



## Rationale of Aceclofenac in Management of Pyrexia in Paediatric Practice

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### Abstract

Pyrexia, a complex physiological response triggered by infection or aseptic stimuli causes increase in Prostaglandin E<sub>2</sub>(PGE<sub>2</sub>) concentration in brain and later firing rate of neurones of thermoregulatory centre i.e. Hypothalamus.

Majority attendance at paediatrician chamber are of children with pyrexia of varied origin and to calm the temperature at optimal level various therapeutics are in vogue but attendance of children with antipyretics adversely presenting as morbidity and mortality necessitated an evaluation of presenting hazards with consuming antipyretics.

**Objective of study:** Analyse the rationality of Aceclofenac paracetamol combination, as antipyretics in paediatric practice.

**Material and Methods:** analysis of datasheet of patients admitted with antipyretics adversely at Centre for Children Disease and Research.

**Result:** children consuming Aceclofenac Sodium Paracetamol presented with grave status of prolonged hypothermia, CNS disturbances like Dizziness, Convulsion, coma in addition to more pronounced other presentation like persistent vomiting, haematemesis, blood dyscrasia, rash, albuminuria than other.

**Conclusion:** Aceclofenac sodium Paracetamol combination must be restricted for paediatrics use considering its dreaded outcome.

**Keywords:** Pyrexia; Prostaglandin; Hypothalamus, Thermoregulatory; CNS Disturbances Hypothermia; Blood Dyscrasia; Albuminuria

### Introduction

Pyrexia, a common clinical presentation of varied clinical conditions estimating 1/3 of all children visit to health care centre and parent usually self-medicate their children with the over the counter (OTC) antipyretics [1].

Fever is a beneficial outcome of the physiologic response triggered by infection or aseptic stimuli as it boosts immunity against the invading pathogen, though beyond certain level it may cause discomfort and organic damage which usually presents with febrile convulsion [2,3].

Fever up to 102° F is considered beneficial but >102° F become harmful and disastrous thus medication needed to keep the temperature <102° F [4,5].

Fever result from an immune response mediated through the action of cytokinin on thermoregulatory centre of the brain or by conserving heat through vaso- constriction manifesting as Chills Or generating heat by active muscular contraction i.e.- rigor (Figure 2).

During fever in addition to specific therapeutics the molecules usually prescribed is antipyretics and the commonly prescribed are – Paracetamol (Acetaminophen); Mefenamic acid, Ibuprofen and Nimesulide either alone or in combination with paracetamol, but these days Aceclofenac and paracetamol being commonly prescribed and sold as over the counter antipyretics in children [6-9].

Fever may be suppressed by antipyretic or by physical cooling. During antipyretics prescription safety profile must be choice as

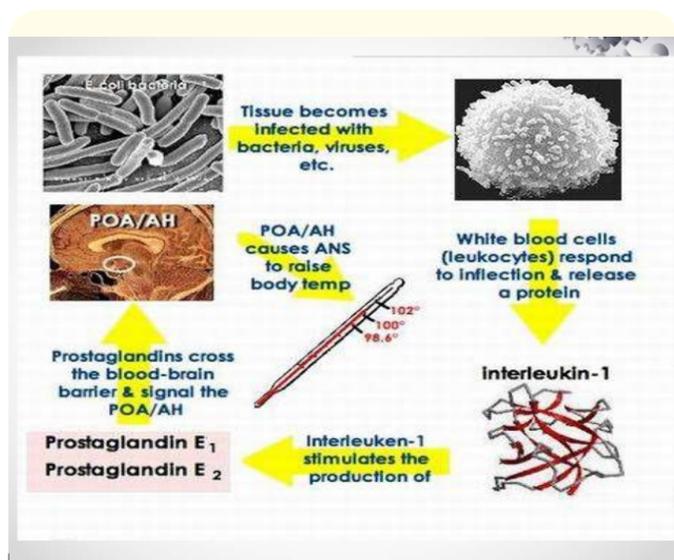


Figure 1: Schematic presentation of Fever generation).

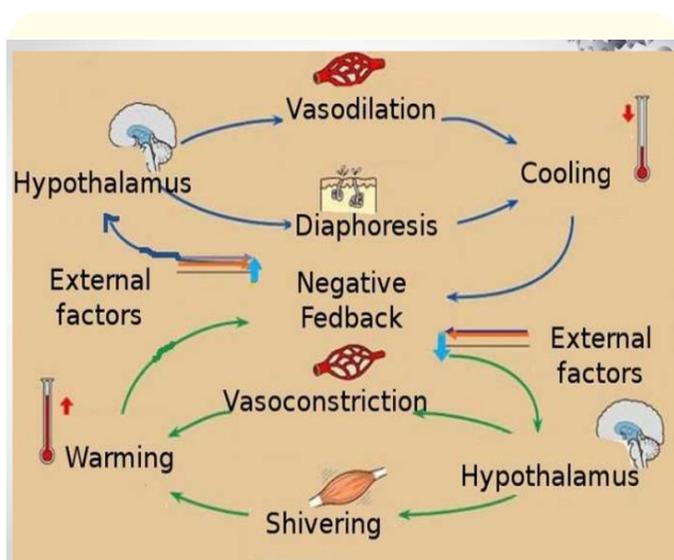


Figure 2: Schematic representation of Thermal haemostasis.

majority of antipyretic are equally effective and their proper dose and administer schedule must be ensured [7,10].

Most antipyretics act by inhibiting the enzyme Cyclo oxygease and reduces PGE2 within the hypothalamus but may be due to reduction of pro inflammatory mediator, increased anti-inflammatory signals or boost antipyretic message within the brain [9,11].

Usually village practitioner follows the prescription of qualified clinician and over the counter drugs are being used only when manufacturer come with these products with due permission from FDA. Availability of Aceclofenac sodium -paracetamol suspension being rampantly used for pyrexia in children.

As drug formulation approval is the responsibility of FDA, this study is being conducted with an intent to assess the rationality of Suspension Aceclofenac with paracetamol as an antipyretic for children.

**Objective of the study**

Analysis of untoward effects observed in children taking Aceclofenac -Paracetamol combination for treatment of fever.

**Duration of study**

Patients attended the centre between January 2016- February 2018.

**Material and Methods**

**Material**

Children suffering with pyrexia and consumed Aceclofenac sodium -paracetamol combination and admitted at Centre For Research in Children Disease, RA. Hospital and Research Centre, Warisaliganj (Nawada) Bihar with unusual presentation been selected for analysis.

**Method**

Patient’s parent or attendant were interrogated for therapeutics taken, its dose administration and appearance of the manifestation, clinically examined and investigated for haematological, hepatic and renal profile.

Patients presenting with hypothermia, perspiration, hypotension, cardiac dysrhythmia unconsciousness and convulsion were treated accordingly

**Observations**

Children consuming various antipyretics for relief of fever and attending at Centre for Children Disease Research were of age group < 1 - > 5 years majority 614 (22.7%) patients of age group 4-5 years (Table 1).

Out of all 1700 were male and 1000 female (Figure 3).

Age group (in years)	Number of patients			
	Male	Female	Total	%
< 1	138	94	232	8.6
1 - 2	238	142	380	
2 - 3	312	212	524	
3 - 4	308	202	510	
4 - 5	406	208	614	
> 5	298	146	444	

Table 1: Age and sex wise distribution of patients.

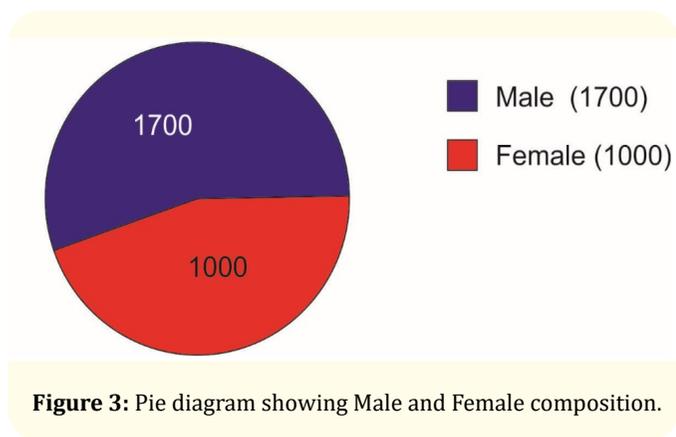


Figure 3: Pie diagram showing Male and Female composition.

Out of all 25% were taking Aceclofenac -paracetamol while 4.2% only paracetamol though 34% patients were taking Nimesulide and paracetamol (Table 2).

Therapeutic group	Number of patients	%
Aceclofenac sodium + Paracetamol	674	25
Nimesulide +Paracetamol	924	34
Ibuprofen +Paracetamol	4745	17.5
Mefinamic acid +Paracetamol	322	12.0
Nimesulide	208	7.3
Paracetamol	98	4.2

Table 2: Distribution of patients as per their therapeutics.

Though nausea remain a common manifestation among all patients of varied therapeutic group, but manifestation like Dizziness, rash, GI bleeding, blood dyscariasis, convulsion, prolonged hypothermia remain more pronounced with marked albuminuria in patients taking Aceclofenac sodium - Paracetamol combination. Patients taking Aceclofenac paracetamol presenting with adversity

like Dizziness, convulsion and sustained hypothermia resulted in an eventful fate i.e. mortality in 20 cases out of 674 but none of another group (Table 3).

Presentations	Number of cases in various group of therapy					
	AP	NP	IP	MP	N	P
	(674)	(925)	(474)	(322)	(208)	(98)
Nausea	425	306	138	102	50	06
Vomiting	288	103	60	32	-	-
Dyspepsia	300	108	68	40	-	-
Abdominal colic	342	110	92	46	-	-
Dizziness	208	-	-	-	-	-
Rash	196	-	-	-	-	-
GI bleeding	12	-	-	-	-	-
Blood dyscariasis	37	-	-	-	-	-
Convulsion	19	-	-	-	-	-
Prolonged hypothermia	78	-	-	-	-	-

Table 3: Presentation observed during therapy.

Onset of antipyretic effect was similar in all the groups sustained prolonged hypothermia was very common in patients consuming Aceclofenac sodium - Paracetamol than Nimesulide -paracetamol (Figure 4).

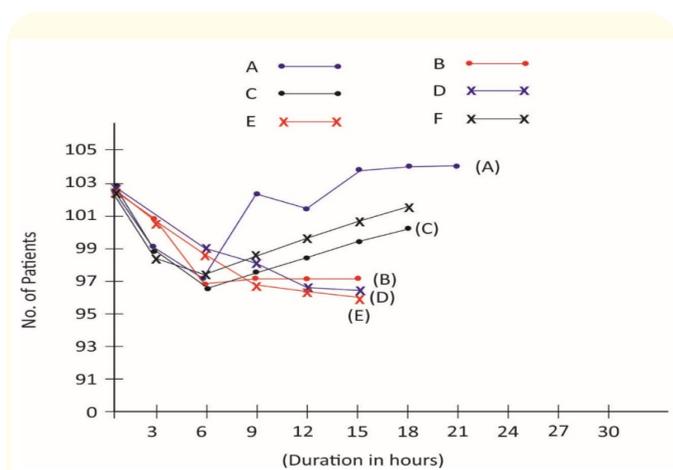


Figure 4: Group showing antipyretic effect of various combinations.

**Result**

Antipyretic available shows equi anti pyretic effect for varied duration. Patients taking Aceclofenac- Paracetamol combination shows highest drug adversivity in children than other anti pyretics, with dreaded toxicity like prolonged and sustained hypothermia resulting in morbidity and mortality, thus must be restricted its use as antipyretics.

**Conclusion**

Considering the untoward effects causing morbidity and mortality with Aceclofenac Sodium -Paracetamol, its advocacy in children must be restricted.

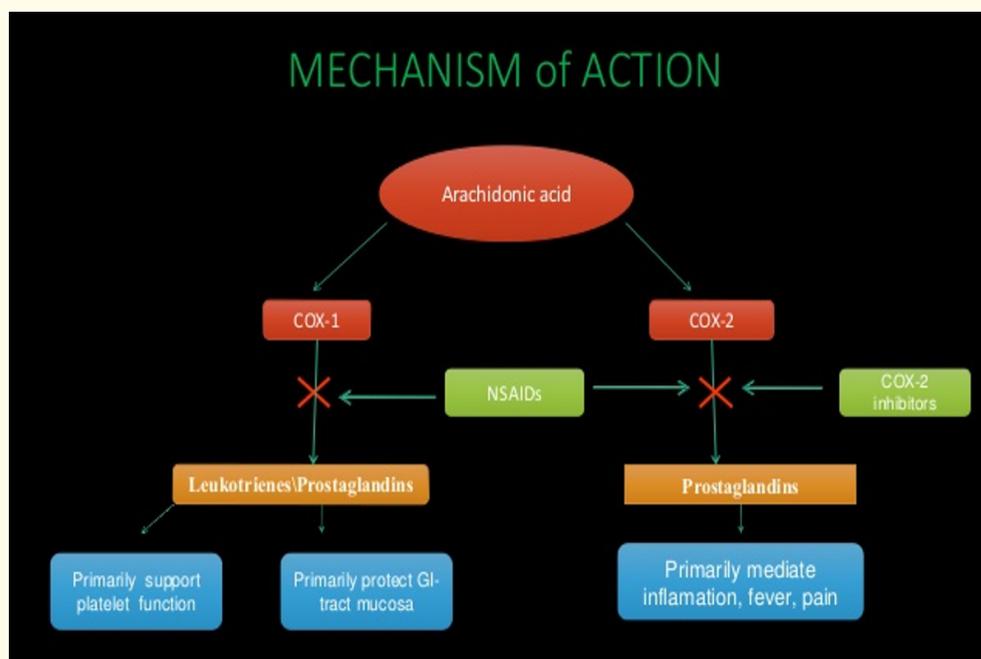
**Discussion**

Pyrexia remain a major cause of children attendance at Clinician chamber and majority comes with use of various over the counter

antipyretics or treated by local practitioners. As to calm the fever use of antipyretic is an Ernest need but must be used with due caution as -Evaluation of data sheet of children presenting with fever of varied origin taking various antipyretic and presenting with sequel suggest pronounced drug adversivity with Aceclofenac sodium -paracetamol combination than other i.e.- dizziness, rash, blood dyskaryosis, marked albuminuria, convulsion, sustained and prolonged hypothermia resulting in brain death.

Most antipyretics act by inhibiting the enzyme Cyclo oxygenase and reducing the level of PGE<sub>2</sub> within the hypothalamus but may be due to reduction of pro inflammatory mediators, increase anti-inflammatory signals or boost anti pyretic messages within the brain (Figure 5).

Aceclofenac sodium is an orally effective non-steroidal anti-inflammatory drug of phenyl acetic acid group possessing remark-



**Figure 5:** Schematic presentation of Antipyretic action.

able anti-inflammatory, analgesic and antipyretic properties but usually a choice prescription for rheumatoid arthritis, osteoarthritis and ankylosing spondylitis, but not recommended in children. Aceclofenac shows more selective effect towards COX<sub>2</sub> than COX<sub>1</sub>

and inhibits synthesis of Prostaglandin (PGE<sub>2</sub>), a product of inflammatory cytokine, interleukin and tumour necrosis factor; in addition also affect cell adhesion molecules from neutrophil [12,13].

This also interrupts the endo cannabinoid system and endocannabinoid [14,15] as COX<sub>2</sub> utilises endo cannabinoid as a substrate and plays key role in producing drug adversity specially in children, pregnant and breast-feeding mother (Figure 6).

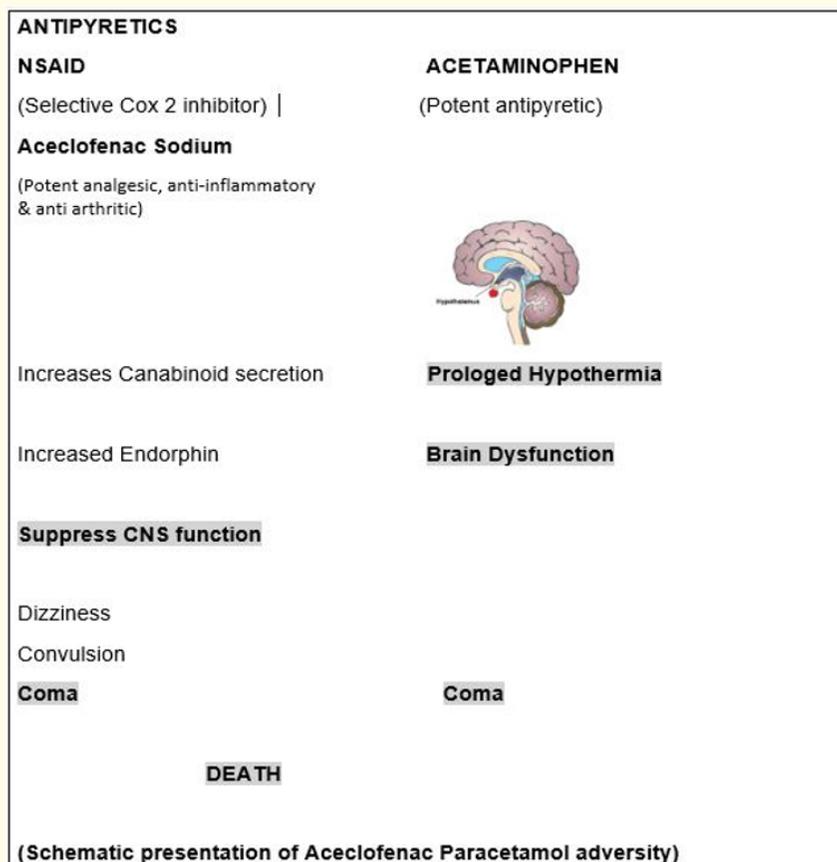


Figure 6: Schematic presentation of Aceclofenac\_paracetamol adversity.

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