Plasma exchange led to a higher rate of renal recovery than intravenous methylpredisolone in severe vasculitis

Jayne DR, Gaskin G, Rasmussen N, et al. **Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis.** J Am Soc Nephrol. 2007;18:2180-8.

Clinical impact ratings: Hospitalists ★★★★★☆☆ Allerg & Immunol ★★★★★★☆ Hematol/Thrombo ★★★★★★☆ Nephrology ★★★★★★★

QUESTION

In patients with severe vasculitis who receive cyclophosphamide and oral prednisolone, does plasma exchange increase renal recovery more than intravenous (IV) methylprednisolone?

METHODS

Design: Randomized controlled trial.
Allocation: Concealed.*
Blinding: Unblinded.*
Follow-up period: 12 months.
Setting: 28 hospitals in 9 countries in Europe.
Patients: 137 patients (median age 66 y, 61% men) with Wegener granulomatosis or microscopic polyangiitis; biopsy-proven, pauci-immune, necrotizing, or crescentic glomerulonephritis; and serum creatinine level > 500 µmol/L (5.8 mg/dL). Exclusion criteria included age < 18 or > 80 years, pregnancy, circulating antiglomerular basement membrane (GBM) antibodies or linear IgG staining of the GBM on renal biopsy, other multisystem autoimmune disease, life-threatening nonrenal manifestations of vasculitis, creatinine > 200 µmol/L (2.3 mg/dL) ≥ 1 year before study entry, dialysis > 2 weeks before study entry, a second cause of renal failure, previous episode of biopsy-proven necrotizing glomerulonephritis, > 2 weeks of cyclophosphamide or azathioprine, > 500 mg of IV methylprednisolone, plasma exchange in the preceding year, and > 3 months of treatment with oral prednisolone.
Intervention: IV methylprednisolone, 1000 mg/d for 3 days (n = 67), or a total of 7 plasma exchanges given within 14 days of study entry, with an exchange volume of 60 mL/kg at each session, and volume replacement with 5% albumin (n = 70). In addition, all patients received oral prednisolone (1 mg/kg per d, tapered to 0.25 mg/kg per d by 10 wk, 15 mg/d by 3 mo, and 10 mg/d between 5 and 12 mo) and oral cyclophosphamide (2.5 mg/kg per d, or 2 mg/kg per d for those aged > 60 y, reduced to 1.5 mg/kg per d at 3 mo, and stopped at 6 mo). Azathioprine, 2 mg/kg per day, was started at 6 months.
Outcomes: Renal recovery (survival, dialysis independence, and serum creatinine < 500 µmol/L [5.8 mg/dL]) at 3 months. Secondary outcomes were survival, end-stage renal disease (ESRD), and adverse events.
Patient follow-up: 84% at 3 months (intention-to-treat analysis).

MAIN RESULTS

At 3 months, renal recovery was higher with plasma exchange than with methylprednisolone (Table). The risk for ESRD at 3 months was lower in the plasma-exchange group than the methylprednisolone group (Table). At 12 months, groups did not differ for survival or adverse events (Table).

CONCLUSION

In patients with severe vasculitis who received cyclophosphamide and prednisolone, plasma exchange led to greater renal recovery than did intravenous methylprednisolone.

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*See Glossary.

Plasma exchange (PE) vs high-dose IV methylprednisolone (Met) in patients with severe vasculitis†

Outcomes	PE	IV Met	RBI (95% CI)	NNT (CI)
Renal recovery at 3 mo	69%	49%	39% (5 to 89)	6 (3 to 36)
			RBR (CI)	NNH (CI)
Survival at 12 mo	73%	76%	4% (–17 to 22)	Not significant
			RRR (CI)	NNT (CI)
ESRD at 3 mo	19%	41%	55% (18 to 76)	5 (3 to 17)
			RRI (CI)	NNH (CI)
Severe or life-threatening adverse events at 12 mo	50%	48%	4.7% (–26 to 48)	Not significant

†ESRD = end-stage renal disease; other abbreviations defined in Glossary. RBI, RBR, RRR, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

As our understanding of the pathogenesis of small-vessel vasculitis (SVV) expands, evidence of a contributory role for antineutrophil cytoplasmic autoantibodies (ANCAs) increases, and a study of therapy directed at elimination of these autoantibodies is timely. Current practice (prompt treatment with glucocorticoids and cyclophosphamide) is supported by several observational studies. Observational data also suggest that induction therapy with pulse steroids is more efficacious than oral steroids alone in reversing inflammation in rapidly progressive glomerulonephritis (1). The addition of plasma exchange to immunosuppressive therapy has been studied in several randomized controlled trials: Renal recovery was increased in dialysis-dependent patients but not in those with less-severe renal disease (2). Furthermore, observational data suggest that mortality due to pulmonary hemorrhage, a strong risk factor for death, can be greatly diminished with the addition of plasmapheresis (3).

The study by Jayne and colleagues showed that plasma exchange was superior to IV methylprednisolone as part of induction for patients with ANCA-SVV and severe renal dysfunction. Speedy removal of presumed pathogenic antibody burden appears to facilitate amelioration of the disease. The report by Jayne and colleagues suggests that when people with ANCA-SVV glomerulonephritis and creatinine > 500 µmol/L are being treated with methylprednisolone, adding plasma exchange to inductive treatment should be considered. However, it should be considered only in patients with advanced severe disease because benefits are unlikely in those with less-severe disease. No evidence to date can support combined treatment with both plasma exchange and IV steroids, even in patients with severe disease.

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