

## **Fixed dose combination of ibuprofen and paracetamol induced toxic epidermal necrolysis**

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### **ABSTRACT**

Toxic Epidermal Necrolysis (TEN) is a serious dermatological disorder and a potential life threatening condition, which can be due to drugs or infections. Fixed dose combination (FDC) of Ibuprofen plus Paracetamol is commonly used as an analgesic and antipyretic over the counter (OTC) in India. We present a case of Toxic Epidermal Necrolysis due to Fixed Drug Combination of Ibuprofen and Paracetamol. Awareness should be there both at the level the consumers and the health care professionals regarding occurrence of such rare but potentially serious side effect associated with such combination.

**Keywords:** FDC, Ibuprofen, OTC drug, Paracetamol, TEN

### **INTRODUCTION**

Fixed drug combinations of Ibuprofen plus Paracetamol are available freely as over the counter medicine in Indian market. Such irrational fixed drug combinations are easiest way to sell two drugs but patient has to pay in terms of extra cost and extra adverse effects.<sup>1</sup> Toxic epidermal necrolysis (TEN) is a rare but fatal disorder of the skin and mucous membranes and present clinically as wide spread erythema, necrosis, bullous formation and detachment of the epidermis from the dermis which may results in exfoliation of skin, sepsis and death. 80-95% of TEN are drug induced.<sup>2</sup> We are presenting a case of TEN in 3yrs old boy due to use of fixed drug combination of syrup combiflam; Sanofi Aventis (Ibuprofen 100mg/5ml and Paracetamol 162.5mg/5ml).

### **CASE REPORT**

A 3 year old boy was admitted in the dermatology ward with complaints of erythematous rashes all over the trunk and abdomen. The child had history of fever for 3 days and local medicine retailer has given syrup Combiflam to the parents. After 2 days of taking the syrup at a dose of 5 ml thrice daily the mother noticed sudden appearance itchy rashes in his body. As the rashes increased rapidly by overnight, she stopped giving him the drug and rushed to the emergency of our Institute the next day. Mother reported that the same medicine was given to him for fever 2 month ago without any allergic manifestation. On physical examination extensive oedematous raised maculo-papular rashes were noted over the trunk and abdomen. The case was provisionally diagnosed as erythema multiformae major and treatment was started with Gentian violet lotion, Hydroxyzine Hydrochloride, Cefixime and Multivitamin. However during the initial hospital stay the rash converted to polymorphic bullous

lesion over the affected part and also affected the face, upper and lower limbs and oral mucosa. However there was no involvement of conjunctiva, scalp, palm and sole. The case was re-assessed and diagnosed clinically as TEN due to involvement of more than 30% of body surface area with blistering in oral mucosa. Nikolsky sign and Asboe Hansen sign were positive. Laboratory investigation shows Total leucocyte count-8,600/mm<sup>3</sup>, Neutrophil-74%, lymphocyte-20%, eosinophil-6%, ESR-90, SGOT-96 U/L, SGPT-112 U/L and serology test for HIV were negative. The boy responded well to the conservative management and discharged home after 3 weeks of hospital stay. The parents are advised not to give the same medicines in the future without consultation with the physician and to inform about the drug reaction.



**Figure 1: Epidermal detachment.**

## DISCUSSION

The diagnosis of TEN is based on both clinical and histological findings. Necrotic keratinocytes with full-thickness epithelial necrosis and detachment is consistent with the diagnosis of TEN. Perivascular and scattered lymphocytic infiltration of the dermis is sometimes demonstrated, although the underlying dermis is not greatly altered. No definitive or specific emergent laboratory tests are indicated for TEN. Basic laboratory tests may be helpful in planning symptomatic or supportive therapy.



**Figure 2: Target lesion.**



**Figure 3: Lesions at various stages of healing.**

Our case was presented with feature of erythema multiformae major but rapidly progressed to full-fledged TEN. The appearance of lesions coincides with the consumption of syrup combiflam and there was no other drug history. Ibuprofen and Paracetamol when used alone are equally effective and well tolerated in the treatment of fever in paediatric age group. Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) of propionic acid derivative and Paracetamol is a para-amino phenol derivative, also known as acetaminophen is not

commonly categorized under NSAID due to its weak anti-inflammatory action. Though cases of ibuprofen induced TEN has been reported in some literature, no such association has been found in relation to paracetamol alone.<sup>3,4</sup> We find out a case of combiflam induced maculo-papular rash in the literature.<sup>5</sup>

In our case diagnosis of TEN was made clinically. In spite of the fact that case of TEN has high mortality, our case responded well with supportive management and patient recovered completely without much serious sequelae. Drug re-challenge was not done due to ethical issue. WHO-UMC causality assessment system pointed towards a “probable” association and Naranjo’s algorithm score+5 also suggestive of probable association.<sup>6</sup>

### CONCLUSION

Although fixed drug combination of Ibuprofen and Paracetamol are commonly used to treat fever in paediatric age group and tolerated well, they are not without detriment and are sometimes associated with serious side effects. Awareness should be there both at the level the consumers and the health care professionals regarding occurrence of potentially serious side effect associated with such combination specially in Indian scenario where this combinations are prescribed frequently and also available over the counter.

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