Steroids and immunoglobulin A nephritis

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To the Editor: We read with much interest the mini review 'Treatment of immunoglobulin A nephropathy' by Barrat and Feehally,[1] and were very pleased to note that, after many debates between us at many meetings, Dr Feehally finally accepts the results of our trial[2,3] strongly suggesting the use of steroids in patients with immunoglobulin A nephropathy and persistent proteinuria (>1 g/24 h), after aiming at a blood pressure target value of 125/75 mmHg using antihypertensive drugs, including angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers at maximum doses and, if necessary, in combination. However, this agreement clearly contradicts what is said in Table 1, which contain no recommendation concerning the use of steroids in patients with proteinuria levels of >1 g/24 h.

It is surprising that the abstract makes no mention of the use of steroids for patients with proteinuria levels of >1 g/24 h and refers to no evidence in favor of using steroids for nephrotic immunoglobulin A nephropathy beyond the group of minimal change nephropathy, whereas the text states that 'the risk attributable to proteinuria is almost certainly a continuum'. We agree that there is no evidence proving the efficacy of steroids in this patient population, but no evidence does not mean they should not be used, but just that there are no randomized studies supporting their use. Nihilism while awaiting the publication of randomized trials (which, to the best of our knowledge, are not even planned) could be very dangerous for the patients because, as the authors say themselves, heavy proteinuria is also the most important factor of progression in patients with immunoglobulin A nephropathy.

1. Barratt J, Feehally J. Treatment of IgA nephropathy. *Kidney Int* 2006; **69**: 1934–1938.
2. Pozzi C, Bolasco PG, Fogazzi GB *et al.* Corticosteroids in IgA nephropathy: a randomised controlled trial. *Lancet* 1999; **353**: 883–887.
3. Pozzi C, Andrulli S, Del Vecchio L *et al.* Corticosteroid effectiveness in IgA nephropathy: long-term results of a randomized, controlled trial. *J Am Soc Nephrol* 2004; **15**: 157–163.

F Locatelli[1], S Andrulli[1] and C Pozzi[1]
[1]*A. Manzoni Hospital, Nephrology and Dialysis, Lecco, Italy*
Correspondence: *F Locatelli, A Manzoni Hospital, Nephrology and Dialysis, Lecco, Italy. E-mail: f.locatelli@ospedale.lecco.it*

Response to 'Steroids and IgA nephritis'

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We appreciate the interest of Dr Locatelli *et al.*[1] in our discussion of the treatment of IgA nephropathy.

It is not surprising, given the relative lack of robust evidence, that there is a range of opinions about the preferred treatment approaches to patients with IgA nephropathy at risk for progressive renal failure, and Dr Locatelli *et al.* have not interpreted our article as we had intended.

We are in agreement that there is evidence that increasing proteinuria marks a continuum of risk; however, the threshold of proteinuria >1 g/24 h was an entry criteria for a number of treatment trials in IgA nephropathy (including the trial of corticosteroids by our correspondents). It might be appropriate to extend the use of treatments effective for proteinuria >1 g/24 h to patients with lesser degrees of proteinuria provided that such treatments are well tolerated with very low toxicity. The dosing regimen for corticosteroids studied by our correspondents is substantial – over 6 months they gave 9 g intravenous methylprednisolone with oral prednisolone 0.5 mg/kg/day. Although in their published study they state this regimen was well tolerated by their patients and with few adverse effects, in our experience such a regimen has considerable short and longer term toxicity, which strengthens our reluctance to recommend it in circumstances where its benefits have not been subject to randomized controlled trial.

The crucial question is whether corticosteroids or other immunosuppressive regimens give added benefit when patients are treated to contemporary blood pressure goals (125/75), with adequate blockade of the renin–angiotensin system, using combination therapy with angiotensin converting enzyme inhibitors and angiotensin receptor blockers. In our opinion, the answer to this question is uncertain since many of the studies we review in our article, including that of Dr Locatelli *et al.*, do not have such contemporary best practice in the control limb of the randomization. The analysis we provided in our article emphasizes the need for caution since those few intervention studies reporting rigorous blood pressure control with effective renin–angiotensin blockade are in general those least likely to show benefit for an additional treatment.

Our observations are not intended to criticize the investigators who undertook these studies, since most were designed and initiated when such standards of care for blood pressure control and renin–angiotensin blockade were not recognized; indeed, their contribution is much to be respected when so few investigators around the world have completed treatment trials in this common glomerular disease.

As we recognize that corticosteroids remains the choice of many nephrologists, we mentioned in the text of our article that their use should be 'considered' but only in circumstances where their use might be considered most logical – if a patient still meets the entry criteria of the trial of Dr Locatelli *et al.* (proteinuria >1 g/24 h) despite