Antithrombotic Drug Therapy for IgA Nephropathy: A Meta Analysis of Randomized Controlled Trials

Xiu-Juan Liu1,2, Yan-Qiu Geng2, Shao-Nan Xin3, Guo-Ming Huang1, Xiao-Wen Tu1, Zhong-Ru Ding1 and Xiang-Mei Chen2

Abstract

Background Antithrombotic agents, including antiplatelet agents, anticoagulants and thrombolysis agents, have been widely used in the management of immunoglobulin A (IgA) nephropathy in Chinese and Japanese populations. To systematically evaluate the effects of antithrombotic agents for IgA nephropathy.

Methods Data sources consisted of MEDLINE, EMBASE, the Cochrane Library, Chinese Biomedical Literature Database (CBM), Chinese Science and Technology Periodicals Databases (CNKI) and Japan Centra Revuo Medicina (http://www.jamas.gr.jp) up to April 5, 2011. The quality of the studies was evaluated from the intention to treat analysis and allocation concealment, as well as by the Jadad method. Meta-analyses were performed on the outcomes of proteinuria and renal function.

Results Six articles met the predetermined inclusion criteria. Antithrombotic agents showed statistically significant effects on proteinuria (p<0.0001) but not on the protection of renal function (p=0.07). The pooled risk ratio for proteinuria was 0.53, [95% confidence intervals (CI): 0.41-0.68; I²=0%] and for renal function it was 0.42 (95% CI 0.17-1.06; I²=72%). Subgroup analysis showed that dipyridamole was beneficial for proteinuria (p=0.0003) but had no significant effects on protecting renal function. Urokinase had statistically significant effects both on the reduction of proteinuria (p=0.0005) and protecting renal function (p<0.00001) when compared with the control group.

Conclusion Antithrombotic agents had statistically significant effects on the reduction of proteinuria but not on the protection of renal function in patients with IgAN. Urokinase had statistically significant effects both on the reduction of proteinuria and on protecting renal function. Urokinase was shown to be a promising medication and should be investigated further.

Key words: Glomerulonephritis, IgA nephropathy, Antithrombotic agents, Meta analysis


Introduction

IgA nephropathy (IgAN) is an immune complex-mediated glomerulonephritis defined immunohistologically by the presence of glomerular IgA deposits accompanied by a variety of lesions identified histopathologically in the absence of systemic disease (1). It has been demonstrated that IgAN is a worldwide disease causing end-stage renal disease (ESRD) in up to 15-20% of affected patients within 10 years from the apparent onset of disease and in up to 30-40% of individuals within 20 years from diagnosis (2, 3), and it is especially frequent in the East among the Chinese and Japanese. The mechanisms involved in the pathogenesis of this disease have remained unclear. Many treatments have been attempted, however, no specific treatment has been established due to wide variations in current practice (4-6).

The most commonly used regimens include immunosuppressive agents such as glucocorticoids or cyclophosphamide and non-immunosuppressive medications including antihy-
pertensive agents and surgical tonsillectomy, anticoagulants and antiplatelet agents, which had been tested in a variety of studies including randomized controlled trials (RCTs). More than two-thirds of Japanese patients (7) and almost half of the Chinese patients with IgA nephropathy received antithrombotic agents, while the use of antithrombotic agents for such patients in non-Asian countries was relatively rare (8). Differences between regions in the use of antithrombotic agents for IgA nephropathy might be attributed to the lack of studies with appropriate designs and sufficiently large sample sizes. Therefore, we conducted a meta-analysis to systematically evaluate the effects of antithrombotic agents for IgA nephropathy based on the currently available data (9-16). We expected that the results could expedite worldwide utilization of antithrombotic agents not only for IgAN but also for other primary GN and even secondary GN.

Materials and Methods

Inclusion and exclusion criteria

To be selected for analysis, a study had to meet all of the following criteria: (i) The study was an RCT; (ii) The study compared antithrombotic drug (any dose, type) vs. placebo/no treatment; (iii) Antithrombotic drug (any dose, type) vs. any other non-immunosuppressive agents; (iv) The first period of randomized, crossover studies shall be included; and (v) Studies with immunosuppressive agents such as cytotoxic agents or steroids in only one arm were excluded; Studies were excluded if they did not clearly report the numbers of patients who recovered, worsened, or had renal replacement therapy.

Search strategy

PubMed/MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), Chinese Science and Technology Periodicals Databases (CNKI), Japan centra revuo medicina (http://www.jamas.gr.jp) were searched up to April 5, 2011. The following medical subject heading items and free-text words were used: glomerulonephritis, IgA, IgA glomerulonephritis, Berger disease and IgA nephropathy, antithrombotic drug, antiplatelet, platelet antiaggregants, platelet aggregation inhibitors, platelet inhibitors, platelet antagonists, anticoagulant, thrombolysis, defibrotide, urokinase, uPA, and UK, t-PA, randomized controlled trial, controlled clinical trial, randomized, randomly, placebo, and trial. Reference lists from identified articles were also searched. The titles and abstracts of the articles were analyzed by two of the authors (Xiujuan Liu, Yanqiu Geng) independently to ascertain conformity with the inclusion criteria. The full text of an article was reviewed carefully if the screening of its title and abstract was unclear as to its admissibility.

Study validity assessment

We evaluated the quality of the studies in terms of allocation concealment and intention-to-treat analysis, blinding of investigators, participants and outcome assessors and completeness to follow-up, as well as the Jadad scale (17-20).

The Jadad scale is an established procedure by which study methodologies are evaluated. Its scale assigns 0 or 1 points to each of the following five items: (i) with or without randomization; (ii) with or without a double-blind design; (iii) the appropriateness of the randomization methods if used; (iv) the appropriateness of double-blinding design if used; and (v) the analysis and reasons for withdrawals and dropouts. Thus, the Jadad scores can range from 0 to 5. The quality of studies to be included was assessed independently by two reviewers. Studies should be scored as excellent quality if they received a Jadad score of five (of a possible five points), good quality if the score was 3 or 4, and poor quality if the score was ≤2.

Data collection and analysis

Data were extracted from all included studies in terms of participant characteristics of the study sample, baseline of study, and intervention characteristics for each group. The level of proteinuria and renal function was considered to measure the effects of antithrombotic drugs in patients with IgA nephropathy. The primary outcome was the decrease of proteinuria, and its end point was a decrease of ≥50% in urinary protein excretion (UPE) compared with the baseline. The secondary outcome was progression of renal disease and its end points were an increase by ≥50% in serum creatinine (Scr), end-stage renal failure or death.

Statistical analysis

All statistics analyses were performed using Review Manager (RevMan) [Computer program] (Version 5.0. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008). The results were expressed as risk ratio (RR) for dichotomous data, and the mean difference (MD) for continuous data, with 95% confidence intervals (95% CI). Heterogeneity among included trials was analyzed using chisquared ($\chi^2$) test. If a p value of >0.10 indicated no heterogeneity across included trials, the Mantel-Haenszel (M-H) method in fixed-effect model was carried out for meta-analyses of dichotomous data and Inverse variance (IV) method for continuous data. Otherwise, M-H and IV methods in Random-effect model were used for dichotomous and continuous data, respectively. The potential publication bias was examined by the funnel plot method.

Results

Selection of the studies

The combined search of MEDLINE, EMBASE, CCTR, CBM and CNKI, which also included some hand-searching
Table 1. Characteristics of the Eight Included Studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Participants</th>
<th>Interventions/Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhuang 2000</td>
<td>N:75 Gender:M57,F18 Age: 30.41±1.80(13-56) UPE:2.76±0.27g/24h; Ccr: &gt;75mL/min; Pathology: Lee’s grade: III(24), IV(39), V(12).</td>
<td>I (n=37): UK+benazepril. C (n=38): benazepril. Follow-up period: 3 months</td>
</tr>
<tr>
<td>Chen 2004</td>
<td>N:71 Gender:M48,F23 Age: 31.31±9.57(12-53) UPE:1.82±0.27g/24h; Ccr: &gt;75mL/min; Pathology: Lee’s grade: III(28), IV(37), V(6).</td>
<td>I (n=35): UK+benazepril. C (n=36): benazepril. Follow-up period: 12 months</td>
</tr>
<tr>
<td>Wu 2006</td>
<td>N:46 UPE:2.15±1.02g/24h; Ccr: &gt;75mL/min; Pathology: Lee’s grade: III(15), IV(16), V(15).</td>
<td>I (n=20): UK + Sodium Ferulate. C (n=26): Sodium Ferulate. Follow-up period: 6 months</td>
</tr>
<tr>
<td>Chan 1987</td>
<td>N:38 UPE: 1.7g/24h; Ccr: 75 mL/min</td>
<td>I (n=19): D+ aspirin. C (n=19): placebo. Follow-up period: 33.2 months</td>
</tr>
<tr>
<td>Tojo 1987</td>
<td>N:122 UPE: 2.1g/24h; Ccr: 60 ml/min</td>
<td>I (n=57): D+ aspirin. C (n=65): placebo. Follow-up period: 6 months</td>
</tr>
<tr>
<td>Lee 1997</td>
<td>N:21 UPE: 1.1g/24h; Ccr: 51 mL/min</td>
<td>I (n=10): D+ warfarin. C (n=11): none. Follow-up period: 36 months</td>
</tr>
</tbody>
</table>

N: number; M: male; F: female; UPE: Urinary protein excretion; Scr: serum creatinine; Ccr: creatinine clearance rate; I: Intervention group; C: Comparison group; UK: urokinase; D: Dipyridamole.

Quality assessment

A quality assessment of the primary studies was summarized in Table 2. The Jadad scores ranged from 0 to 5 points. Study quality on the whole was not good; only four studies had a Jadad score of ≥3. Only one study’s blinding was confirmed, however, the outcome and outcome measurement were not likely to be influenced by lack of blinding. Sufficient details of drop-outs and withdrawals were described in all trials; two studies met allocation concealment and four studies met the intention-to-treat analysis criteria.

Concomitant drugs (Table 1)

In the studies of Zhuang et al (9) and Chen et al (10), the two groups evenly received benazepril. In the studies of Wu et al (11), the two groups evenly received sodium Ferulate. In the study of Tojo et al (14), the two groups evenly received cytotoxic agents, steroids, anticoagulants, or antihypertensive agents that had been administered before entry to the study. And the agents were continued until the end of the study. In the study by Chan et al (13), both groups were treated with antihypertensive agents when indicated, and the intervention group also received aspirin. In the study by Lee et al (16), the intervention group also received warfarin, and hypertension was controlled without angiotensin-converting enzyme inhibitors.

of relevant nephrology journals, retrieved sixty-five citations. After discarding a number of duplicates retrieved by individual searches and reviewing all titles and abstracts, forty-nine studies were excluded because they were not RCTs, or were not meant to investigate any of the outcomes of interest to this study, or were animal or basic research studies or review articles.

For a total of thirteen articles the full text was reviewed to further assess their eligibility. Two studies were excluded because they did not report the actual number of cases (21); two studies (Chen et al (22), Liu et al (23)) used the same material as Chen et al (10) were excluded; the study of Yoshikawa et al (24) used prednisolone and azathioprine in only one arm was excluded. The studies of Woo et al (15) and Yagame et al (12) were excluded because these two studies were not randomized. Thus, only six RCTs, enrolling a total of 320 patients, fulfilled the inclusion criteria of this meta-analysis (9-16). Three trials compared UK with non-UK in the treatment of IgAN (9-11), and three trails compared antiplatelet and/or warfarin with non-antiplatelet and/or warfarin in the treatment of IgAN (13-16), were included in this analysis. The details of characteristics of the six studies are summarized in Table 1. Judging from the biopsy findings and the laboratory data, such as urinary protein excretion and mean creatinine clearance, the severity of all the study cohorts seemed to be in the moderate to severe stages of IgA nephropathy. The study period ranged from 3 months to 36 months.
Table 2. Quality Assessment of RCTs Included in the Review

<table>
<thead>
<tr>
<th>References</th>
<th>Jadad score</th>
<th>Randomisation</th>
<th>Appropriateness of randomisation</th>
<th>Double blind</th>
<th>Appropriateness of double blind</th>
<th>The analysis reasons for withdrawals</th>
<th>Sum of Jadad score</th>
<th>Lost at follow-up (%)</th>
<th>Intention to treat analysis</th>
<th>Allocation concealment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhuang 2000</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>No</td>
<td>Adequate</td>
<td>Adequate</td>
</tr>
<tr>
<td>Chen 2004</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>No</td>
<td>Adequate</td>
<td>Adequate</td>
</tr>
<tr>
<td>Wu 2006</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>2/46</td>
<td>No</td>
<td>Adequate</td>
<td>Adequate</td>
</tr>
<tr>
<td>Chan 1987</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>Yes</td>
<td>No</td>
<td>Adequate</td>
</tr>
<tr>
<td>Tojo 1987</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>No</td>
<td>Adequate</td>
<td>Adequate</td>
</tr>
<tr>
<td>Lee 1997</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>Yes</td>
<td>No</td>
<td>Adequate</td>
</tr>
</tbody>
</table>

Experimental vs Control Risk Ratio

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total</th>
<th>Weight</th>
<th>M-H, Fixed, 95% CI</th>
<th>M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen 2004</td>
<td>19</td>
<td>37</td>
<td>29.4%</td>
<td>0.67 [0.47, 0.96]</td>
<td></td>
</tr>
<tr>
<td>Wu 2006</td>
<td>17</td>
<td>57</td>
<td>41.3%</td>
<td>0.45 [0.29, 0.70]</td>
<td></td>
</tr>
<tr>
<td>Zhuang 2000</td>
<td>10</td>
<td>35</td>
<td>20.3%</td>
<td>0.51 [0.28, 0.94]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>142</td>
<td>153</td>
<td>100.0%</td>
<td>0.53 [0.41, 0.68]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>50</td>
<td>101</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 2.26, df = 3 (p = 0.52); I^2 = 0$
Test for overall effect: $Z = 4.98 (p < 0.00001)$

Figure 1. Comparison of antithrombotic agents vs controls on proteinuria.

Effect on proteinuria (Fig. 1)

Four studies assessed proteinuria in a total of 295 patients, and 142 were assigned to treatment groups, while 153 were in the control groups. A deterioration in proteinuria was seen in 50 of 142 patients in the treatment groups, and in 101 of 153 patients in the control groups. Among the four studies, dipyridamole was evaluated in one study, and UK in the other three studies. Because heterogeneity was not significant ($p=0.52$), we used the Mantel-Haenszel (M-H) method in Random-effect model. The pooled risk ratio for proteinuria was 0.53, and a statistical analysis showed that this estimate was statistically significant (95% CI: 0.41-0.68; $p<0.0001$).

Effect on renal function (Fig. 2)

Six studies assessed renal function in a total of 320 patients, and 151 were assigned to treatment groups, while 169 were in the control groups. A deterioration in renal function was seen in 32 of 151 patients in the treatment groups, and in 72 of 169 patients in the control groups. Among the six studies, dipyridamole was evaluated in three studies and urokinase in the other three studies. Because heterogeneity was significant ($p=0.003$), we used the Mantel-Haenszel (M-H) method in Random-effect model. The pooled risk ratio for renal function was 0.42, and it was not statistically significant (95% CI: 0.17-1.06; $p=0.07$).
Adverse effects of treatment

Adverse events were recorded in three trials which compared urokinase with non-urokinase in the treatment of IgAN. High serum potassium and bleeding were the most common adverse events in the urokinase group with an incidence of 9.8% (9/92) and 7.6% (7/92), respectively. These did not influence the planned therapy, because they were mild and temporary. Only two participants discontinued the trial in the urokinase group because of gross hematuria. Headache was reported to be observed significantly frequently in the dipyridamole group compared with the control group in the study by Tojo et al (14). Other studies investigating dipyridamole did not report headache or any other side effects.

Subgroup analyses (Fig. 4, 5 and 6)

Subgroup analyses were performed using the studies that included antiplatelet agents or urokinase. Subgroup analyses which included antiplatelet agents (dipyridamole) demonstrated a deterioration in renal function in 26 of 58 patients. Because heterogeneity was not significant (p=0.5), we used the Mantel-Haenszel (M-H) method in the fixed-effect model. The pooled risk ratio was 0.80 for renal function and it was not statistically significant (95% CI: 0.61-1.04, p=0.09). Only one study (14) assessed the effects of dipyridamole on proteinuria. The deterioration in proteinuria was seen in 17 of 57 patients in the treatment groups, and in 43 of 65 patients in the control groups. The risk ratio was 0.45, it was statistically significant (95% CI: 0.29-0.70, p=0.0003).

Subgroup analyses which included urokinase demon-
stratified a deterioration in proteinuria in 91 of 173 patients. Because heterogeneity was not significant (p=0.63), we used the Mantel-Haenszel (M-H) method in Fixed-effect model. The pooled risk ratio was 0.59 for proteinuria, and it was statistically significant (95% CI: 0.44-0.79, p=0.0005; Fig. 5). The three studies assessed renal function by serum creatinine in a total of 193 patients, and 93 patients were assigned to the treatment groups, 100 patients were in the control group. Because heterogeneity was significant (p=0.006, I²=81%), we used the Inverse variance (IV) method in the Random-effect model. Overall, according to this analysis, the urokinase treatment induced a greater reduction in serum creatinine when compared with the control group (WMD, -17.29; 95% CI, -23.74-10.84, p<0.00001; Fig. 6).

Sensitivity analysis and publication bias

Our analyses were robust in both the choices of models and the statistical methods. The substitution of a random effects model for a fixed model did not change our initial qualitative interpretation of the pooled treatment effect on renal function and proteinuria. Likewise, removal of studies "with a Jadad score of below 3" from our analysis did not alter the results for the effects of antithrombotic agents when compared with control group on renal function and proteinuria. The funnel plots of four trials exhibited symmetric patterns for proteinuria (Fig. 3), which indicated the absence of publication bias.

Discussion

Evidence-based recommendations for the management of IgAN have been published since 1999 (25), but most evidence-based recommendations are based on immunosuppressive treatments for IgAN (26-29). At present, steroids may be the most promising intervention in terms of both renal function and proteinuria (28). For non-immunosuppressive agents, meta analysis of fish oil and antiplatelet therapy for IgAN has been published (30, 31). Evidence-based recommendations indicate that fish oils are not beneficial in this population, while antiplatelet agents can reduce proteinuria and protect renal function in patients with IgA nephropathy. But these recommendations have been somewhat criticized by subsequent studies. The main criticism of these recommendations was that they were based on a variety of sources including non-randomised controlled trial data.

In this meta analysis, we identified six RCTs that compared antithrombotic agents, including antiplatelet agents and thrombolysis agents, with the control group, and antithrombotic agents had statistically significant effects on the reduction of proteinuria, but the effect of protecting renal function was not significant in patients with IgAN when compared with the control group. In the subgroup analysis, dipyridamole also seemed to be not beneficial for renal function. But urokinase seemed to be beneficial for both proteinuria and renal function. Judging from the biopsy findings and the laboratory data, including urinary protein excretion and mean creatinine clearance, the severity of all the study cohorts seemed to be in the moderate to severe stages of IgA nephropathy. Our analysis showed that urokinase was beneficial for proteinuria and renal function in moderate to severe stages of IgA nephropathy. Taj et al (31) reported that dipyridamole was beneficial for proteinuria and renal function in moderate to severe stages of IgA nephropathy. But, the studies included in their study were not good, two studies of Yagame et al (12) and Woo et al (15) were not randomized. The role of dipyridamole in moderate to severe stages of IgA nephropathy needs further research.

Antithrombotic agents were well tolerated. The use of antithrombotic agents was not found to be associated with a significant increase in the risk of adverse events and withdrawal of study medication. However, it should be noted that reports of adverse events were few or absent in some trials, and it is unclear whether this is because there were no events or because they were not properly recorded.

Although the mechanism of the effects of antithrombotic agents on IgA nephropathy is not fully understand yet, several pathophysiological processes have been considered. Intraglomerular fibrin deposition is a documented feature of IgAN. Studies have suggested that intravascular thrombosis is promoted by endothelial cell activation or injury, resulting in the release of endothelial cell-derived tissue factor procoagulant, fibrinolytic inhibitors, platelet-activating factor and large multimers of von Willebrand factor. Glomerular fibrin may be removed by fibrinolytic or phagocytic mechanisms or may persist and lead to glomerular obsolescence (32). Therefore, anticoagulant (including antiplatelet agents, anticoagulants and thrombolysis agents) strategies were proposed to protect against accelerated sclerosis. Our meta analysis showed that urokinase was effective and safe for moderate to severe stages of IgA nephropathy which could reduce proteinuria and protect renal function.

The mechanism of the effects of urokinase on IgA nephropathy involves several aspects as follows: First, urokinase
removes intra-glomerular fibrin-related antigen (FRA) which can lead to glomerular endothelial cell hyperplasia and edema; it may be related to glomerular sclerosis and crescent formation; Second, it’s effect of fibrinolysis. Third, it can mediate proteolysis in the mesangial extracellular matrix (33).

The mechanism of the effects of antiplatelet agents on IgA nephropathy involves several other aspects as follows: First, antiplatelet agents prevent the release of various chemical mediators from platelets such as serotonin and platelet-derived growth factor (34). Second, they attenuate the decrease in the anionic charge in the glomerular basement membrane (35). Third, they inhibit glomerular mesangial cell proliferation (36). Fourth, they can induce efferent renal vasodilatation, possibly through an increase in intrarenal adenosine (37). Only one study (14) assessed the effects of dipyridamole on proteinuria and it showed that dipyridamole was beneficial for proteinuria. The quality of this study was very good; it had a Jadad score of 4, and it was confirmed to be a blinded study. The results could be adopted. Our meta analysis showed that dipyridamole was safe and beneficial for proteinuria, but it was not as effective as urokinase in protecting renal function.

Although our analysis provides strong recommendations for IgAN treatment, our meta analysis had several limitations that should be considered. First, the quality of the individual controlled trials was not essentially high. Only four of six RCTs had a Jadad score ≥3. Therefore, we conducted a quality assessment of the studies and clearly showed the details of each study. A high-quality trials design (such as antithrombotic agents vs. placebo) should be used. Studies should have a sufficiently long follow-up time, and clearly report the numbers of patients who recovered, worsened or had renal replacement therapy. Second, the drugs used in treatment group were different. Some studies used antithrombotic agents as the treatment group, while other treatment group drugs were co-administration of antithrombotic agents. At the same time, the primary endpoint of the studies was different. As the study periods were not long enough to evaluate this slowly progressive chronic disease, most studies did not assess the true outcome of renal death (defined as ESRD). Long-term follow-up studies with true outcome might yield different results. Finally, most of the studies included patients receiving concomitant drugs, such as antihypertension agents. Although we included this kind of study with such concomitant drugs in the same way for both intervention and control groups, studies to assess the effect of antithrombotic agents alone in patients not receiving other therapy are needed.

In conclusion, our meta analysis showed that antithrombotic agents seem to be beneficial for proteinuria but not renal function in patients with moderate to severe stages of IgA nephropathy. But in the subgroup analysis, urokinase seemed to be beneficial for both proteinuria and renal function. The use of antithrombotic agents, expecially urokinase, was a promising strategy in patients with moderate to severe stages of IgA nephropathy and should be investigated further. Current evidence-based practice guidelines should continue to emphasise antithrombotic agents as the primary pharmacological therapy for patients with IgAN.

The authors state that they have no Conflict of Interest (COI).

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References