

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 E₂(PGE₂) 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 adversity 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 adversity at Centre for Children Disease & 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 dyscrasias, 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 dyscrasias, albuminuria

1. 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.^{1,2}

Fever is a beneficial outcome of the physiologic response triggered by infection or aseptic stimuli as it boost immunity against the invading pathogen, though beyond certain level it may cause discomfort and organic damage which usually presents with febrile convulsion.^{3,4}

Fever up to 102⁰F is considered beneficial but >102⁰F become harmful and disastrous thus medication needed to keep the temperature <102⁰F.^{5,6}

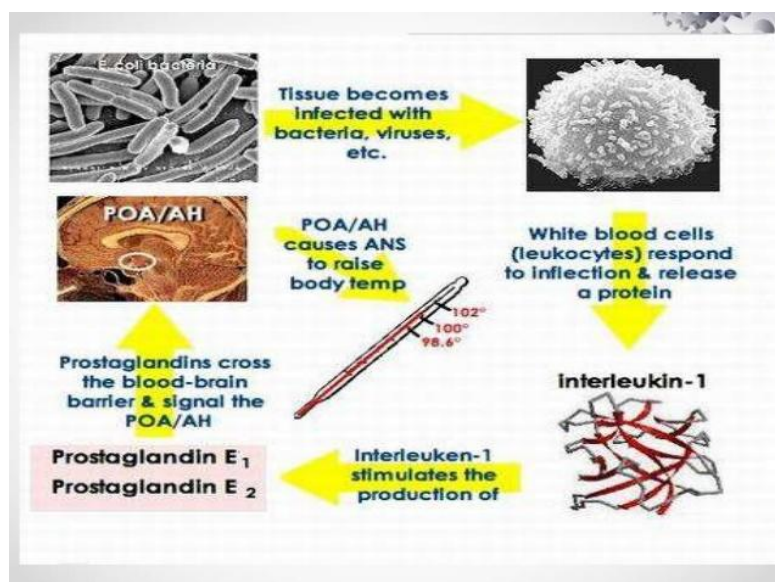


Figure 1. Schematic presentation of Fever generation

Fever results from an immune response mediated through the action of cytokines on the thermoregulatory centre of the brain. Or by conserving heat through vasoconstriction manifesting as chills. Or generating heat by active muscular contraction i.e. - rigor (Figure -2)

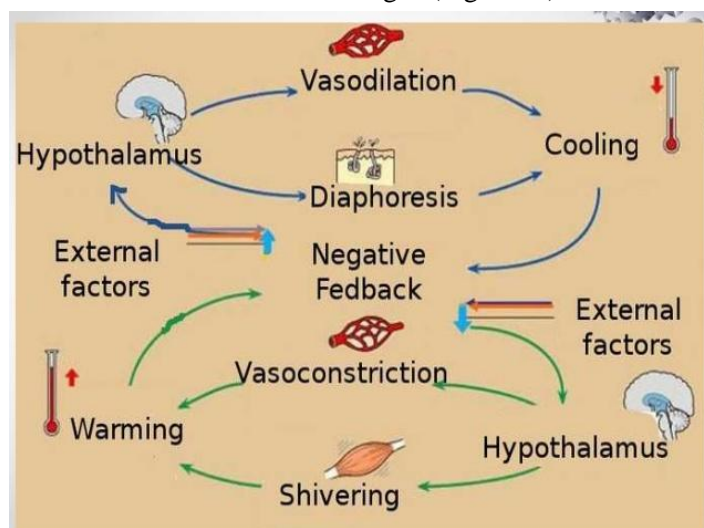


Figure 2. Schematic representation of Thermal haemostasis

During fever, in addition to specific therapeutics, the molecules usually prescribed are 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 are being commonly prescribed and sold as over-the-counter antipyretics in children^{7,8,9,10}

Fever may be suppressed by antipyretic or by physical cooling. During antipyretic prescription, safety profile must be chosen as the majority of antipyretics are equally effective and their proper dose and administration schedule must be ensured.^{11,12}

Most antipyretics act by inhibiting the enzyme Cyclooxygenase and reduce 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.^{13,14}

Usually village practitioners follow the prescription of a qualified clinician and over-the-counter drugs are being used only when manufacturers come with these products with due permission from FDA. Availability of Aceclofenac sodium-paracetamol suspension is 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.

2. OBJECTIVE OF THE STUDY

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

3. DURATION OF STUDY

Patients attended the centre between January 2016- February 2018

4. MATERIAL & METHODS

4.1. Material

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

4.2. 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

5. OBSERVATIONS

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

Table1.Age & sex wise distribution of patients

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	

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

Pie diagram showing Male Female Composition

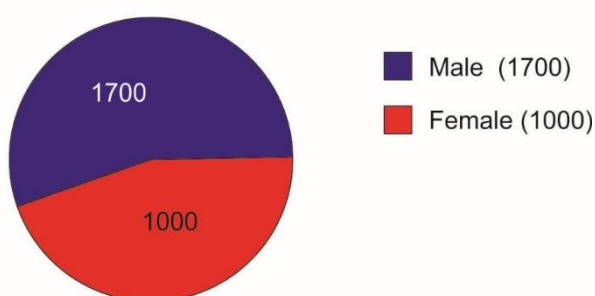


Figure3

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

Table2. Distribution of patients as per their therapeutics

Therapeutic group	Number of Patients	%
Acceclofenac sodium + Paracetamol	674	25
Nimesulide +Paracetamol	924	34
Ibuprofen +Paracetamol	474	17.5
Mefinamic acid +Paracetamol	322	12.0
Nimesulide	208	7.3
Paracetamol	98	4.2

Though nausea remain a common manifestation among all patients of varied therapeutic group, but manifestation like Dizziness, rash, GI bleeding, blood dyscrasias, 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 non of other group. (Table -3)

Table 3. Presentation observed during therapy

Presentations	Number of cases in various group of therapy					
	AP (674)	NP (925)	IP (474)	MP (322)	N (208)	P (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 dyscrasias	37	-	-	-	-	-
Convulsion	19	-	-	-	-	-
Prolonged hypothermia	78	-	-	-	-	-

(Key: AP: Aceclofenac Sodium -Paracetamol, NP: Nimesulide-Paracetamol, IP: Ibuprofen -Paracetamol, MP: Mefenamic acid-paracetamol, N: Nimesulide, P: Paracetamol)

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)

Group Showing Antipyretic effect of various combinations

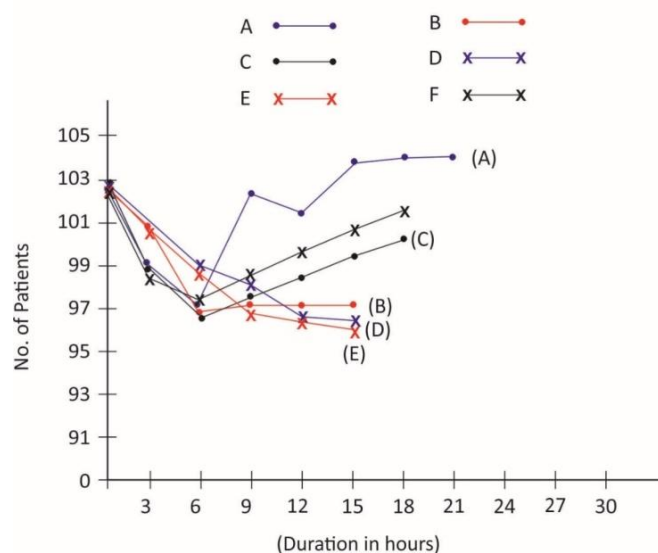


Figure 4

6. RESULT

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

7. CONCLUSION

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

8. 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 adversity 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 PGE2 within the hypothalamus,but may be due to reduction of pro inflammatory mediators, increase antiinflammatory signals Or boost anti pyretic messages within the brain (Figure 5).

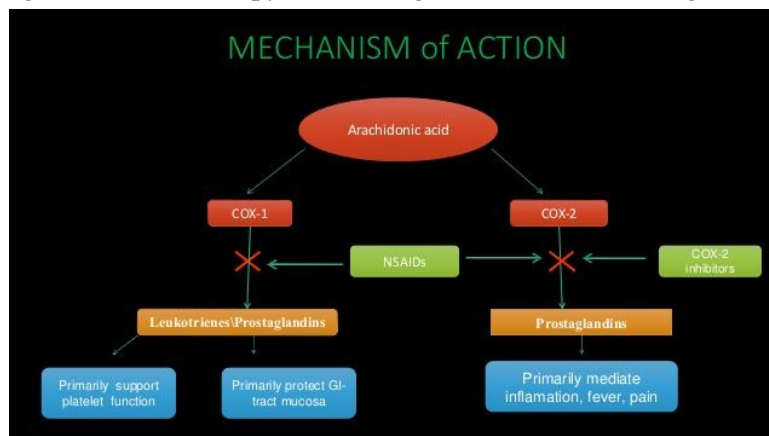


Figure5. Schematic presentation of Antipyretic action

Aceclofenac sodium is an orally effective nonsteroidalanti inflammatory drug of phenyl acetic acid group possessing remarkable 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 COX2 than COX 1 and inhibits synthesis of Prostaglandin (PGE2), a product of inflammatory cytokine,interleukin and tumour necrosis factor, in addition also affect cell adhesion molecules from neutrophil.15,16

This also interrupts the endo cannabinoid system and endocannabinoid 17,18 as COX2 utilises endo cannabinoid as a substrate and plays key role in producing drug adversity specially in children,pregnant and breast feeding mother. (Figure 6)

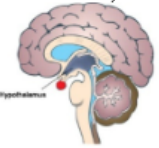
<p>ANTIPYRETICS NSAID (Selective Cox 2 inhibitor) Aceclofenac Sodium (Potent analgesic, anti inflammatory &anti arthritic)</p>  <p>Increases Canabinoid secretion Increased Endorphin Suppress CNS function Dizziness Convulsion ComaComa DEATH (Schematic presentation of AceclofenacParacetamol adversity)</p>	<p>ACETAMINOPHEN (Potent antipyretic)</p> <p>Prologed Hypothermia Brain Dysfunction</p>
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Figure6. Schematic presentation of Aceclofenac_paracetamol adversity)

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