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Prescription Pattern of Antipyretics for Infection Induced Fever in Pediatric Ward of Nedjo General Hospital, Nedjo Town, West Ethiopia

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Abstract

Background

Antipyretic therapy administration to patients who develop fever due to infection is controversial and its impact on clinical outcomes has yielded mixed results. We aimed to assess the prescription pattern and rational use of antipyretics for infection induced fever among hospitalized pediatric patients.

Materials and Methods

A retrospective cross-sectional study design was conducted to describe the use of antipyretics in hospitalized fever develop infectious patients from 2015 to 2016. A total of 290 patients were included in the study using random sampling method. Data was collected from the patients' cards from February to March, 2016 at Nedjo general hospital, Ethiopia.

Results

Of the 290 patients, 164(56.6%) were males while 126 (43.4%) were females. The mean age of the patients was 3.41±2.65 years with mean temperature of 37.21C^0. The average hospital stay of patients was 4.65±1.82 days and a total of 201 antipyretics were prescribed. Among the patients' cases, pneumonia accounts 96 (33.1%) of morbidity and 8 (42.1% of all mortality while neonatal sepsis accounts 79(27.24%) of morbidity and 7(36.8%) of all cause of mortality. During the study period there were 19(6.6%) in hospital mortality was recorded. The antipyretics ordered were Paracetamol, Diclofenac and Ibuprofen. From these, Paracetamol was the most frequent ordered drug, (96.5%) and 98.5% of the antipyretics were ordered as required basis (PRN).

Conclusion

The pattern of antipyretic prescription during the study depends on the diagnosis of the infection identified. Further studies are needed to demonstrate the effect of antipyretics on clinically relevant outcomes in fever developed hospitalized infectious patients.

Key Words: Antipyretics, Ethiopia, Infection, Prescription pattern, Pediatrics.

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1- INTRODUCTION

Fever is elevated body temperature (> 37.8° C orally or > 38.2° C rectally) or an elevation above a person's known normal daily value. Normally, the hypothalamic thermoregulatory censer maintains the internal temperature between 37°C and 38°C (1 – 4). Fever is an extremely common sign in pediatric patients and the most common cause for a child to be taken to the doctor. The different literatures indicated that physicians and parents have too many misconceptions and conflicting results about fever management (5-6).

Paracetamol, aspirin, and other non-steroidal anti-inflammatory drugs (NSAIDs) are all effective antipyretic agents. They work by inhibiting production of prostaglandin E2 in the anterior hypothalamus in response to endogenous pyrogens, although stimulation of endogenous "cryogens" (Antipyrogens such as vasopressin and melanocyte-stimulating hormone) may also play a role (7). Aspirin is an effective antipyretic, but its use in children is associated with adverse effects greater than those of paracetamol. Overdose (usually with the adult-strength tablets) leads to a syndrome called salicylism, which is characterized by hyperventilation, depressed level of consciousness, and severe metabolic acidosis (8).

After sufficient evidence emerged of an association between salicylates and Reye syndrome, acetaminophen essentially replaced aspirin as the primary treatment of fever (9). Although hepatotoxicity with acetaminophen at recommended doses has been reported rarely, hepatotoxicity is most commonly seen in the setting of an acute overdose. In addition, there is significant concern over the possibility of acetaminophen-related hepatitis in the setting of a chronic overdose (10, 11). Other NSAIDs have also been used as antipyretic agents in children, the most common being Ibuprofen. Current evidence indicates that in doses of 5-10 mg/kg ibuprofen is of comparable antipyretic efficacy to recommended doses of aspirin or paracetamol. In acute overdoses, ibuprofen appears to be much safer than paracetamol or aspirin. The use of Ibuprofen to manage fever has been increasing, because it seems to have a longer clinical effect related to lowering of the body temperature (12, 13). A practice frequently used to control fever is the alternating or combined use of acetaminophen and ibuprofen. Although the aforementioned studies provide some evidence that combination therapy may be more effective at lowering temperature for a greater period of time, questions remain regarding the safety of this practice as well as the effectiveness in improving discomfort, which is the primary treatment end point (14).

Despite the enhanced immune function that occurs at febrile temperatures, studies in humans have not convincingly demonstrated clinically important risks with the use of antipyretic therapy in common viral and bacterial infections (13, 14). In Ethiopia, management of fever varies across different areas and among physicians. As a result, there is a perceived need to improve the recognition, assessment, and management of fever with underlying infectious illnesses in children.

To promote effective management of fever it would be important for a study to be undertaken to determine the current practices toward fever management with antipyretics. Findings from this study will enable health practitioners to reflect upon their practices and examine the determinants of these practices, leading to informed decision making and effective practice in the fever management of hospitalized infectious patients.

2- MATERIALS AND METHODS

2-1. Method

The study was conducted in Nedjo general hospital (NGH) found in Nedjo city, Oromia region which is located 506 km from Addis Ababa capital city of Ethiopia. A retrospective cross-sectional study design was conducted to explore and describe the use of antipyretics in hospitalized fever develop infectious patients from 2015 to 2016. The source population was all pediatric patients visiting NGH and the study population was consisting of all patients who aged from 1 day to15 years and admitted to pediatrics ward with diagnosis of infection. A total of 290 patients were included in the study using random sampling method. The following patients were excluded from the study for various reasons:

- Patients known to be immune-suppressed or with pre-existing neurological or oncological condition.
- Patients who were afebrile during the first 24 hours in the ward.
- Patients who stayed in the ward for less than one day.
- Patients with signs of cerebral irritation on admission.
- Patient with seizure and/aura diagnosis of epilepsy.
- Patient cards which do not include one of the study variables

2-2. Variables of the study

The independent variables included were: age, gender, weight diagnosis, temperature on admission, temperature when antipyretics administered, White blood cells (WBCs), date of drug administration, co-morbid disease and co-medication. The dependent variables were antipyretic use pattern and outcome variables which includes length of hospitalization and in hospital mortality.

2-3. Data collection Process

A semi-structured data collection format containing the variables to be measured was designed, developed and utilized by the principal investigator or data collector after permission obtained from pediatric ward of NGH. The data was collected from the patients' cards. The collected data includes; Demographic information (such as gender, age, etc.), Diagnoses and co morbidities, Temperatures and antipyretic ordered early in the ward, Temperatures and antipyretic ordered lately in the ward, Antibiotics administered during the hospital stay, White Cell Count (WCC) on admission, Length of hospitalization and weight of the patients. Before starting actual data collection, small scale data collection was done on the questionnaires for having full required information of the study and to maintain quality of the study.

2-4. Data Quality Control and Management

The clarity and completeness checkup of data collection formats was under taken before the actual data collection and data clearing was done every day, formats with insufficient information was excluded from the study to avoid error. Then collected data was processed and retained cautiously in the line of its objective.

2-5. Data Processing and Analysis

Once all necessary data was obtained, data was checked for completeness, sorted and categorized accordingly to the needed direction. Then the data was processed analyzed (using SPSS software version 16.0) and interpreted. The final result was compared with the standard criteria and was presented using tables. P-value less than 0.05 were statistically significant.

2-6. Operational definition

- **Fever:** a rise in body temperature above the normal, i.e. above an oral temperature of 37ºC or a rectal temperature of 37.2 ^{0}C (1),

- **Febrile seizure**: an epileptic type of seizure associated with a fever (4),
- **Antipyretics**: a drug that reduces fever by lowering body temperature (9, 10).

2-7. Ethics approval and consent to participate

The study was conducted after approval by pharmacy department of Wollega University and hospital administration of Nedjo general hospital. The confidentiality of patients was assured throughout by removing identifiers from data collection tools. Not applicable. No individual person's personal details, images or videos are being used in this study.

3- RESULTS

A total of 290 participants were involved in the study, 164(56.6%) were males, while 126 (43.4%) were females. The mean age of the patients was 3.41± 2.65 years and mean temperature of the patients was 37.21^0C. The average stay of patients in hospital was 4.65 ± 2.82 days and a total of 201(69.3%) antipyretics prescription were used. There was a large range in the recorded temperatures, 36.1°C to 40.1°C in which individual children's mean temperature was 36.25°C on admission and 38.2°C for those on antipyretic medication at the order time (**Table.1**).

Table-1: The age characteristics for pediatric patients in pediatrics' ward of Nedjo general hospital, 2015 to 2016.

Age, year	Male, number (%)	Female, number (%)	Total, number (%)
< 1	92(31.72%)	46(15.86%)	138(47.58%)
1-5	50(17.24%)	50(17.24%)	100 (34.48%)
6-15	21(7.24%)	31(10.69%)	52 (17.93%
Total patients	163(56.2%)	127(43.79%)	290(99.99%)

3-1. Comorbidity and mortality rate of the patients

Among the participant's cases, pneumonia accounts 96 (33.1%) of morbidity and 8 (42.1% of all mortality, while neonatal sepsis accounts 79(27.24%) of morbidity and 7(36.8%) of all mortality. In general during the study period there were 19(6.6%) in hospital mortality was recorded (**Table.2**). From the 19 patients who died during the hospitalization 15(78.95%) of them took antipyretic therapy.

Table-2: Morality rate of the pediatric patients with respective of their disease in pediatrics' ward of Nedjo general hospital, 2015 to 2016.

Disease	Individuals affected (morbidity), Number (%)	Number of mortality Number (%)
Pneumonia	96(33.1)	8(42.1%)
Neonatal sepsis	79(27.24)	7(36.8%)
Acute febrile illness	51(17.59)	2(10.5%)
Malaria	51(17.59)	1(5.3%)
Tonsillitis	6(2.1)	1(5.3%)
Others	7(2.4%0	0(0%)
Total	290	19

3-2. Pattern of antipyretic medication use among the patients

Of the total incidence where fever was observed (n = 290) many of the children 210(72.4%) had a medical order for at least one type of antipyretic and some children had an order for more than one antipyretic during the audit period. The antipyretics ordered were Paracetamol, Diclofenac and Ibuprofen. Among antipyretic ordered to children, paracetamol was the most frequent ordered drug, (96.5%) and 98.5% of the antipyretics were ordered as required basis (PRN, i.e., every 4 hours when required). The mostly ordered dosage form was suppository, 86.21%, as indicated in **Table.3**.

Table-3: The pattern of antipyretics used among pediatric patients in pediatrics' ward of Nedjo general hospital, 2015 to 2016.

Antipyretics	Order (%)	Dosage form				Dose frequency
		Suppository	Tablet	Injection	Syrup	
Paracetamol	96.5	86.21	2.2	-	4	as needed
Diclofenac	2.41	-	1.6	2	-	as needed
Ibuprofen	1.03	-	2.2	-	-	as needed

3-3. Length of Hospital Stay of the patients

The length of stay in hospital ranged from 1 to 8 days (mean 4.65$\pm$ 2.82 days). Younger children, under the age of 60 months, were hospitalized for longer ($\geq$ 2 days) than children 60 months and older. Mean hospitalization for younger children was 3.22 $\pm$ 1.52 days and for those 60 months and older, 1.5 $\pm$ 0.73 days. In this study, 96(45.7%) patients received the antipyretic on early basis.

4- DISCUSSION

This study was intended to describe current antipyretic therapy practice in patients with infection induced fever, to identify patterns in patients who were treated with antipyretic medications and to identify the impact of antipyretic in length of hospitalization. One of the interesting findings is that there is wide practice variability in which patients are treated, such variability in prescribing is likely a reflection of the absence of strong evidence-based guidelines with which to guide decision making about fever treatment in infection. If antipyretic therapy were shown definitively to affect infection outcomes, however, most would agree that wide practice variation is undesirable. Data conflict on the potential protective role of fever in human infections. Clearly, failure to mount fever is a marker for worse clinical outcomes, but whether therapeutically attenuating fever has a similar effect is unclear (5). Furthermore, understanding clinicians' choices in treating patients with fever may lend new insight to factors that play a role in the unique risk-benefit trade-off for a therapy of uncertain utility. There was a large range in the recorded temperatures, 36.1°C to 40.1°C, with individual children's mean temperature 36.25°C on admission and 38.2°C for those antipyretic were ordered at the order time. With no definite temperature in the literature one would expect some variation in the temperatures health professional use. Numerous studies support that fever is beneficial in promoting host defenses, yet, physicians continue to prescribe antipyretic therapy (15). Of the time

periods where fever was observed (n = 290) many of the children 210 (72.4 %) had a medical order for at least one type of antipyretic and some children had an order for more than one antipyretic during the study period. The antipyretic ordered in this study was lower than that discovered in another studies (6, 15-16). The difference could be related to with number of participants included, study design and the study period. As rationales for antipyretic administration were not documented in the charts, and there was no differentiation in medication order for fever or pain. But it was assumed that antipyretics administered when temperatures were below 37°C were not for fever management. Most authorities on fever agree that only high fever, 40.0°C or higher, do not enhance the immune process and should be avoided in weak or debilitated patients. Temperatures below 39°C were regarded as mild fever (15, 17).

The health professionals seem to be administering antipyretics for mild fever, halting the body's natural defenses. Ultimately, the treatment of fever is an individualized clinical decision. Physiologically, some patients may have clinical factors that favor antipyretic treatment based on evidence of shock, tissue hypo perfusion, or risk factors for myocardial ischemia. Some of these factors may drive clinicians to seek to attenuate tachycardia or other physiologic squeal, such as increased Carbon dioxide (CO2) production, by administering antipyretics. The metabolic load of fever is significant, and patients expected to withstand the demands may benefit from forgoing antipyretic treatment (15-18).

It is impossible to know from this retrospective study whether end-of-life care does not include antipyretic therapy or whether antipyretic therapy decreases mortality. The greatest limitation of the study was being retrospective associated with incomplete data. Another limitation was the inability to ascertain the indication for administration of antipyretic drugs. Finally, a factor that may contribute for hospital stays are broad but the only investigated was the role of antipyretic identified which may be difficult to generalize.

5- CONCLUSION

This research has faced a deficit in documentation practices and a lack of clarity in the ordering of medications that have dual actions, i.e., antipyretic and analgesic. Among the participants cases Pneumonia accounts for highest morbidity and mortality. During the study period there was about one fifth in hospital mortality was recorded. Appropriate counseling on the management of fever begins by helping parents understand that fever is not known to endanger a generally healthy child. In contrast, fever may actually be of benefit; thus, the real goal of antipyretic therapy is not simply to normalize body temperature but to improve the overall comfort and well-being of the child.

Acetaminophen and ibuprofen, when used in appropriate doses, are generally regarded as safe and effective agents in most clinical situations. The systematic review of fever management also recommended that the purpose, when intervening in fever management, must be clearly identified through documentation. This series does not answer the ultimate question of which patients, if any, benefit from antipyretics. Further studies are needed to demonstrate the effect of antipyretics on clinically relevant outcomes in fever developed hospitalized infectious patients.

6- AUTHORS' CONTRIBUTIONS

GF contributes in the proposal preparation, study design, analysis and write up the manuscript. ET and DD contributed to the design of the study and edition of the

manuscripts. All authors read and approved the final version of the manuscript and 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.

7- CONFLICT OF INTEREST: None.

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