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# Efficacy of Steroid Therapy in Management of Sydenham's Chorea in Children: A Comparative Prospective Study

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## ABSTRACT

***Objective:*** To determine the efficacy of steroid therapy in Sydenham's chorea in children.
***Study Design:*** Comparative prospective study.
***Place and Duration of Study:*** Inpatient and Outpatient Department of Pediatric Neurology, Children Hospital and Institute of Child Health, Lahore Pakistan, from Dec 2019 to May 2020.
***Methodology:*** Sixty-eight children of Sydenham's chorea were divided in Group A and B. Each Group was treated with Diazepam (0.3mg-1mg/kg/day) and an injection of Benzathine Penicillin. Group-B was given additional oral prednisolone (2mg/kg/day) for four weeks, with tapering in the next two weeks. Epidemiological data, clinical features and laboratory parameters were collected. The Universiade Federal de Minas Gerais Sydenham's chorea Rating Scale (USCRS) was applied to both groups at the presentation after two weeks and four weeks.
***Results:*** Out of 68 patients, the mean Universidade Federal de Minas Gerais (UFMG) Sydenham's Chorea Rating Scale (USCRS) got progressively better in Group-B (mean score improvement was 25.73±5.56 at two weeks and 41.06±6.89 at four weeks) than in Group-A (mean score improvement was 9.12±3.75 at two weeks and 17.97±3.89 at four weeks) with *p*-value of <0.05.
***Conclusion:*** Steroid therapy significantly improved patients with Sydenham's chorea compared to those who did not receive any steroid therapy.

**Keywords:** Efficacy, Steroid therapy, Sydenham chorea.

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## INTRODUCTION

Sydenham's chorea is an autoimmune hyperkinetic movement disorder and a major neuropsychiatric presentation of acute rheumatic fever.[1] It occurs weeks to months after Group A beta haemolytic streptococcal infection (GABHS).[2,3] It is the most prevailing chorea in children, even in developed areas. In underprivileged regions like Pakistan incidence rate of Rheumatic fever is nearly 46.1/100,000 population.[4,5] Sydenham chorea is found in almost 10% of patients with rheumatic fever and is more common in girls than boys. It can present both alone and, in some cases, with carditis.[6]

The Universidade Federal de Minas Gerais Sydenham's chorea Rating Scale (USCRS) is a valuable tool for evaluating the clinical changes in Sydenham's chorea patients related to natural history or therapeutic intervention.[7] It gives the quantitative interpretation of the performance of daily life activities like handwriting, cutting food, dressing, walking, and hygiene; behavioural problems like irritability, attention deficit, hyperactivity, obsessions, compulsions, and reduced verbal fluency; and motor function like oculomotor function, motor persistence, dysarthria, chorea in the face and all limbs, bradykinesia, muscle tone, and gait of patients with Sydenham's chorea.[8]

Treatment choices early in chorea include antiepileptic drugs like phenobarbital, valproic acid and carbamazepine etc. Neuroleptics like Haloperidol, Pimozide, Chlorpromazine, etc.[9] Secondary prophylaxis comprises one intramuscular injection of benzathine penicillin at three to four weekly intervals in higher endemic regions and is typically continued for five years. However, patients with carditis must continue for 25 years.[10]

This study was designed to determine the efficacy of steroids in children with Sydenham chorea in the Neurology Department of Children Hospital and Institute of Child Health so that we may revise protocols of Sydenham chorea treatment according to the efficacy of steroids.

## METHODOLOGY

The prospective comparative study was conducted in the Inpatient and Outpatient Departments of Pediatric Neurology, Children Hospital and Institute of Child Health, Lahore Pakistan, from December 2019

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to May 2020. Institutional Ethical Review Board approved the study (Reference number: 2020-103-CHICH). The sample size was calculated by taking population proportion as 4.6/100000,[11] population via Open Epi, Version 3.01, open-source calculator. Non-probability, consecutive sampling was utilized as a sampling technique.

**Inclusion Criteria**: Children aged 5 years to 18 years, irrespective of gender, who was diagnosed with Sydenham's chorea according to Modified Jones Criteria for Rheumatic Fever7, having a duration of illness of 1 week, were included in the study.

**Exclusion Criteria**: Children with other causes of chorea (antinuclear factor, anti-double-stranded DNA antibodies, antiphospholipid antibodies, serum glucose, thyroid function, Kayser-Fleischer ring, ceruloplasmin, and computed tomography or magnetic resonance imaging of brain) were excluded from the study.

Informed consent was taken from parents. Tests, i.e. throat culture, acute phase tests (C-reactive protein, erythrocyte sedimentation rate), antistreptolysin O titers, electrocardiogram, and two-dimensional Echo-Doppler cardiography, were done in all patients. The selected 68 patients were assigned to two groups, Group-A & Group-B, comprising 34 patients in each irrespective of gender by lottery method. USCRS was applied to both groups at the time of the presentation. No placebo was used in this study. As per protocol of the neurology department, The Children's Hospital and The Institute of Child Health, Lahore, medications (diazepam 0.3mg-1mg/kg/day and injection Benzathine Penicillin prophylaxis) were given to both groups. Children in group B were given steroid therapy in the form of oral Prednisolone 2mg/kg/day (maximum 60mg) for four weeks, followed by tapering it off in the next two weeks, in addition to Diazepam. The treating physicians supervised that the study drug was given accurately, and a Penicillin administration card evaluated compliance with the injection of Benzathine Penicillin prophylaxis. USCRS was applied to both groups after two and four follow-up weeks. The percentage of USCRS improvement was assessed for each group, applying the formula (USCRS X week–USCRS 0-week/USCRS 0-week) X100. Parents were asked about any side effects of Prednisone, i.e. weight gain, cushingoid appearance, gastrointestinal symptoms and high blood pressure. The pediatric examination was done in all patients, including weight and blood pressure measurements. Data was collected in pre-designed proforma for clinical features, laboratory parameters, and USCRS at the presentation after two weeks and four weeks on follow-up and side effects of steroid therapy.

Data was entered and analyzed through Statistical Package for the Social Sciences (SPSS) version 20:00. Quantitative variables were expressed as mean and standard deviation. Qualitative variables were expressed as frequency and percentage. Differences between groups were evaluated by t-test and the *p*-value of <0.05 was considered significant.

## RESULTS

The total sample involved 68 patients, of which 32(47.06%) were males, and 36(52.94%) were females. Patients were divided into two Groups-A and B having 34 patients in each group. In Group-A, 32(94.11%) had generalized chorea, 2(5.89%) had hemichorea [2(100.00%) with right-sided hemichorea], 18(52.94%) had carditis, out of which 17(94.44%) were with mild carditis, and 1(5.56%) was with moderate carditis. In comparison, 16(47.06%) did not have carditis, Erythrocyte Sedimentation Rate(ESR) was >30mm/hr in 22(64.70%), C-Reactive Protein (CRP) was >3mg/dl in 28(82.35%), and Antistreptolysin O Titer (ASOT) was >250IU in 24(70.58%). In Group B, 32(94.11%) had generalized chorea, 2(5.89%) had hemichorea [1(50%) with right-sided hemichorea and 1(50%) with left-sided hemichorea], 16(47.06%) had carditis out of which 15(93.75%) were with mild carditis, and 1 (6.25%) was with moderate carditis. In comparison, 18(52.94%) did not have carditis, ESR was >30mm/hr in 20(58.82%), CRP was >3mg/dl in 20(82.35%), and ASOT was >250IU in 18(52.94%) (Table-I).

**Table-I: Clinical and Laboratory Parameters (n=68)**

| Clinical and Laboratory Parameters | Group-A (n=34) Mean±SD | Group-B (n=34) Mean±SD | *p*-value |
|---|---|---|---|
| Type of Chorea | 1.05±0.23 | 1.50±0.56 | 1.000 |
| Carditis | 1.55±0.56 | 1.05±0.23 | 0.689 |
| Erythrocyte Sedimentation Rate >30 mm/hr | 35.95±9.85 | 33.32±14.47 | 0.364 |
| C-Reactive Protein >3mg/dl | 10.52±12.10 | 8.11±12.58 | 0.469 |
| Antistreptolysin O Titer >250IU | 654.91±462.92 | 505.11±441.90 | 0.114 |

There was continuous improvement in both Groups (A and B) at the follow-up time at two weeks and four weeks. However, in Group-A, only 13 (38.23%) children had USCRS score improvement >

50% from their USCRS score at presentation (Figure-1). There was a more significant improvement in USCRS score at four weeks' follow-up in Group-B having USCRS score improvement >50% in 34(100%) children from their USCRS score at presentation (Figure-2).

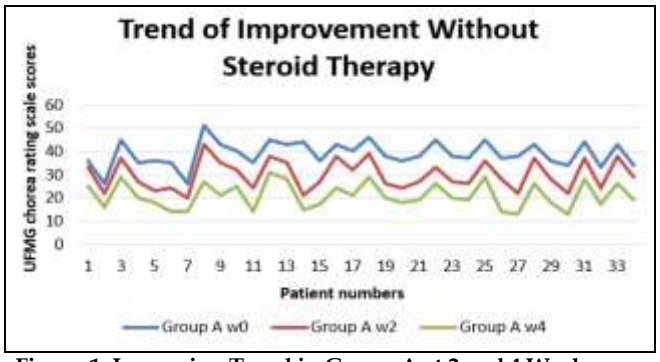


**Figure-1: Improving Trend in Group-A at 2 and 4 Weeks**

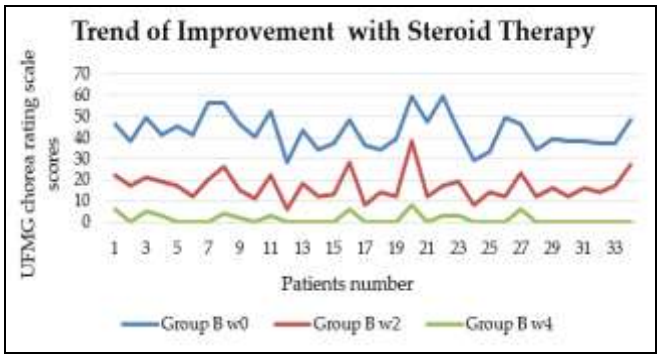


**Figure-2: Improving trend in Group-B at 2 and 4 Weeks**

A significant difference between both groups was noted in the percentage of 2 and 4 weekly USCRS score rate improvement (Table-II).

**Table-ll: Comparison of USCRS Score Improvement in Study Groups at 2 and 4 Weeks (n=68)**

| Week | Group A (n=34) | Group B (n=34) | *p*-value |
|---|---|---|---|
| | Mean±SD | Mean±SD | |
| 2 | 9.12±3.75 | 25.73±5.56 | <0.001 |
| 4 | 17.97±3.89 | 41.06±6.89 | <0.001 |

Utilizing repeated measurements on USCRS at 2 & 4 weeks, the mean USCRS score got better in Group-B (mean score improvement was 25.73±5.56 at two weeks and 41.06±6.89 at four weeks) more significantly than in Group-A (mean score improvement was 9.12±3.75 at two weeks and 17.97±3.89 at four weeks).

Prednisolone-induced side effects were observed in Group-B in weight gain, cushingoid features (moon face) and gastrointestinal upset. Weight gain was noted in 34(100%), moon face was observed in 28 (82.35%), and gastrointestinal upset was noted in 2 (5.88%), whereas hypertension was not observed in any case.

## DISCUSSION

This study shows that Sydenham's chorea treatment with Prednisone decreased the severity and duration of symptoms more significantly than treatment without steroids. In addition, there is a more significant improvement in USCRS score at 4-week follow-up in the steroid therapy group having USCRS score improvement >50% in 100% of children from their USCRS score at presentation as compared to those without steroid therapy group in which only 38.23% of children had USCRS score improvement >50% from their USCRS score at presentation.

Another study illustrated a significant response by steroids in the form of decreased chorea duration and fast recovery in symptoms. Oral Prednisone was used as steroid therapy, and the chorea intensity scale was used for the chorea rating, which did not include the psychological aspects.[12]

A small case series by Fusco *et al.* revealed the effectiveness of steroids in the severe paralytic form of chorea. Steroid therapy was given in the form of intravenous methylprednisolone pulses followed by deflazacort, and USCRS was used for measurement of chorea intensity.[13]

A retrospective analysis by Walker *et al.* indicated that steroids significantly decreased the period of chorea by about 5.0-weeks. Oral Prednisone was used as steroid therapy, but no proper scale was utilized for chorea intensity measurement.[14] Favaretto *et al.* demonstrated the effectiveness of corticosteroid therapy in Sydenham's chorea patients in terms of faster resolution of symptoms in a retrospective observational study in which Prednisone was used as steroid therapy in a single administration for 14 days and then tapered off.[15]

Teixeira *et al.* described the effectiveness of steroid therapy in four patients with the severe form of Sydenham's chorea, which was given in the form of intravenous methylprednisolone therapy followed by oral Prednisone.[16] Fusco *et al.* described five cases where steroids were given as oral deflazacort in mild and moderate cases. In contrast, intravenous methylprednisolone pulses followed by oral deflazacort in severe cases of Sydenham's chorea, apart from symptomatic treatment, revealed the effectiveness of steroid therapy with no significant side effects.[17]

Garvey *et al.* established a non-blinded, randomized controlled trial by comparing immunomodulatory therapies, including Prednisone, intravenous immunoglobulin and plasmapheresis. The results revealed that the mean chorea severity score was reduced by 72% in the intravenous Immunoglobulin Group and 50% in the plasmapheresis Group and 29% in the Prednisone Group.[18]

In future, studies should be done to compare the effectiveness of Prednisone with other steroids like methylprednisolone pulse and deflazacort.

## CONCLUSION

We concluded that USCRS applied to both groups on two weeks and four weeks follow-ups showed progressive betterment in the score, which is more remarkable in the steroid therapy group. So, this study supports that steroid therapy is effective in Sydenham's chorea. Therefore, we propose that prednisolone should be considered when managing Sydenham's chorea.

**Conflict of Interest:** None.

**Author's Contribution**

Following authors have made substantial contributions to the manuscript as under:

MA & JRA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

ZR & TS: Conception, study design, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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