

**IBUPROFEN INDUCED STEVEN JOHNSON SYNDROME**

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**ABSTRACT**

Stevens Johnson Syndrome (SJS) is a hypersensitivity reaction characterized by skin rashes with hyperpigmentation and cutaneous target lesions involving blistering/erosions over face, trunk & limbs. The mortality rates of SJS/Toxic Epidermal Necrolysis (TEN) is ranging between 10% and 75 %. Nonsteroidal antiinflammatory drugs (NSAIDs), analgesic agents and nonsulfonamide antibiotics are associated with SJS/TEN is controversial.<sup>[5]</sup> **Case report:** A 2years old male child was admitted in hospital with chief complaints of swelling, discolouration of lips and skin lesion since 4 days. Flexon suspension (ibuprofen 100mg+ paracetamol 125mg) was used for fever. The condition was managed with Intravenous fluids, oral corticosteroids prednisolone, fusidic cream and liquid paraffin. **Conclusion:** Early identification and discontinuation of the causative drug is very important as it helps to avoid secondary infection and other complications.

**KEYWORDS:** Ibuprofen, NSAIDs, Steven Johnson syndrome.**INTRODUCTION**

Adverse drug reaction is an unexpected, undesired, and unintended or a toxic consequence of drug administration.<sup>[1]</sup>

Stevens Johnson Syndrome (SJS) is a hypersensitivity reaction characterized by skin rashes with hyperpigmentation and cutaneous target lesions involving blistering/erosions over face, trunk & limbs.

The incidence of SJS is more in male compare to female and ranges from 7 to 49 cases per million persons per year.<sup>[2]</sup>

The mortality rates of SJS/Toxic Epidermal Necrolysis (TEN) is ranging between 10% and 75 %.<sup>[3]</sup>

SJS involves less than 10% and more than 30% of the body surface area. The third condition named as SJS - TEN overlap falls in between SJS and TEN. Patient may initially present with SJS, which subsequently evolves into TEN or SJS - TEN overlap.<sup>[4]</sup>

Drugs are an important cause of Stevens-Johnson syndrome, but infections or a combination of infections and drugs has also been implicated.

A limited number of drugs like sulphonamides, anticonvulsant agents and allopurinol are most consistently associated with conditions like SJS and

TEN; whether nonsteroidal antiinflammatory drugs (NSAIDs), analgesic agents and nonsulfonamide antibiotics are associated with them is controversial.<sup>[5]</sup>

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used to control pain and fever and to treat various inflammatory diseases, by inhibiting the synthesis of prostaglandins, they can induce both beneficial effects and adverse reactions, including type B reactions, which are not dose-dependent. Type B reactions encompass drug hypersensitivity reactions (DHRs) which affect all age groups.<sup>[6]</sup>

Ibuprofen is a common over-the-counter antipyretic-analgesic nonsteroidal anti-inflammatory drug whose principal effect is inhibition of cyclooxygenase (prostaglandin-synthase), thus impairing the final transformation of arachidonic acid to prostaglandins, prostacyclin, and thromboxanes. Hypersensitivity-syndrome associated with ibuprofen is a host-dependent idiosyncratic drug-reaction.<sup>[7]</sup>

**CASE REPORT**

A 2years old male child was admitted in hospital with chief complaints of swelling, discolouration of lips and skin lesion since 4 days. Blackish discolouration started over face then spread all over the body which was sudden in onset.

History of fever since 2 weeks on and off for which treatment was done at local hospital.

Past medication history: Paracetamol syrup was given for 4 days as the fever was not subsided it is replaced with flexon suspension (ibuprofen 100mg+ paracetamol 125mg).

On examination the child was conscious irritable, on systemic examination pulse rate was 116beats/min, B.P. was 100/70mmHg, RR was 24/min, all other organ systems were normal. Crusting over the lips and generalised maculopapular rash was present. Clinically a case of SJS.

Laboratory findings shows haemoglobin 8.9g /dl (12-14 g/dl), WBC 13,200(4000- 12000) Neutrophils- 71% Lymphocytes- 25% Serum electrolytes were normal. ESR 1<sup>st</sup> hour 55mm 2<sup>nd</sup> hour 60mm.

On day 1 Intravenous fluids with isolyte p, oral corticosteroids prednisolone and Listerine mouth wash for gargling were started.

On 2<sup>nd</sup> day Liquid paraffin, fusidic cream calosofe plus lotion were given for local application and syrup paracetamol was added.

They continued the same treatment for 6 days and the patient was discharged. Discharge medication include fusidic cream, liquid paraffin and Listerine mouthwash for gargling.

## DISCUSSION

SJS is a severe life threatening mucocutaneous syndrome caused by hypersensitivity to drugs and is associated with significant morbidity and mortality.<sup>[8]</sup>

Among the NSAIDs, paracetamol and nimesulide are most commonly reported in the study conducted by Patel. Severe Cutaneous Adverse Reactions (SCAR) study has found an overall risk of SJS with oximac derivatives. There is no increased risk with diclofenac, salicylates and pyrazolone derivatives. Euro SCAR study found weak association of paracetamol with SJS.<sup>[4]</sup>

The first case report on Stevens Johnson syndrome with hepatitis secondary to Ibuprofen was reported in the USA in 1978 by Sternlieb *et al.* In 1984, Stern *et al.*, reported case series of 135 cutaneous reactions secondary to use of non-steroidal anti-inflammatory agents to NSAIDs in USA. The study showed high incidence of fixed drug eruption secondary to ibuprofen first time.<sup>[2]</sup>

The mechanism has still not been understood and is complex that how NSAIDs develop SJS. Evidence has shown various pathological mechanisms are involved like drug specific CD8+ cytotoxic lymphocytes, natural killer cell activation, cytokines including perforin/granzyme and Tumour Necrosis Factor (TNF) alpha.<sup>[9]</sup>

Cytokines play a role in the immunopathological and molecular mechanisms of drug-induced hypersensitivity reactions (HSR). A study of ibuprofen induced SJS showed that in SJS patients there will be high level of lymphocytes and cytokine secretion with high level of TNF alpha as high as in TEN patients.<sup>[10]</sup>

Prompt removal of the causative drug is the main priority and alternative drug should be given. Hence flexon (ibuprofen + paracetamol) was discontinued and only paracetamol syrup was given. In this case WBC and Erythrocyte Sedimentation Rate were increased. Corticosteroids helps in improving the condition by suppressing T lymphocytes activity.



Fig 1: Skin lesion and discolouration of lips.



Fig 2: Rashes and hyperpigmentation on the first day.

## CONCLUSION

Early identification and discontinuation of the causative drug is very important as it helps to avoid secondary infection and other complications. Patient education and having an information chart related to drug reaction may be helpful in reducing the number of adverse drug reactions.

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