiency (n = 2), and hemiplegia (n = 1). The modified Rankin scores were reduced to 1.5 (95% CI 1 to 2) and 3 (95% CI 2 to 4) in the treatment and control groups, with a statistically significant difference between the two groups (p < 0.04, Mann-Whitney U test). In all of the patients in the treatment group, EMG-ENG examinations documented, to a variable degree, a progressive, although slow, re-innervation process. In the control group, two patients with asymmetrical polyneuropathy displayed a persistent denervation in leg and foot muscles.

There was a clearcut difference in the frequency of relapses, 1/9 for the treatment group and 4/9 for the control group, which occurred in all cases during the first 12 months of treatment. Of the six relapsed patients, four had received cyclophosphamide and the other two had not. Clinical remission was achieved following an increase in the corticosteroid dose.

Neither asthma nor sinusitis was affected by our study protocol.

**Side effects**

Table 3 shows the number and type of adverse events recorded during the study period. Only mild side effects such as headache or minor gastrointestinal intolerance were documented following the IVIg infusions or PP sessions, and they did not require modification of the treatment.

Steroid related side effects were the most frequent. We documented a tendency, even though not statistically significant, toward lower incidence of osteoporosis in the treatment group compared with the control group (p = 0.057, Fisher’s exact test). In this regard, only two patients for each group had osteoporosis at the beginning of the treatment. At the end of the follow up period, the cumulative steroid doses were 11.7 and 16.1 g for the treatment and control groups.

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid related</td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>2</td>
</tr>
<tr>
<td>Myopathy</td>
<td>1</td>
</tr>
<tr>
<td>Cushingoid habitus</td>
<td>1</td>
</tr>
<tr>
<td>Cyclophosphamide related</td>
<td>0</td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td>0</td>
</tr>
<tr>
<td>Permanent lymphopenia</td>
<td>1</td>
</tr>
<tr>
<td>Bacterial pneumonia</td>
<td>1</td>
</tr>
</tbody>
</table>

* p < 0.057, Fisher’s exact test.
Intravenous immunoglobulin in Churg-Strauss syndrome

Impact of corticosteroids on the neurological involvement

ableing problems from which recovery is usually long and
between the two groups. These data are at variance with
modified Rankin score medians were significantly different
even at long term evaluation. At the last assessment, the
disease manifestations: systemic symptoms, alveolitis, myo-
After initiation of the immunoglobulin infusions, we
with a lower incidence of adverse effects.

specific laboratory markers, and the overall disease severity,
statistically significant difference in the clinical recovery, the
short follow up. Compared with the "standard" treatment
reserved for patients with severe disease. This combined
We treated nine patients with CSS with IVIg and PP

DISCUSSION
We treated nine patients with CSS with IVIg and PP
associated with oral prednisone. Cyclophosphamide was
reserved for patients with severe disease. This combined
therapy achieved a remission that was maintained at long
treatment and control groups, respectively. Among the
cyclophosphamide related side effects, only one woman in
each group had menstrual irregularities, lasting less than
6 months. None of patients treated with cyclophosphamide
developed unexplained microhaematuria during long term
follow up.

In our series of 18 patients with CSS, the vasculitis scores
indicated a mean for active and severe vasculitis, respectively.
After initiation of the immunoglobulin infusions, we
documented a rapid and sustained recovery. The clinical
and biochemical improvement occurring during the first two
infusions persisted at long term follow up (a mean of 3 years).
We thus documented the resolution of the main
disease manifestations: systemic symptoms, alveolitis, myo-
carditis, renal impairment, cutaneous vasculitis, polyserositis,
and arthritis. For the peripheral nervous system, our study
demonstrated that the functional recovery was significantly
better in patients treated with IVIg than in the control group,
even at long term evaluation. At the last assessment, the
modified Rankin score medians were significantly different
between the two groups. These data are at variance with
previous reports. Vasculitis neuropathy causes severe disab-
abling problems from which recovery is usually long and
partial, if at all. A delay in the diagnosis or in the start of the
treatment could increase the burden of the vasculitic damage
in the nerve trunks. As previously reported, the clinical
impact of corticosteroids on the neurological involvement
may be incomplete.2 23

During the disease course, relapses occurred less frequently
in the treatment group than in the control group. It should be
emphasised that the reported incidence is higher, ranging
from 23 to 50%.12 10 Furthermore, the strongest probability of
relapse occurs in the first 2 years of disease.12 The long term
favourable course obtained in our patients may be a result of
a synergistic effect of the drugs when used as combined
rather than single agents.

After a median follow up period of 44 months all of the
patients in the treatment group maintained clinical remis-
sion, thus permitting a significantly better recovery of
peripheral nerve system dysfunction with a statistically signifi-
cant lower corticosteroid dose in comparison with patients
receiving the "standard" treatment. This is further confirmed
by the higher incidence of steroid dependent adverse effects
(in particular osteoporosis) in this group of patients.
Finally, permanent damage was less prevalent in patients
 treated with IVIg. At the last assessment, the median SNVDI
values were significantly lower in the treatment than in the
control group. Considering that baseline characteristics of
the patients were similar in both groups, it is conceivable that
the lower frequency and severity of disease and/or treatment
associated sequelae in the treatment group could be ascribed
to a reduced total exposure to corticosteroids and/or
immunosuppressive drugs.

In the literature, few studies have been specifically
performed in groups of patients with CSS only.12 12 The
"standard" treatment for CSS is based on corticosteroids and
cyclophosphamide. Steroids achieve a good clinical response
with a significant decrease in main functional parameters;
however, they are associated with a high relapse rate and a
greater frequency of side effects. Review of the ample series
by Guillevin et al failed to demonstrate that cyclophos-
phamide could modify long term survival rates.30 In
addition, corticosteroids alone should be considered only in
the absence of manifestations that could result in mortality
or severe morbidity.21

Other studies have documented an important role for IVIg
in the treatment of ANCA associated systemic vasculitis and
other immune mediated neuropathies. Despite its limitation
as therapy because of availability and cost, IVIg has been
shown to be effective alone or as add on therapy. In a recent
randomised, placebo controlled trial, Jayne et al documented
the efficacy and safety of a single course of IVIg in previously
treated ANCA associated systemic vasculitis with persistent
disease activity.12 To our knowledge, only single case reports
have been published on the use of IVIg treatment in CSS.14–16
The rationale for the use of IVIg involves the idiotype–anti-
idiotype mechanism between ANCs and their antigen(s)13
and the blockade of specific ANCA receptor(s) implicated in
neutrophil activation and cytokine release in vitro.31 In
addition, Yu and Lennon postulated that the acceleration of
the rate of the IgG catabolism is probably the most relevant
mechanism to explain the benefit of action of IVIg in some
autoimmune diseases.27 In neuropathies, taking into account
evidence from various human and experimental studies, IVIg
could also act at other levels, such as suppressing pathogenic
cytokines, inhibiting complement binding, preventing mem-
branolytic attack complex formation, modulating T lympho-
cytes and neutralising bacterial and viral superantigens.13

Synchronised therapy has previously been proposed for severe
immune mediated diseases.18 PP and IVIg could permit
the rapid removal and solubilisation, respectively, from the
circulation of the immune complexes formed by ANCA and
the antigen MPO.12 However, in our study we could not
document any beneficial effect for the addition of PP, in
agreement with others.3 7

In conclusion, our major findings were the complete
improvement and long term stable remission with lower side
effect rates, as further confirmed by review of previous
publications. The limitations of our study are the small
sample, the lack of randomisation, and the retrospective
analyses of the control group, all linked to the rarity of the
disease. In particular, there could be bias because of the
retrospective evaluation of BVAS in some subjects in the
control group. However, the homogenous clinical and
serological features in the two populations, the standardised
protocol employed to collect the data, and the results of the
longitudinal and statistical analyses should have reduced
the relevance of this methodological bias. A randomised con-
trolled trial is warranted to confirm the benefit and safety of
IVIg in CSS.

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REFERENCES


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