Henoch-Schönlein purpura in children

Limited benefit of corticosteroids

Joel Bluman  Ran D. Goldman MD FRCPC

Abstract

**Question** A child recently presented to my office with lower limb petechiae, arthralgia, and abdominal pain characteristic of Henoch-Schönlein purpura (HSP). Will systemic corticosteroids help relieve these symptoms and prevent potential HSP complications such as intussusception and nephritis?

**Answer** Henoch-Schönlein purpura is a common and self-limiting disease in children. Current evidence does not support universal treatment of HSP with corticosteroids. Recent trials and meta-analyses found that corticosteroids do not prevent the onset of renal disease or abdominal complications. However, corticosteroids are effective as treatment of abdominal pain, arthralgia, and purpura. Clinicians are advised to use their discretion in choosing which patients might benefit most from oral corticosteroid treatment.

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Henoch-Schönlein purpura (HSP) is the most common vasculitis in children, affecting 8 to 20 children per 100,000 annually. It has a male predominance (male-to-female ratio of 1.5:1), and typically affects children aged 3 to 8 years. Henoch-Schönlein purpura is an immunoglobulin A (IgA)-mediated systemic small-vessel vasculitis, with IgA deposition in vessel walls leading to symptoms involving the skin, joints, intestines, and kidneys. Although the cause is unknown, HSP is often preceded by an acute infectious illness and has a seasonal pattern (nonsummer months), providing strong evidence for an infectious trigger.

The diagnosis of HSP is best determined by the presence of purpura or petechiae (usually palpable) with a lower limb predominance in addition to 1 or more of the following 4 findings:

- abdominal pain (diffuse and colicky),
- arthritis or arthralgia,
- renal involvement (proteinuria > 0.3 g in 24 hours, morning urine albumin or creatinine levels of >30 µmol/L, or positive dipstick results for hematuria, and positive histopathologic findings (leukocytoclastic vasculitis with predominant IgA deposits on skin biopsy, or proliferative glomerulonephritis with predominant IgA deposit on kidney biopsy).

Additional symptoms include fever, scrotal pain, and edema in boys, and rarely pulmonary, cardiac, or neurologic manifestations.

Henoch-Schönlein purpura is a self-limiting condition, usually resolving within 6 to 8 weeks, but complications might arise. Renal involvement occurs in 37% of cases; only 1% of cases result in end-stage renal
failure.\textsuperscript{1,2} Sixty-six percent of children experience gastrointestinal symptoms such as abdominal pain (44%), intestinal bleeding (22%), or intussusception (≤3%).\textsuperscript{2,3,6-8}

Treatment is symptomatic and might include mild analgesics such as acetaminophen and nonsteroidal anti-inflammatory drugs for joint pain and fever.\textsuperscript{2,4} However, nonsteroidal anti-inflammatory drugs should be avoided in the presence of gastrointestinal or renal manifestations, as they have been shown to aggravate these symptoms.\textsuperscript{2,4} All patients should undergo blood pressure measurement and urinalysis at the time of diagnosis followed by periodic urinalysis for 6 months, with further urinalysis if abnormalities are present.\textsuperscript{9}

**Treatment with corticosteroids**

**Renal complications.** Although little is known about disease-modifying treatment of HSP, corticosteroids have been suggested owing to their immunosuppressive properties and their usefulness in treating other childhood vasculitides.\textsuperscript{10,11} Four randomized, double-blind, placebo-controlled trials have assessed the effectiveness of corticosteroids in preventing HSP nephritis.\textsuperscript{6,12-14} Prednisone (1 mg/kg daily for 2 weeks followed by a 2-week weaning period, or 2 mg/kg daily for 1 week plus a 1-week weaning period) resulted in no reduction in the severity of hematuria, proteinuria, or urine protein-to-urine creatinine ratio.\textsuperscript{6,12,14} A 2009 Cochrane meta-analysis that evaluated 3 of these studies (N = 569) determined that prednisone did not prevent the development of kidney disease at 1 month, 3 months, 6 months, or 1 year after the onset of HSP.\textsuperscript{15} In a 2012 study, Jauhola and colleagues\textsuperscript{16} investigated the long-term renal outcomes of steroids through reassessing 138 of 171 patients a mean of 7.7 years after their treatment in one of the above-mentioned randomized controlled trials (RCTs).\textsuperscript{14} They reported no long-term renal protective effects of prednisone (1 mg/kg daily for 2 weeks plus a 2-week weaning period) versus placebo, determined by urinalysis and blood pressure.\textsuperscript{16}

Pediatric therapies for established severe HSP nephritis include corticosteroids, immunosuppressants, angiotensin-converting enzyme inhibitors, plasma exchange, and tonsillectomy.\textsuperscript{17} In a systematic review, Zaffanello and Fanos\textsuperscript{17} evaluated 34 English publications that assessed the effectiveness of these various treatment options using end-stage renal disease, increasing proteinuria, and increasing serum creatinine as end points. Although studies have provided evidence for the effectiveness of the above-mentioned treatments, the lack of prospective RCTs, the small sample sizes of studies (ranging from N = 3 to N = 56), and the heterogeneity in severity of renal disease cloud the findings.\textsuperscript{17} Therefore, the ideal treatment regimen, including the role of corticosteroids for children with severe HSP nephritis, remains inconclusive.\textsuperscript{17}

**Purpura and arthralgia.** A small body of literature speaks to the role of corticosteroids in treating purpura and arthralgia symptoms.\textsuperscript{12,14,18} Although the findings from one small RCT\textsuperscript{12} (N = 40) were not statistically significant, 2 larger RCTs\textsuperscript{14,18} (N = 171 and N = 176) reported improvement of purpura and arthralgia in patients receiving prednisone (1 mg/kg daily for 2 weeks) versus placebo. Specifically, prednisone decreased both the prevalence of purpura during the first month after onset and the patient-reported severity and duration of joint pain.\textsuperscript{14,18}

**Gastrointestinal symptoms.** The RCTs performed by Ronkainen et al\textsuperscript{14} and Jauhola et al\textsuperscript{18} demonstrate that prednisone reduces both the severity and the duration of abdominal pain during the first 2 weeks of treatment, with Ronkainen and colleagues
reporting a decrease in mean pain duration from 2.7 to 1.5 days (1.2-day decrease, 95% CI 0.1 to 2.3). Another systematic review analyzed results from 3 retrospective studies and reported that corticosteroids in slightly higher doses (1 to 2 mg/kg daily) were effective in reducing abdominal pain within 24 hours after corticosteroid administration.

No RCTs to date have found a statistically significant relationship between early prednisone treatment and a decrease in abdominal complications, namely hospitalization, intussusception, or surgery. However, as these complications are quite rare, statistical significance might be difficult to achieve even in large RCTs. A 2010 large retrospective study of hospitalized HSP patients from the United States found that early corticosteroid use reduced the risk of patients undergoing abdominal investigations such as endoscopy and abdominal imaging, but did not reduce the risk of abdominal surgery. Because abdominal complications are rare in HSP and extant research does not show a significant or practical benefit, corticosteroids should not be administered generally as abdominal complication prophylaxis.

**Recurrent HSP.** Henoch-Schönlein purpura might recur in up to 33% of affected children. Recurrences appear to be more common in older children (>8 years of age at onset) and in children with renal involvement. Current research indicates placebo is as good as prednisone in preventing HSP recurrence after 1 month, with 1 RCT finding recurrence rates of 17% and 25% in the placebo and prednisone (1 mg/kg daily) groups, respectively (P = .22). A second RCT, as well as a systematic review of both prospective and retrospective trials, supported these findings, reporting no statistically significant difference in recurrence rates after 1 month between the placebo and prednisone groups, with considerable heterogeneity in the retrospective observational trials.

**Conclusion**

Current evidence does not support universal treatment of HSP with corticosteroids, as they do not appear to prevent the onset of renal disease or abdominal complications, nor do they alter recurrence rates. However, corticosteroids do seem to have a role in the symptomatic management of HSP, specifically in treating abdominal pain, arthralgia, and purpura. As research is limited, clinicians are advised to use their discretion when choosing which patients would benefit most from corticosteroids. If prednisone is used, doses of 1 to 2 mg/kg daily given for 1 to 2 weeks (followed by an appropriate weaning period) appear to be effective, but further research is required to determine the optimal dose. Patients with severe renal symptoms, specifically nephrotic syndrome, nephritic syndrome, or rapidly worsening proteinuria or hematuria should be urgently referred to a pediatric nephrologist for prompt assessment and treatment.

**Competing interests**

None declared.

**Correspondence**

Dr Ran D. Goldman, BC Children's Hospital, Department of Pediatrics, Room KA-226, Ambulatory Care Bldg. 4480 Oak St, Vancouver, BC V6H 3V4; telephone 604 875-2345, extension 7333, fax 604 875-2414; e-mail rgoldman@cw.bc.ca.

**References**