

The Role of Prophylactic Corticosteroids in Henoch Schonlein Purpura

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Introduction

Henoch Schonlein Purpura (HSP) is the commonest vasculitis seen in the pediatric population [1], with an incidence of 10-20 per 100, 000 children. Although treatment with corticosteroids is routine during the acute phase of the disease, controversy remains as to the merit of corticosteroids in preventing persistent renal disease in children presenting with HSP. Although several sporadic case series have claim demonstration of efficacious usage of prednisone and immuomodulators in preventing development of HSP nephropathies, data from randomized controlled trials are limited.

Case Presentation

John¹, a 7 years old Indian male, presented with a 3-day history of bilateral knee pain and swelling, associated with a 5-day history of non-itchy, non-painful rash over the lower limbs and a week history of fever and coryza, in the absence of trauma. Rest of the systems review was negative. Apart from the recent upper respiratory tract infection, which spontaneously resolved, John has been well with no past history of similar episodes. He was not on any medications and has no known allergies. Perinatal history was unremarkable: spontaneous vertex delivery at term with birth weight of 3.4 kg. His development has been up to age, with satisfactory performance in school. His immunization was up to date. Family history was unremarkable. He was a single child, looked after by his parents in a comfortable home environment.

Vital Signs: Pulse: 75 beats per minute, with regular rhythm and good volume, Blood

Pressure: 110/70, Respiratory Rate: 16 and Temperature: 37.5°C

Upon examination, John appeared alert, active, oriented, responsive and non-toxic. Knees were bilaterally tender with periarticular edema, but neither hot nor erythematous. Crops of palpable, non-blanching, purpuric rash were distributed over the extensor surfaces of the lower extremities and buttocks. Rest of examination findings were within normal limits. Relevant negative findings included the absence of lip-cracking, cervical lymphadenopathy, peeling of skin over the extremities and organomegaly.

Provisional diagnosis was HSP and differential diagnoses included meningococemia, ITP, Reactive/Post infective Arthritis, JIA², Septic Arthritis and connective tissue diseases. Laboratory work up including full blood count (Hb, WBC differential & platelet count), blood culture, coagulation studies, renal profile (BUSE³, Creatinine), CRP, and autoantibody screen (ANA, ANCA to rule out collagen vascular diseases) yielded normal results. Urine dipstick revealed 2+ blood and 1+ protein in the absence of nitrites and WBC, and consequent Urine FEME revealed microscopic hematuria and mild proteinuria – suggesting glomerulonephritis. In this context, given a normal renal profile (which ruled out alarming causes of proteinuria), raised ASOT⁴ and reduced C3, John was diagnosed to have HSP and appropriately treated with Steroids. Follow up for a period of six months from the initial presentation, with regular urinalysis and a minimum of 2 blood pressure checkups,

¹ Patient is de-identified to protect confidentiality

² Juvenile Idiopathic Arthritis

³ Blood Urea & Serum Electrolytes

⁴ Anti-Streptolysin O Titre

has been planned. Prompt referral to a paediatric nephrologist for long term follow up in a situation of persistent renal involvement has been discussed with the family.

Discussion

Though the general consensus remains that HSP resolves spontaneously, with the use of appropriate analgesics (simple analgesics for joint pain, and corticosteroids for severe abdominal colic), is the prophylactic use of corticosteroids or other immunomodulators warranted to prevent persistent renal disease? Systematic review of 10 Randomised Controlled Trials by W Chartapisak et al [1], which involved 1230 children aged less than 18 years, in a setting of Secondary and tertiary paediatric and paediatric nephrology services, with the main outcome measures persistent proteinuria and/or haematuria, concluded that short-term prednisone has not been shown to be effective in treating or preventing renal involvement in HSP: Meta-analyses of four well designed placebo-controlled RCTs revealed insignificant difference in the risk of persistent kidney disease at 6 months (n=379; RR: 0.51 with 95% CI: 0.24-1.11, CI spans across 1) and 12 months (n=498; RR: 1.02 with 95% CI: 0.40- 2.62, CI spans across 1) in children given prednisone for 14–28 days at presentation of HSP in comparison to those who received supportive treatment or placebo. All 4 studies demonstrated adequate allocation concealment with computer-generated random allocation sequence, blinding of participants, investigators and outcome assessors and attrition bias was nominal with loss to following-up patients ranging from 0% - 10%. However, none of the studies adopted an intention-to treat analysis.

A Cochrane review by Opastirakul S et al [2] of RCTs and quasi-RCTs from the Cochrane Renal Group's specialised register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE concluded that cyclophosphamide does not offer any additional protection against renal

diseases in children with HSP who were given supportive treatment (n=56; RR: 1.07 with 95% CI: 0.65-1.78, CI spans across 1) or methylprednisolone (n=19; RR: 0.39 with 95% CI: 0.14-1.06, CI spans across 1). However, the data offered by both the studies are questionable because of small sample sizes.

A randomized, double-blind, placebo controlled study by Huber AM [3] involving 40 children with HSP, seen in the setting of emergency room of a tertiary-care, paediatric centre, compared co-primary outcomes of the rates of renal involvement at 1 year using Fisher's Exact test. Huber AM states that there were no significant difference [$P > 0.05 (=1.0)$] in the rate of renal involvement between the prednisone group (3/21) and placebo group (2/19). The study, however, showed some benefit in the prednisone group in reducing risk of intussusception, though not statistically significant [$(P > 0.05 (=0.2))$].

A randomized, double-blind, placebo-controlled trial by Ronkainen J [4,5] to evaluate the efficacy of early prednisone therapy in both preventing and treating renal symptoms included 171 patients (prednisone=84; placebo=87) and was conducted on an intent-to-treat basis. After 6 months follow-up with endpoints as renal involvement at either 1, 3, or 6 months, revealed that, though prednisone was not effective in preventing renal involvement, it was effective in treating them [(difference=27%; 95% CI: 3% to 47%; $P < 0.05 (=0.024)$] – thereby playing a crucial role of altering the course of the renal involvement.

Conclusion

In conclusion, current literatures [1-3] do not demonstrate any statistically significant benefits that are rendered by prednisone or other immunomodulators in preventing the development of persistent renal disease in children diagnosed with HSP, when administered at the time of presentation. Therefore, routine prophylactic usage prednisone in uncomplicated HSP should not

be recommended at this moment as any apparent benefits offered by such drugs could well be due to chance or other unknown confounders. However, the role of prednisone in altering the disease course in HSP complicated with nephropathy is well-known and is warranted by evidences conferred by literatures discussed above. Hence, continuous monitoring and early identification of children who develop HSP nephropathy and prompt treatment with prednisone is the ideal management to reduce disease burden of HSP.

References

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