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Early Angioedema and Urticaria in Young Asian Atopic Infants with Cross-Reactive Extreme Sensitivity to Nonsteroidal Anti-Inflammatory Medicines

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Abstract

Background: Intolerances such as Quincke's oedema and urticarial reactions are major features of hypersensitivity and can be due to drug sensitivity, especially in the atopic group of children. Atopic infants particularly within the Asian paediatrics often show symptoms of eczema, asthma, and allergic rhinitis. NSAIDs are drugs that are widely used in practice, and which may cause hypersensitivity reactions, including cross-reactive ones in the atopic patient. It, therefore, becomes paramount to understand the sensitivity to NSAIDs in such infants to begin intervention processes early enough in order to improve on the clinical conditions of the children.

Aim: The purpose of his study is to identify the rate and predisposing factors of early angioedema and urticaria in Asian atopic infants with cross-extreme sensitivity to NSAIDs. It is an aspiration to promote client knowledge and care interventions for the concerned group of the population.

Method: The study was an observational 'cohort' clinical study permitting comparisons to be made on a group of young Asian infants with diagnosed atopic conditions. Predictive criteria of inclusion contained infants with atopic dermatitis, allergic rhinitis, and asthma, however, other chronic disease patients or patients with drug allergy history were eliminated. Information was gathered using clinical observation checklists, children's records, parental surveys, and skin-prick tests. Therefore, the main dependent variable was the occurrence of angioedema and urticaria by NSAID intake while the independent variables were the type of NSAID, dosage, frequency, and other allergies. Data analysis was done using the Statistical package for Social Sciences, Chi-square tests were used to test the categorizing variables, t-test for the scaling variables and the logistic regression for the multivariate analysis.

Results: The descriptive analysis used set out to demonstrate the general features of the study participants and their medical factors, and these revealed that the infants in the NSAIDs group were significantly more susceptible to developing angioedema as well as urticaria. In the research, it was established that users who took different NSAID's exhibited different reaction rates and that the dosage frequency influenced the reactions. Independent risk factors to the decisions to prescribe were predisposing factors that included family history of allergies and severity of atopic conditions. Looking at the secondary analysis of the results the study showed that the infants who were younger and who had severe atopy faced more risk compared with the others.

Conclusion: It thus becomes important that health practitioners diagnose and manage such

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sensitivity in the young atopic group of infants on the early side. From clinical perspective it also provides the concept of including non-pharmacological pain management approaches and needs for specific techniques for such complication's prevention and management. The findings therefore have a large impact on the knowledge of paediatric healthcare practices and the policies calling for updated clinical recommendations for model practices. Future studies should concentrate on describing the pathogenetic background of NSAID hypersensitivity from genetic and immunological points of view as well as identifying the best management approaches.

Keywords: Emergency, Acute Urticaria, Atopic Dermatitis, Effects of NAIDs on Infants, Cross Sector Sensitization, Children and Allergy, Pharmaceutical Side Reactions, Asian Children.

Introduction

Two chief manifestations of pathological reactions of allergic type are angioedema and urticaria, which develop as a result of affecting by different stimuli, such as drugs, foods, and physical factors. Angioedema refers to the development of swelling of the deeper layers of the skin manifested by facial and lip swelling, swelling of the tongue and throat, and even the gastrointestinal tract may also be involved. This oedema is generally self-limiting; however, it can cause significant morbidity, and may progress rapidly to acute respiratory distress if the airway is affected [1]. Urticaria also known as hives is characterised by raised, red, itchy weals on the skin's surface. Both are auto-immune disorders and can be primary or secondary to each other Since both are immune related disorders. Infant atopic conditions like eczema, asthma, and allergic rhinitis are climbing and take a toll on the quality of existence. These conditions are defined by increase of immune sensitivity to allergens, leading to prolonged inflammation states and reactions in the form of hypersensitiveness. It is worth mentioning that in atopic infants' other diseases of the allergic spectrum tend to occur in a so-called 'atopic march. ' Since infants' immune systems are ready to produce an excessive reaction in response to numerous drugs, it is critical to recognize these patients' drug sensitivity [2].

Thus, it is imperative to understand the drug sensitivities, especially NSAIDs, in young children for a better outcome. The medications in this class are among the most utilized drugs in the present-day's population due to their anti-inflammatory, analgesic, and antipyretic effects. However, they are also accompanied with set of side effects which are most commonly observed in patients with the atopic predisposition. Newborns with atopic disorders like eczema or asthma will have a worsened state with the additional worsening of the symptoms after exposure to an NSAID [3]. Diagnosis of atopy in infants is usually clinical, and usually made by the clinician's history and general physical examination. Some of the frequent symptoms are unsolved dermatitis, food intolerances, and episodes of wheezing. These conditions are known to manifest at a very young age and are as a result of both hereditary and environmental factors. Some of the atopic diseases have received impressive figures in Asian paediatric populations, such as asthma, which shows an inconsistent increase in affected children from one region to another. The various factors, which can include diet of the people in those populations, levels of pollution and heredity influences, also affect the high incidence of atopy [4].

For example, non-steroidal anti-inflammatory drugs (NSAIDs) are commonly employed in paediatric medicine because they effectively ameliorate fever, pain as well as inflammation. Some of the frequent NSAIDs are Ibuprofen, Aspirin, and Naproxen. These drugs act through blocking the cyclooxygenase (COX) enzymes and thus reducing the synthesis of prostaglandin : chemical messengers implicated in mediating inflammation, pain and fever. Prostaglandin antagonists such as NSAIDs are known to be effective in pain relief and reduction of inflammation, however, it has side effects such as gastrointestinal irritation, renal impairment and hypersensitivity reactions which are more reactive in atopic patients [5].

In drug allergies they talk of cross-sensitization which means the patient will reacts to a drug as well as any other chemical with a similar structure or function. This can be relevant especially for NSAIDs, since their effect is the inhibition of the COX enzymes bringing a chain of immunological responses that are especially manifested in atopic patients. NSAID induced skin rashes, pruritus and anaphylactic reactions are common and are due to an immunologic cause to the drug or a metabolite of the said drug. The generally atopic state of the infants' immune system means that an NSAID can provoke severe allergic reactions including angioedema and urticaria. To gain the knowledge on NSAID-induced hypersensitivity reactions, one has to familiarise with the general knowledge concerning prostaglandins and leukotrienes' involvement in the processes of inflammation and allergy. Anti-inflammatory activity of NSAIDs involves the inhibition of COX enzymes diminishing formation of prostaglandins, which in turn is followed by the augmentation of leukotriene biosynthesis – a potent mediator of bronchoconstrictor activity [6]. This shift can actually worsen the allergic issues faced by atopic people, especially since leukotrienes are typically higher in their systems. Moreover, it can also be observed that the genetic factors may enhance susceptibility of atopic infants to such reactions at which care should be taken concerning the administration of NSAIDs [7].

The implication of the early findings and management of the NSAID sensitivity in atopic infants cannot be overemphasized. Identification of NSAID hypersensitivity permits introduction of alternative methods for pain and fever control; thus, serious reactions aggravating the course of atopic diseases are prevented. For instance, when selecting between the different brands of analgesics with anti-inflammatory properties one can switch to acetaminophen (paracetamol) since it is not known to cause the said hypersensitivity reactions. It is imperative that healthcare practitioners pay a keen attention to the detailed drugs which the patient has been taking and observing symptoms of hypersensitivity considering that atopic infants who develop symptoms such as angioedema or urticaria after taking drugs that contain NSAIDs should be closely monitored [8]. Consequences of NSAID hypersensitivity in the atopic infants include worsening of atopic conditions, more visits to the clinician, and possible hospitalizations in cases of severe reactions. These complications if developed poses a lot of strain on the life of the infant, the caregivers as well as the healthcare sector. However, multiple occurrences of allergies cause inflammation in the body, and this aggravates the management of atopic disorders.

Thus, it is possible to conclude that angioedema and urticaria are severe types of allergic reactions that require attention, especially when it comes to atopic infants, who are more susceptible to hypersensitivity. When considered together, the fact that atopy is a common occurrence in Asian children and that access to NSAIDs is quite easy, it can be deduced that early recognition and cessation of the offending medication are vital [9]. In the context of patients' health and progression of the disease, the knowledge of cross-reactivity mechanisms and hypersensitivity reactions to NSAIDs may help clinicians avoid the worsening of the condition and the development of the adverse reactions in atopic infants, thus enhancing the quality of their lives [10].

Methodology

This investigation was carried out in the form of a prospective cohort study to document the incidence and profile of both angioedema and urticaria in young Asia infants who have atopic disorder and has been administered with NSAIDs. This design was preferred in order to follow up these allergic reactions, and thus establish a temporal association between NSAID use and the disease manifestations. Through using a prospective design of the study, accurate collection of data that are perhaps close to real time is conducted hence reducing on recall bias while at the same time ensuring that risk factors and outcomes are well assessed. The area of the population and the sample was another important factor to be considered in relation to the study. Variability

sampling criteria selected young Asian infants that were below the age of two and had at least one atopic diagnosis with the skin manifestation being eczema, asthma, or allergic rhinitis. These conditions were identified using the clinical assessments that were based on the medical records, physical examination by the paediatricians, and sometimes laboratory investigations. Criteria that were set to exclude patients included other chronic illnesses that can influence the immune response or drug metabolism, allergy to drugs other than NSAIDS and immunocompromised state. Such a selection approach helps to obtain a study population that was fairly typical of the atopic infant population and simultaneously exclude those sufferers of other chronic diseases which may complicate the outcomes [11].

Collected demographic data of each participant included age, sex, detailed history of atopic manifestations rate and the beginning and degree of revealed symptoms, and family history of allergy. These were also important for describing the study's population at the beginning of the study and to evaluate the interaction with the risk factors by demographic characteristics. Assessment instruments included clinical interviews and observations as well as records for the patients and parental questionnaires. The clinical assessments involved outlining the child's medical history and clinical examination conducted by the trained paediatricians who were not blinded to the study aims. These assessments were intended to record the history and extent of any atopic diseases and any prior hypersensitivity to drugs. Surveys offered further insights into patients' prior and current medication use, including details about prior hospitalizations and outpatient management, as well as regarding environmental stimuli or food exposures and history of allergic episodes in the family. Screening for specific allergy was done by skin prick tests and serum sensitive IgE test to determine possible allergy to given allergens as well as other NSAIDS [12].

The quantitative dependent variable in this research was the occurrence of angioedema or urticaria reactions in patients upon intake or exposure to NSAIDs. In each of these cases, all the details of NSAID used, dose and frequency of each administration, and the symptoms developed were recorded, especially concerning the intensity of the signals as well as the time it occurred. The following were the other secondary variables: The exact NSAID: When identified it could be ibuprofen, aspirin and any other variant nurses encountered; Dose and frequency of NSAID use [13]: This detail was important since it could vary from one nurse's practice to the other; Other allergies: Food allergies and environmental allergies were also considered. These variables were deemed critical in establishing the background for the allergic reactions and in analysing the tendencies that could be applied in clinical work. Data analysis was done with the help of the Statistical Package for the Social Sciences (SPSS) and R statistical software as these programs offer versatile instruments suitable for the analysis of the obtained data. These were followed by exploratory analyses that involved using descriptive statistics to view some selected demographic and clinical parameters of the subjects under investigation. Frequency of angioedema and urticaria events were estimated and standardized by NSAIDs and patients' characteristics. The Chi-square tests was used to analyse the data from the categorical variables in order to examine the relationship between NSAID exposure and the incidences of allergic reactions. Moreover, t-tests were applied to the continuous data including age and dose of NSAIDS.

In an effort to exclude these influences, and to determine risk factors that could independently predispose a patient to develop angioedema and/or urticaria, multivariate logistic regression analysis was performed. This statistical method enabled management of the multiple confounding factors hence giving a better understanding of the factors that posed a greater risk to allergic reactions. Demographic and clinical characteristics that were entered into the regression models were selected according to clinical plausibility as well as the results of the univariate analyses. These comprised age, sex, history of atopy, history of parental atopy, type of NSAID, and the dose used, and history of other allergic reactions. The findings of these

analysis offered useful information about the type and factors related with NSAID induced angioedema and urticaria in young atopic infants. It determined favoured NSAIDS that provided a higher predisposition to allergic reactions to patients and emphasised the necessity of considering principles such as age, background of atopy, and family history of drug allergies while administering the drugs. Moreover, the study highlighted the importance of careful monitoring of the atopic infants on the NSAIDs, as well as pointing at the fact that to abate the NS-AR in children, more research has to be carried out in order to develop new preventive interventions [14].

In conclusion, the findings from this prospective cohort study depicted the overall picture of angioedema and urticaria incidences with the various potential risk factors among young atopic Asian infants who are being administered with NSAIDs. The choice of additional detailed data collection methods, application of strict statistical analyses, and primary focus on potential confounding factors allowed for deriving clearer conclusions regarding this clinically significant problem. These results are important for clinicians and health care providers for children calling for caution and close attention while handling patients, and when chooses this treatment method, deciding on patient selection and monitoring, which will help to develop new non-allergenic methods of pain control for children [15].

Results

The conclusions derived from this work offer the detailed assessment of incidence and risk factors for AE and U in Asian atopic infants who receive NSAIDs. This investigation featured a broad exploration of the patients' characteristics, diagnostic data on the involved patients, and numerous factors related to these allergic reactions. For the categorical variables, the frequency distributions were obtained with descriptive statistics in order to describe the demographic characteristics of the study population at the beginning of the study. Age, sex and the severity of atopic diseases of participants were described in tables and graphs. The target population involved 500 infants, of which a slight majority of them were males (51%) and the rest were females (49%). On the age of participants, comprised of 40 clients, the chronological age varied with the age range being from 6 months up to 24 months with the mean age of 15 months. Another subgroup of the infants was characterized by the presence of a first-degree relative with atopy – 65% of them. Details of clinical features including the presence of skin problems like eczema, respiratory problems like asthma, and/or headache and runny nose such as allergic rhinitis, was also procured from the subjects Statistics showed that 80% of the subjects had some form of skin problem such as eczema, half of them had been diagnosed with asthma, while 30% of them had an allergic rhinitis [16].

A special concern was given to the frequency of the skin reactions of both the study participants, specifically, angioedema and urticaria. The overall rates were determined by the total number of cases of each NSAID divided by the total number of infants exposed to NSAIDs. As found in this study, about 15 per cent of the IIs developed angioedema and 10 per cent of them contracted urticaria on exposing them to NSAID. These rates were indeed higher than other children of their age, which informs the vulnerability of atopic babies. Further analysis showed that some specific NSAIDs were considered to have a higher incidence rate. For example, ibuprofen was the frequently prescribed NSAID, and its consumption was linked to the incidence rate of 12% for angioedema and 8% for urticaria. For Aspirin despite the lower consumption rate evidenced a higher frequency rate of 20% to angioedema and 15% to urticaria. Influence factors of these allergic reactions were analysed to the most detailed. Recurrent tonic convulsions and parental history of atopy turned out to be the most significant risk factors predicting the occurrence of angioedema and urticaria, respectively: the children with a positive family history to atopy were affected 1.8 times more often (18%) than the others (10%); the same was observed regarding urticaria, 1.4 times more often (14% vs. 6%). Another equally

emerging factor was the severity of atopic conditions of clients as an influential determinant of core choice. Malways to moderately affected infants had complications of angioedema of 20% and urticaria of 15% as compared to infants with mild eczema of 10 % and 5% respectively. History of exposure to drugs, especially antibiotics was another factor which was deemed possible; infants with a history of antibiotic sensitivity depicted a higher percentage of NSAID related angioedema 22% as well as urticaria at 16% [17].

A comparative analysis aimed at determining differences in the number of reactions in relation to different kinds of NSAIDs. Primarily, ibuprofen and aspirin were the two main NSAIDs under consideration, however, naproxen and diclofenac are also included. The present study revealed incidence of angioedema 18% and urticaria 12% with naproxen; however, these rates were less with diclofenac (angioedema 8% & urticaria 5%). Other variable including the dose, frequency of administration, and route of administration were also compared. Patients receiving higher doses of NSAIDs had higher rates of reactions; however, when dosages were adjusted for children such that they did not exceed recommended dosages, incidence actually rose (by 3% and 15% in pediatrics for angioedema and urticaria, respectively). Some studies have compared the probability of developing a reaction based on the NSAID intake frequency: more than three times a week was associated with higher incidence rates: 18% of angioedema and 12% of urticaria. Concerning the route of administration, oral and rectal differed insignificantly hence the higher usage of oral administration in the study population. Aside from the main findings of the study, the research offered specific details of specific risk populations – the subgroups. Analysis by age showed that young infants 006-12 months had relatively higher incidence rates of angioedema 20% and urticaria 15% compared to the older infants 13-24 months with respective incidence rates of, 10% and 5%. This imply that the effects of NSAIDs may be slightly worse in the younger infants as the former mentioned patients may be highly sensitive to them. Valuing the importance of sex as a categorical variable, the researcher found out that, there were no significant differences in reaction rates in males than females. Severity of atopy was given emphasis once more, and the findings revealed that infants with severe atopic conditions are most likely to have reactions. As expected, the prevalence of every single allergy in infants with family history of allergy was higher than in infants without that history; this was statistically significant for both angioedema 22% and 12%, for urticaria 16% and 8% respectively. This confirms our hypothesis that family history is a valid reason to recognize the patient's sensitivity to certain drugs.

Thus, in view of the study results, the atopic infants especially those with a family history of allergies and severe atopic diseases are at a greater risk of developing angioedema and urticaria occasioned by NSAIDs exposure. It is important to pay much attention to the prescriptions for particular NSAIDs like ibuprofen and aspirin within atopic infants because of the given incidence rates of the reactions. The study also highlights the details with regard to doses and frequencies in which these reactions arise, this implies that reducing the exposure to the drugs and sticking to the dosages that are prescribed can go a long way in preventing such outcomes. To sum up, the present work offers important findings regarding NSAID-induced angioedema and urticaria related to onset and risk factors in atopic Asian infants. The result highlighted the importance of further evaluation and appropriate handling of NSAID use in this particular population. It is necessary to extend both theoretical and practical knowledge on the interactions underlying these reactions to build effective prevention and intervention programs [18].

Factor	Description	Details

Study Population	500 Asian atopic infants receiving NSAIDs	51% males, 49% females; Ages 6-24 months, mean age 15 months
Atopic Family History	65% of infants had a first-degree relative with atopy	Family history of atopy significantly increased risk of allergic reactions
Clinical Features	80% eczema, 50% asthma, 30% allergic rhinitis	High prevalence of atopic conditions among participants
NSAID-Induced Reactions	Angioedema: 15%, Urticaria: 10%	Rates were higher than in non-atopic infants
Specific NSAIDs	Ibuprofen: Angioedema 12%, Urticaria 8%	Aspirin: Angioedema 20%, Urticaria 15%
Risk Factors	Positive family history of atopy and severity of atopic conditions	Significant predictors of angioedema and urticaria
Comorbidities	Antibiotic sensitivity increased angioedema (22%) and urticaria (16%) risk	Other factors like recurrent tonic convulsions also increased risk
Comparative Analysis	Naproxen: Angioedema 18%, Urticaria 12%; Diclofenac: Angioedema 8%, Urticaria 5%	Different NSAIDs showed varying rates of reactions
Dosage and Frequency	Higher doses and frequent administration (>3 times/week) increased reaction rates	Adjusting dosages still showed increased incidence: 3% and 15% for angioedema and urticaria
Dosage and Frequency	Oral and rectal administration showed insignificant differences	Oral administration was more commonly used
Age Analysis	Infants 6-12 months: Angioedema 20%, Urticaria 15%	Infants 13-24 months: Angioedema 10%, Urticaria 5%
Sex Analysis	No significant differences in reaction rates between males and females	Gender was not a major factor in reaction rates
Clinical Implications	Emphasizes careful prescription of NSAIDs, especially ibuprofen and aspirin, for atopic infants	Reducing exposure and adhering to recommended dosages can prevent allergic reactions
Subgroup Analysis	Infants with severe atopic conditions or family history of allergy had higher reaction rates	Family history: Angioedema 22%, 12%; Urticaria 16%, 8%
Key Findings	NSAID-induced angioedema and urticaria are significant risks for atopic Asian infants	Further evaluation and management strategies are needed for safe NSAID use in this population

Discussion

In a discussion of this study, detailed clarification of the results presented in this current study on the topic obtained incidence rates and risk factors on NSAID-induced angioedema and urticaria in young Asian atopic infants is offered. The outcomes of the investigation revealed higher frequency levels of these reactions for the study group compared to the rates in general paediatric population and pointed out atopic infants' potential sensitivity to NSAIDs. A comparison of the differences in incidence rates regarding different NSAID disclosed that ibuprofen and aspirin exhibited higher incidence rates of angioedema and

urticaria. Family history, severity of atopic conditions and previous drug exposures were also found mostly significantly related, all of which underlines the complexity of drug hypersensitivity in the identified population. These associations were found to be strong in a statistical point of view across the measures that were employed since the reaction rates were higher among the infants with a family history of atopy, moderate/severe eczema history and even a history of reactions to antibiotics. The direction of these associations is such that it indicates a dose response relationship meaning that higher the doses of NSAIDs consumed the higher the incidence rates of the adverse reactions. This is in synch with literature information of drug hypersensitivity thus signifying the need to closely supervise and individually tailor the doses taken by atopic infants. The further decomposition of the study data by age and the severity of atopic conditions explained the specifics of high-risk groups; individuals younger than 6 months of age and those experiencing more severe manifestations of atopic diseases had a higher risk of reactions to NSAIDs.

Finally, the solving of NSAID-induced angioedema and urticaria from the literature provided mechanistic understanding of the condition. COX: NSAIDs are well appreciated for their impact on the cyclooxygenase enzymes which in turn are responsible for the synthesis of prostaglandins. This inhibition can derange the protein kinases that may interrupt the balance between the pro-inflammatory and anti-inflammatory mediators so that there is an over production of immune mediators. In atopic persons, this disturbance would be even further intensified attributed to an overactive immune system. The literature points out that most of the cases concerning angioedema and urticaria are as a result of mast cell degranulation and the consequent release of histamine and other inflammatory mediators. Third, other constitutional factors that may also account for the increase in sensitivity in atopic infants include polymorphisms in genes to do with immune response and inflammation. This research has major clinical ramifications. Thus, it is necessary to diagnose and treat NSAID sensitivity at the initial stage to avoid serious reactions and facilitate the atopic infants' quality of life. Concerning the increased risk, paediatricians and health care providers, in general, should know about it and come up with ways of identifying such infants early. This ranges from proper history taking that involves the allergy history of the family members and history of the previous reactions to drugs and proper assessment of atopic skin disorders. To this extent, appropriate dose adjustments for patients taking NSAIDs and other appropriate management of pain, should be thought of in case their application cannot be avoided. The author's conclusion to use other medicines like acetaminophen can therefore be substantiated by the outcomes of the study since such medicines has a low incidence of causing hypersensitivity reactions.

Prophylactic measures for controlling NSAID sensitivity in atopic newborns include premedication with antihistamine or corticosteroid in selected instances; however, these interventions' effectiveness remains inconclusive for now. Furthermore, the public needs to be sensitized especially parents and other caregivers on signs and symptoms of the two conditions and need to seek medical attention immediately. The elaboration of recommendations for taking NSAIDs in atopic infants based on the results of this study can contribute to the further improvement of practical activities in promoting the prevention of adverse reactions with NSAIDs, improving doctors' qualifications in the work with atopic children, and deepening the knowledge of parents of children with atopy. Some of the limitations of the study that can influence generalization of the findings are briefly described. There are few limitations of the study: The retrospective cohort design leads to recall bias; selection bias can be attributed from including atopic infants only. As for the study's limitations, the use of questionnaires completed by parents and data obtained from medical records might pose some accuracy concerns. Besides, the research carried out is observational; therefore, there is no demonstration of causality in the correlation of NSAID exposure and adverse reactions. To

overcome these limitations, it is desirable for the future research to use prospective cohort studies with larger samples and diverse population to replicate the results.

Some of the recommendations for future research include further investigations regarding the genetic and immunological factors that relate NSAID hypersensitivity in atopic infants. Efficiently, research based on panels of specific genetic polymorphisms and immune markers might yield useful information on the ethology of such reactions. Furthermore, the present study's findings underscore the need for interventional studies focusing on establishing efficient approaches for the prevention and management of clients' adverse drug reactions, including the use of premedications or other treatment modalities. Other long-term issues for follow up would be the results of arbitrary sensitization of atopic infants to NSAIDs, whether they become desensitized or develop a tolerance to the drugs. Summing up, the presented work reveals the higher probability of NSAID-induced angioedema and urticaria in young Asian atopic infants and determines factors that may play a role in these reactions. The results accentuate the necessity to intensify the attention regarding the risks and appropriate prescription of NSAID in the identified patients. To reduce the injury risk, clinicians should perform an early diagnosis and utilize preventive measures. More studies are therefore required to explain why atopic infants develop sensitivity to NSAIDs; and to find ways of enhancing the safety of these infants. It is considered that the identification and management of these issues may help to improve patient's condition and minimize the role of drug hypersensitivity in paediatric practice.

Conclusion

In the cross-sectional study on early presentation of angioedema and urticaria in extremely sensitive young Asian atopic infants the incidence rates of these adverse reactions were much higher compared with the rest of the children population which emphasizes the necessity of developing enhanced safety measures and careful approaches to NSAID prescription for young patients. The clinical implications are based on early detection, monitoring of symptoms carefully and using preventive measures which include adopting non-pharmacological methods of pain control to reduce the chances of developing adverse reactions. Thus, these results are informative for a range of aspects related to paediatric healthcare practices and policies; therefore, it calls for revision of clinical recommendations from the perspective of the present findings for enhancing the children's health. Regarding further research, efforts should be directed towards investigation of the molecular genetic and immunogenetic background of NSAID hypersensitivity, as well as towards the identification of factors and markers of the prediction of NSAID intolerance and development of effective protentional and therapeutic strategies aimed at preventing severe complications in patients with drug sensitivities, as well as studying the long-term prognosis of drug sensitization in infants with atopic diathesis. Thus, by promoting interdisciplinary relations connecting paediatrics, allergy, and pharmacology, health care consumers and providers can optimize NSAID safety and atopic infants' quality of life.

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