Medical Students’ Knowledge Of Risk Factors For Adverse Drug Reactions In Children

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Abstract
Adverse drug reaction (ADR) is a global problem that affects all age groups. Poor perceptions of doctors about ADRs and risk management have contributed to high rate of ADR under-reporting in Nigeria. The focus of this study was to assess the knowledge of medical students on the risk factors for ADRs in children and to identify the classes of medicines most likely be involved. Assessment was done before and after a didactic lecture on ADRs and pharmacovigilance. Forty four medical students in their fourth year, comprising of 25 males and 19 females, were assessed with a structured questionnaire for their knowledge of possible risk factors for ADRs in children, knowledge of pre-existing diseases that may predispose a child to having ADRs, and their ability to identify the classes of medicines that are most likely involved. Before the lectures on ADRs and pharmacovigilance, the risk factors were well identified except medication dose error, age and gender of a child that were wrongly perceived. The perception was much improved in the post lecture assessment. In both the pre- and post- lecture assessments, atopy, asthma, immunodeficiency, malignancy, sickle cell anaemia, and tuberculosis were all considered diseases that may likely be associated with adverse reactions. However, the proportions of students with correct perceptions of these diseases were significantly higher in the post –lecture assessment (P< 0.05 in all cases). Medicines with potentials for ADRs that were highly ranked in the pre- and post- lecture assessments include antibiotics (88.6% vs 100%), antimalarials (84.1% vs 100%) and immunosuppressive drugs (84.1% vs 100%), respectively. It was concluded that teaching ADRs and pharmacovigilance in pharmacology enhanced the previously acquired knowledge in junior clinical postings.

INTRODUCTION
Adverse drug reaction in children is a global public health problem that requires concerted efforts to tackle. The Adverse Effects Methods Group, registered as part of the Cochrane Collaboration (http://www.cochrane.org/contact/mwfield.htm) [1], was developed in an attempt to drastically reduce the problem of ADRs globally. The main objectives of the Group are to develop and implement methods for systematic reviews of the adverse effects of therapeutic interventions and to develop an agenda for research on adverse drug reactions (ADRs). Education on ADRs for public, health-care workers, and medical students was one of the potential key topics proposed by the Group for research on ADRs. It is believed that good knowledge of ADRs may be the beginning of good steps to adequate and proper pharmacovigilance.

Earlier studies in Nigeria have shown that ADRs in children are under-reported [2] probably as a result of lack of awareness of ADRs and lack of facilities for their monitoring. An awareness of the risk factors for ADRs in children, amongst medical students and doctors, is necessary to preventing ADRs occurrences. Studies like this may therefore contribute to the steps to managing ADRs [3]. Patients do not always have the same perception of the risks of using medicines as health professionals. The risks perception is also different among health professionals themselves [4]. Such differences in ADR risk perception has been illustrated in a study of French medical students [5]. The study assessed the effect of education on students’ perception of ADR risks factors. Before taking a pharmacology course the students ranked hypnotics as the most dangerous drugs with high potentials for ADRs, followed by antidepressants and anticoagulants, similar to the perception of non-health professionals in France [4]. After the course the order of risk perceptions changed to antidepressants, anticoagulants, and hypnotics. Their perception of the risks for ADRs of other drugs also changed. These results therefore reinforced the importance of education on improving medication prescribing [6].
Adverse drug reactions are taught as a special topic in pharmacology at the Lagos State University College of Medicine (LASUCOM), Ikeja. The teaching is general and encompasses teaching the subtle differences in drug properties that put them at risk of adverse reactions and teaching the predisposing factors for ADRs in both children and adults. In the past, medical students are taught pharmacology, pathology and other laboratory medicines at the LASUCOM partly in their third year and the whole of fourth year. However, very recently, the programme has been modified. Introductory pharmacology is now taught in the first 2 months at the beginning of third year. Thereafter, the students proceed to anaesthesia posting for another 2 months, and junior clinical postings in medicine and surgery for about 6 months. These postings commence in the later part of third year through the early part of fourth year. During the clinical posting the students are privileged to observe medical emergency cases which may include patients with ADRs. The students are also taught patient management at the bedside during ward rounds. The teaching often include principles of clinical pharmacology and therapeutics.

The perceptions of health care workers and medical students perceptions about ADRs have been previously studied in developed countries in social pharmacology [7,8]; an integral part of clinical pharmacology. However, these studies were specifically focused on adults. Awareness of social pharmacology is not very common in Nigeria, hence the limited research on ADRs monitoring and pharmacovigilance. Children constitute a very large proportion of population of developing countries, yet only a few studies have focused exclusively on ADRs in children [2]. This study is therefore aimed at assessing the knowledge of medical students at the LASUCOM on the risk factors for ADRs in children and the likely medicines involved.

METHODS

This is a cross-sectional study involving the fourth year medical students of the LASUCOM, Ikeja. The students had completed a three month introductory lectures in pharmacology. They had also completed a three month posting in each of anaesthesia, junior clinical medicine and surgery. Upon resuming the pharmacology class after the junior clinical postings, the students were lectured basic pharmacology for about four months. During this period, ADRs and pharmacovigilance were taught, both theoretically and practically, for six hours.

The assessments were performed before and after teaching ADRs and pharmacovigilance to the students. The pre-lecture assessment was performed in April 2007 and the post-lecture assessment six months later, towards the period of their professional M.B; B.S examinations. A structured questionnaire was used to assess the students’ knowledge. The questionnaire was divided into three parts; the demographics of the students, their knowledge of risk factors for ADRs in children, and their knowledge of classes of medicines likely responsible for ADRs in children.

A list of possible risk factors was provided for the students to rank in descending order of importance. In-depth knowledge of the risk factors was further assessed by providing some statements on risk factors for ADRs to be answered as a ‘yes’ or ‘no’ options. A list of classes of medicines that include antibiotics, antimalarials, cardioactive medicines, anti-epileptic medicines, immunosuppressants, antituberculosis medicines, herbal medicines and dietary supplements, analgesics, multivitamins, and haematinics was also provided for ranking in descending order of potential for ADRs.

A total of 44 students who participated in the pre-lecture assessment also participated in the post-lecture assessment. The same questionnaire was used for both the pre- and post-lecture assessments. Questionnaire was administered for the pre- and post-lecture assessments when the students were about to have lectures in pharmacology. The questionnaire was filled-in and returned on the spot to the researchers in order to eliminate bias from filtering of information among the students. The students were not aware of the study until the time of questionnaire administration.

The ethical committee of the college approved the study. Data was analysed with SPSS version 13. Continuous data was expressed as mean ± S.D. Pre- and post-lecture responses were compared using chi-square at a significance level of P < 0.05

RESULTS

Of the 58 medical students in the fourth year, 44 participated in the study. Their mean age was 24.46 ± 2.44 years with a range of 18-32 years. Most of the students (32, 72.7%) were in the age range of 20-24 years. Twenty five (56.8%) of them were males.

Before the lectures, most of the students (40, 90.9%) claimed they were aware of the risks factors for ADRs in children.
Table 1 shows how the students ranked the risk factors for ADRs in children. All the factors were considered risks for ADRs in children except age, medicine dose error and gender which were perceived non-risk factors in the post-lecture assessment. In the pre-lecture assessment, self-medication was ranked the highest and genders of a child the least.

Immaturity of organs of drug metabolism (42, 95.5%) and developmental changes from childhood to adulthood (40, 90.9%) were age related risk factors identified by the students. Among the few students who perceived gender a risk factor in the pre-lecture assessment, 7(53.8%) believed females were more at risk than males. There was an equal perception that medicines could adversely interact with diseases in the body (41, 93.2%) in both the pre- and post-lecture assessments. However, there was a higher perception in the pre-lecture assessment (40, 90.9%) than in the post-lecture assessment (27, 61.4%) that drug-disease interaction occurs more frequently in children than adults (P< 0.001).

Lack of information about medicines and their untoward effects on children (40, 90.9%), concomitant use of herbal and orthodox medicines (38, 86.4%), previous adverse reaction to an old medicine (37, 84.1%), differences in the anatomy and physiology of children and adults (36, 81.8%), inability of children to explain their experience of adverse effects of a medicine (31, 70.5%), and previous adverse reaction to a new medicine (25, 56.8%) were additional risk factors identified by the students in the pre-lecture assessment. However, the perception was 100% for each of these factors after the lecture.

Pre-existing diseases in a child that may likely be associated with ADRs as ranked by the students is presented in Table 2. Initially, all the diseases were perceived as risks for ADRs but only three were later perceived as risks factors. There were significant differences in the risk perceptions for the three diseases in both the pre- and post-lecture assessments.

The perception that multiple ADRs could occur to a single medicine was significantly lower in the pre-lecture assessment (29, 65.9%) than in the post-lecture assessment (41, 93.2%) (P<0.001).

Table 3 shows the ranking of different classes of medicines in decreasing order of potential for ADRs. Initially, all the medicine classes were considered potentially hazardous to children but four classes were later considered non-hazardous.
DISCUSSION

Previous studies in Nigeria have not assessed the perception of parents, health-care providers and medical students about the risks for ADRs in children. However, such studies had been performed in developed countries [5,7,8] with focus on risk factors for ADRs in adults. Adverse drug reactions are common among paediatric population in Nigeria [2] and were a contributory factor to child morbidity and mortality [2]. Parental self medication for children [9] and irrational medicine prescriptions by health and non-health professionals [10, 11] were the most common predisposing factors for ADRs in children. Inadequate training of doctors in pharmacovigilance and ADRs is known to induce irrational prescribing and ADR-under-reporting in Nigeria [12]. This study was about the first to evaluate the perceived risk of ADRs in undergraduate medical students in Nigeria that focused specifically on paediatric age group. Thus it would serve as a database for comparison with future studies on pharmacovigilance in Nigeria.

The perception of the students was assessed twice, immediately after clinical exposure following an introductory lecture in basic pharmacology and towards the end of their pharmacology course during the same university year (i.e. 6 months later). During the first assessment, they showed a fair understanding of risk factors for ADRs, however, the proportion of students who perceived the risk factors correctly were significantly lower than the proportion after the assessment (Table 1). The initial fair knowledge demonstrated by the students may be as a result of the knowledge of ADRs acquired during the junior clinical postings. This therefore emphasizes the need for clinical exposure of undergraduate medical students before completing their basic and clinical pharmacology courses [13-15].

Surprisingly, age, medication dose error and gender were not considered risk factors by the students after ADRs and pharmacovigilance lectures. Although, age and gender are important risk factors for ADRs in adults. Age per se is not an important risk factor in a population of adults but age-related changes are the consequence of a number of individual factors such as polypharmacy, decline in renal or liver function in the elderly, hypoalbuminaemia and reduced body weight. Therefore ADRs risk is higher in the elderly [16]. Similarly, ADRs are more common in women than in men [17]. It is well known that infants and very young children are at high risk of adverse drug reactions because their capacity to metabolise drugs is not fully developed [18]. However, inconsistent results have been published by different authors about the roles of age and gender as risk factors for ADRs children. Some studies have reported a statistically significant association between age or gender and ADRs [19, 20], and others did not find any relationship [21-24]. Perhaps, this might explain the negative response of the students in the post-lecture assessment to the questions of age and gender as risk factors for ADRs in children. It is very likely that ADR was defined to the students in pharmacology lecture according to the definition of the World Health Organization (WHO) [25]. However, this definition has been criticized by some experts of pharmacovigilance [26] because of exclusion of important causes of ADR such as medication errors, overdosing and drug toxicity. This might have informed the wrong perception of the students in the post-lecture assessment that medicine dose error was not a risk for ADRs.

Taking several medicines, whether prescription or over-the-counter, contributes to the risk of having an adverse drug reaction. The number and severity of adverse drug reactions increase disproportionately as the number of medicines taken increases [27]. Immunodeficiency, malignancy, sickle cell anaemia, and tuberculosis are chronic health conditions that require multiple drug therapy. This may therefore explain why these diseases were highly ranked as risk factors for ADRs in both assessments (Table 2). Most anticonvulsants, as well as corticosteroids; the mainstay

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**Figure 3**

Table 3: Ranking of classes of medicines in descending order of potentials for adverse effects

<table>
<thead>
<tr>
<th>Class of medicines</th>
<th>Pre-lecture ranking</th>
<th>Post-lecture ranking</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>39</td>
<td>44</td>
<td>0.097</td>
</tr>
<tr>
<td>Immunomodulators</td>
<td>37</td>
<td>44</td>
<td>0.041</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>37</td>
<td>44</td>
<td>0.041</td>
</tr>
<tr>
<td>Vaccines</td>
<td>35</td>
<td>44</td>
<td>0.018</td>
</tr>
<tr>
<td>Cardiotonics</td>
<td>24</td>
<td>44</td>
<td>0.035</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>32</td>
<td>44</td>
<td>-0.001</td>
</tr>
<tr>
<td>Herbal medicines and dietary supplements</td>
<td>30</td>
<td>44</td>
<td>0.002</td>
</tr>
<tr>
<td>Antibacterials</td>
<td>30</td>
<td>44</td>
<td>0.002</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>27</td>
<td>44</td>
<td>-0.001</td>
</tr>
<tr>
<td>Over the counter medicines</td>
<td>24</td>
<td>44</td>
<td>-</td>
</tr>
<tr>
<td>Haeatomics</td>
<td>15</td>
<td>44</td>
<td>-</td>
</tr>
<tr>
<td>Multivitamins</td>
<td>12</td>
<td>44</td>
<td>-</td>
</tr>
</tbody>
</table>
treatment of atopic diseases and asthma, are frequently associated with ADRs [28, 29]. Asthma and epilepsy are two common childhood emergencies that were likely seen by the students during their early junior clinical postings. Therefore, it is most probably that they had observed the drug therapy of these health conditions which may have influenced their high ranking of the conditions as risk factors for ADRs. Even though the ranking of the diseases was comparably high in both the pre- and post-lecture assessments, the proportion of students who ranked the diseases correctly was significantly higher in the post-lecture assessment. Thus, underscoring the significance of reinforce teaching in enhancing students’ assimilation and retention.

Antibiotics, antimalarials and immunosuppressive medicines consistently remained the likely medicines to be associated with ADRs in children as they remained highly ranked by the students in both the pre- and post-lecture assessments. A study from Nigeria had previously implicated these medicines in ADRs among paediatric population [2]. Our result was, however, contrasting to that of a similar study involving students from a French medical school in Toulouse, France [5]. Although, the French study was focused on medicines used for adults, antibiotics were consistently ranked low before and after their pharmacology lecture on ADRs. This is not surprising because the disease pattern, access to medicines, medicine use patterns, and patient management in developing countries are known to significantly differ from those of developed countries [30].

CONCLUSION

Early clinical exposure appears to contribute to the understanding of risk factors for ADRs before medical students were formally taught the topic in pharmacology. Their perception of the risk factors was much better after teaching ADRs and pharmacovigilance in pharmacology. A larger study that will include students from most medical schools in Nigeria will be necessary to enable the findings in this study to be generalised.

References


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