



Parental Experience of Potential Adverse Drug Reactions Related to Their Oral Administration of Antipyretic Analgesic Medicines in Children in Saudi Arabia

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ABSTRACT

Background: Oral antipyretic analgesic medicines are commonly used in children and have the potential for adverse drug reactions (ADRs).

Objective: The aim of this study was to explore parental experiences of potential ADRs related to their oral administration of antipyretic analgesics in children in the Kingdom of Saudi Arabia.

Methods: For this cross-sectional survey, a paper-based questionnaire, consent form and information sheet were handed out to 1000 parents who had administered an oral antipyretic analgesic medicine to their children during the previous 3 months. Data were entered and analyzed using SPSS version 21.0 (IBM-SPSS Inc, Armonk, NY). Simple descriptive and inferential statistics were used. Management and ethical approvals were attained.

Results: During March to April 2017, 661 parents agreed to participate, giving a response rate of 66.1%. Of the surveyed sample, 208 parents had observed 1 or more potential ADRs (31.5%, n = 208 out of 661). Parents' (n = 208) most commonly reported potential ADRs (n = 523) were loss of appetite (23%, n = 120 out of 523), stomachache (20.3%, n = 106 out of 523), abdominal colic (13%, n = 68 out of 523), and diarrhea (10.3%, n = 54 out of 523). Parents described severity of the ADRs as slight (71.8%, n = 342 out of 476), annoying to the child (7.9%, n = 85 out of 476), significant and affecting daily tasks (3.6%, n = 17 out of 476) and significant and led to the hospital (6.7%, n = 32 out of 476). Fever was the top-ranked reason for using antipyretic analgesic medicines (41.0%, n = 271 out of 661), followed by toothache (25.0%, n = 165 out of 661) and tonsillitis/laryngitis (24.7%, n = 163 out of 661). Among parents, 34.7% (n = 165 out of 476) did not seek medical attention when a potential ADR occurred, whereas 26.3% (n = 125 out of 476) of parents took their children to hospital clinics.

Conclusions: Although the majority of parentally reported (but not proven) ADRs were mild, a number of significant ADRs were reported. Future research should consider whether there is a role for physicians and pharmacists in educating parents in Saudi Arabia, and perhaps more widely, about the optimal use of oral antipyretic and analgesic medicines in children. (*Curr Ther Res Clin Exp.* 2020; 81:XXX-XXX)

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Introduction

Oral antipyretic analgesics, including acetaminophen (also known as paracetamol) and the nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, are commonly used medicines

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in children, with established evidence of efficacy and effectiveness.¹⁻⁴ Both are classified in many countries, including the Kingdom of Saudi Arabia, as over-the-counter medicines with ease of availability and access to parents for oral administration to their children. Antipyretic analgesic medicines are reported as being the most common over-the-counter medicines purchased by the public in Saudi Arabia and freely available on prescription from governmental hospitals or for a charge from private pharmacies.⁵ However, this ease of availability has led to cases of incorrect dose administration by parents to their children, resulting in potential adverse drug reactions (ADRs).⁶ ADR is defined by the UK Medicines and Healthcare products Regulatory Agency as “an unwanted or harmful reaction which occurs after administration of a drug or drugs.”⁷

Children are prone to issues of drug misuse and overdose of medicines.^{8,9} Described by Torissi et al¹⁰ as a challenging-to-research population because children are “very sensitive to the undesirable effects of the drugs due to their physiological differences.”¹⁰ ADRs account for between 4% and 6% of hospital admissions, with incorrect drug dose constituting among the leading causes for ADRs.^{7,8} Several studies reported ADRs in children when administered higher than recommended doses.^{1-6,8-14} These reactions included gastrointestinal, renal, and hepatic system ADRs. Several factors affect the exposure of children to antipyretic analgesic agents rendering children more vulnerable to potential ADRs.⁸⁻¹⁰ A major determinant was parental misconceptions about the potentially harmful effects of fever on their children. Hence the perceived need to act quickly in reducing a raised temperature by administering oral antipyretic analgesic medicines.⁶ Furthermore, because children are a diverse group in terms of weight and age they experience variable responses to drugs resulting in potential ADRs.⁸⁻¹⁰ Li et al¹⁵ reported that the highest percentage of drug overdose cases seen in hospital emergency departments were in children younger than age 5 years.

Several factors contributed to the overdose and misuse of medicines, which included parents' lack of knowledge and inexperience in how to correctly administer oral antipyretic analgesic medicines.^{6,15} Miscalculation of the dose based on weight, individualized dosing, and medication liquid formulation, can lead to greater risk of dosing errors in children.^{16,17} A study conducted to assess parental ability to correctly calculate the appropriate acetaminophen dose found that only 30 out of 100 parents were able to do so.¹⁸ Inappropriate storage and disposal of medicines is another cause of misuse.¹⁹ A large study comprising 1641 households from 22 cities reported that 80% of Saudi homes had an average of at least 2 expired or unused medicines, with oral antipyretic analgesic agents constituting half of these medicines.²⁰ Recently, the Saudi Food and Drug Authority warned against overdosing children younger than age 12 years with paracetamol and there are ongoing concerns about the misuse of analgesics and other medicines by the public in Saudi Arabia.²¹

The aim of this study was to explore parental experiences of potential ADRs related to their oral administration of antipyretic analgesic medications in children in Saudi Arabia.

Methods

Research design

A cross-sectional survey using a paper-based questionnaire was handed out with an information sheet and consent form to the parents of children who had used an oral antipyretic analgesic, with or without a prescription, during the previous 3 months.

Setting and recruitment process

Data collection was conducted in March through April 2017 in pediatric outpatient clinics, pediatric emergency rooms, and hospital waiting areas at 4 hospitals in Jeddah, Saudi Arabia: the Maternity and Children's Hospital, the East Jeddah General Hospital, the King Abdul-Aziz Hospital, and the Maternity and Children's Hospital Al-Aziah. Parents were recruited by convenience sampling without any stratification. The researcher handing out the study materials offered assistance to any parents who needed help completing the questionnaire.

Questionnaire

The questionnaire was based on a recent study of ADRs conducted by members of the research team.^{21,22} It included the following items: demographic characteristics (parent filled in the questionnaire, providing age of child, gender, number of siblings, and parents' levels of education), symptoms, and frequency of any previously experienced ADRs, severity of each ADR, and if the child had previously experienced ADRs that parents believed were attributable to the use of antipyretic analgesic agents. The severity of the potential ADR was categorized by parent respondents as slight, or annoying to the child or an allergy but they were still able to perform their daily tasks, or significant and affecting daily tasks, or significant and led to the hospital, or lastly, fatal. Other items collected in the questionnaire focused on parents' reasons for administering oral antipyretic analgesic medications, where parents would obtain these medicines, who parents would consult on use of these medicines, whether parents read the medicine's information leaflet, under which circumstances parents would re-use remaining prescribed oral antipyretic analgesic medicines, and parents' experience of providing the right dose of antipyretic analgesic medications.

The questionnaire was tested for face and content validity by a panel of 10 academic and health care staff and then piloted with 12 parents. No changes were made to the questionnaire after the pilot, so these responses were included in the final dataset. Completed questionnaires were collected by clinical staff and stored securely for research team collection.

Data analysis

Questionnaire data were entered and analyzed using SPSS version 21.0 (IBM-SPSS Inc, Armonk, NY). Simple descriptive and inferential statistics were used in reporting the results.

Ethical approval

Management authorization was gained from the Ministry of Health (reference No. 892225) and ethical approval from the National Committee of Bio and Medical Ethics (reference No. 872863).

Results

One thousand information sheets, consent forms, and questionnaires were handed out with 661 parents agreeing to participate in the survey, giving a response rate of 66.1%. Mothers accounted for 63.8% (n = 422 out of 661), and 27.8% (n = 184 out of 661) were fathers with the remainder (8.3%, n = 55 out of 661) not disclosed. Demographic characteristics and experience of administering antipyretic analgesic medications are reported in [Table 1](#) with details of potential ADRs in [Table 2](#). Parents' responses related more to sons (44.8%, n = 296 out of 661) than daughters (38.1%, n = 252 out of 661) with the remainder again not disclosed (17.1%, n = 113 out of 661). The children were younger than age 5 years (29%, n = 192

Table 1
Demographic characteristics of participants and experience of administering oral antipyretic analgesic medicines in children.

Characteristic (n = 661)	No. of parents (%)
Mother's education	
Illiterate	100 (15.1)
Primary	4 (0.6)
Intermediate	8 (1.2)
Secondary	193 (29.2)
University	348 (52.6)
Higher studies	8 (1.2)
Father's education	
Illiterate	25 (3.8)
Primary	10 (1.5)
Intermediate	19 (2.9)
Secondary	212 (32.1)
University	386 (58.4)
Higher studies	9 (1.4)
Age of child attending pediatric outpatient clinic (y)	
<5	192 (29.0)
5-10	38 (5.9)
≥10	80 (12.1)
Do you have experience of providing the correct dose of antipyretic analgesic medicine?	
Yes	467 (70.7)
No	128 (19.3)
Maybe	66 (10.0)
Who did you consult before using the antipyretic analgesic medicine?	
Family	83 (12.6)
Physician	427 (64.6)
Pharmacist	131 (19.8)
Friend	12 (1.8)
Internet	8 (1.2)
Did you read the enclosed leaflet attached to the antipyretic analgesic medicine?	
Yes	530 (80.2)
No	131 (19.8)
How did you obtain the antipyretic analgesic medicine?	
Physician's prescription	478 (72.3)
Without prescription	175 (26.5)
The supermarket	7 (1.1)
From the internet	1 (0.2)
Would you reuse an antipyretic analgesic previously prescribed to your child for another illness without medical consultation?	
Yes	381 (57.7)
No	209 (31.6)
Maybe	71 (10.7)
Reasons for using antipyretic analgesic medicine for your child?	
Fever	271 (41.0)
Toothache	165 (25.0)
Tonsillitis and laryngitis	163 (24.7)
Earache	46 (7.0)
After traumas, burns, or rashes	6 (0.9)
After trauma or bruises	3 (0.5)
Other	7 (1.1)

out of 661), with 58.9% in the 5 years to younger than age 10 years group (n = 389 out of 661), whereas 12.1% of the children were aged 10 years or older (n = 80 out of 661). Most were from families of 2 to 5 children (57.5%, n = 380 out of 661). The majority of mothers (52.6%, n = 348 out of 661) and fathers 58.4% (n = 386 out of 661) had completed higher education. However, some mothers (15.1%, n = 100 out of 661) and fathers (3.8%, n = 25 out of 661) described themselves as illiterate. Assistance was offered in completing the questionnaire.

Frequency of potential ADRs, severity, and causality

Of the surveyed sample, 208 parents had observed 1 or more potential ADRs (31.5%, n = 208 out of 661). The most commonly reported potential ADRs (n = 523) were loss of appetite (23%, n = 120 out of 523), stomachache (20.3%, n = 106 out of 523), abdominal colic (13%, n = 68 out of 523), diarrhea (10.3%, n = 54 out of 523), bloody stool (7.6%, n = 40 out of 523), and anxiety (5.4%, n = 28 out

Table 2
Parents' experience of adverse drug reactions (ADRs) following administration of an oral antipyretic analgesic medicine in children.

ADR	Result
ADRs observed by parents in their children (n = 523)*	
Appetite loss	120 (22.9)
Stomach ache	106 (20.3)
Abdominal colic	68 (13.0)
Diarrhea	54 (10.3)
Blood in stool	40 (7.6)
Anxiety	28 (5.4)
Rash	28 (5.4)
Weight loss	27 (5.2)
Isolation	26 (5.0)
Anemia	19 (3.6)
Fatigue	7 (1.3)
Severity of the ADRs affecting the children (n = 476)*	
Slight	342 (71.8)
Annoying to the child or an allergy but they were still able to perform their daily tasks	85 (17.9)
Significant and affecting daily life tasks	17 (3.6)
Significant and led to the hospital	32 (6.7)
Fatal	0 (0.0)
Do you think that the antipyretic analgesic used caused these adverse effects? (n = 661)*	
Yes	224 (33.9)
No	185 (28.0)
Uncertain	252 (38.1)
What was your decision when an ADR occurred with your child? (n = 476)*	
I didn't do anything	165 (34.7)
I went to the hospital clinic	125 (26.3)
I went to an emergency department	35 (7.4)
I stopped the medication	79 (16.6)
I consulted a pharmacist	11 (2.3)
I consulted a physician	48 (10.1)
The physician changed the medication	2 (0.4)
The physician lowered the dose	8 (1.7)
Other	3 (0.6)

* Values are presented as n (%) but values may not add up to total because not all parents observed an ADR, whereas some parents observed multiple ADRs.

of 523). Less frequent potential ADRs were rash (5.4%, n = 28 out of 523) and weight loss (5.2%, n = 27 out of 523), feeling of isolation (5.0%, n = 26 out of 523), anemia (3.6%, n = 19 out of 523), and fatigue (1.3%, n = 7 out of 523). Regarding the severity of the potential ADRs, 71.8% (n = 342 out of 476) were perceived by parents as slight, 17.9% (n = 85 out of 476) perceived the ADRs as annoying to the child or an allergy but they were still able to perform their daily tasks, significant and affecting daily life tasks (3.6%, n = 17 out of 476) when describing the potential ADR, and 6.7% (n = 32 out of 476) perceived them as significant and led to the hospital; none reported experiencing a fatal potential ADR. Respondents were either certain that the antipyretic analgesic had caused the adverse reaction (33.9%, n = 224 out of 661) or disagreed (28%, n = 185 out of 661) or were uncertain (38.1%, n = 252 out of 661). Only 40.4% of parents (n = 84 out of 208) were able to name the medication they believed had caused the potential ADR as acetaminophen (paracetamol) and/or ibuprofen, carrying different brand names and concentrations.

Reasons to use antipyretic analgesic medicines

Fever was the top-ranked reason for using antipyretic analgesic medications (41.0%, n = 271 out of 661), followed by toothache (25.0%, n = 165 out of 661) and tonsillitis/laryngitis (24.7%, n = 163 out of 661).

Parents' knowledge of the correct dose of antipyretic analgesic medicines

Among all respondents, 71% (n = 467 out of 661) believed they were experienced in giving the right dose of medicines. However,

19.3% (n = 128 out of 661) stated they were not and 10.0% (n = 66 out of 661) indicated maybe.

Consultation on use and purchasing of antipyretic analgesic medicines

Among parents surveyed, 64.7% (n = 427 out of 661) consulted a doctor before using oral antipyretic analgesic medicines and 19.8% consulted a pharmacist (n = 131 out of 661), whereas 12.6% consulted family members (n = 83 out of 661) and very few asked friends (1.8%, n = 12 out of 661) or searched on the Internet (1.2%, n = 8 out of 661). Most parents (80.2%, n = 530 out of 661) read the enclosed medication leaflet; however, 19.8% did not (n = 131 out of 661). Parents most commonly obtained oral antipyretic analgesic medicines through a physician's prescription (72.3%, n = 478 out of 661) and 26.5% purchased these medicines without a prescription (n = 175 out of 661). Very few bought directly from supermarkets (1.1%, n = 7 out of 661) or online (0.2%, n = 1 out of 661).

Re-use of previously prescribed antipyretic analgesic medicines for their child for another illness without medical consultation

Among parents, 57.7% (n = 381 out of 661) stated that they would re-use an oral antipyretic analgesic agent previously prescribed for their child for another illness without medical consultation. The remainder would not re-use the medication (31.6%, n = 209 out of 661) or did not respond to this question (10.7%, n = 71 out of 661).

Parents' response following a potential ADR affecting their children

Among parents, 34.7% (n = 165 out of 476) stated that they did not seek medical attention when a potential ADR occurred, whereas 26.3% of parents (n = 125 out of 476) took their child to hospital. The remainder either stopped giving the medicine (16.6%, n = 79 out of 476) or would take their child to the hospital emergency department (7.4%, n = 35 out of 476). When parents were asked whether they believed that the medication they gave to their children caused the potential ADR, responses were yes (33.9%, n = 224 out of 661), no (28%, n = 185 out of 661), and uncertain (38.1%, n = 252 out of 661).

Discussion

This research study investigated parental experience of potential ADRs related to their oral administration of antipyretic analgesic medications in children in Saudi Arabia. The results show that some parents were aware their child experiencing 1 or more potential ADRs, a small proportion of which were sufficiently severe the concerned parents took their child to hospital. Given that 1 in 5 parents admitted not reading the enclosed information leaflet, it can be concluded that they were either unsure or did not have the experience to provide the correct dose of oral antipyretic analgesic. Together with more than half of the parents re-using medications prescribed for a possibly different condition, it is incumbent on pharmacists to counsel thoroughly using short, clear, nontechnical messages.

Parents reported common and less common ADRs associated with their child's antipyretic analgesic medicines use. Most were mild and commonly recognized in clinical trials and postmarketing surveillance studies.^{3,4} The most common potential ADRs reported by parents in this study were loss of appetite, stomachache, and abdominal colic. Less frequent potential ADRs were rash, weight loss, and anemia. Although rashes were reported in this study, nonetheless they are considered in the literature as rare potential ADRs in response to NSAIDs.²³ Of great concern were the 268 (51.2%) cases of gastrointestinal tract ADRs with complications, including rectal bleeding and anemia reported in this study (Table 2).

Gastrointestinal tract adverse effects, including peptic ulcer, bleeding, and perforation are known to be associated with the use of NSAIDs occurring due to mucosal prostaglandin depletion and are considered as rare ADRs.²⁴ A population-based survey conducted in France to describe upper gastrointestinal bleeding reported in 177 children, aged between 2 months and 16 years, revealed that 83 children were prescribed at least 1 NSAID during the 7 days preceding the admission and one-third of the upper gastrointestinal bleeding reports were deemed attributable to use of ibuprofen or aspirin at analgesic or antipyretic dose.²⁵

Other determinants such as parental level of education clearly had an effect on the administration of oral antipyretic analgesic medications. Surprisingly in this study, parents with a high level of education, such as college or university degree, still did not read the medication leaflet and often consulted family members rather than medical professionals before administering the antipyretic analgesic agents. It would be expected that level of literacy would play an important role in understanding drug-related instructions. However, parents could still be confused and miscalculate doses.²⁶⁻²⁸ We suggest providing education and clear instructions to parents, as well as health care professionals, on the appropriate use of oral antipyretic analgesic agents in children. Fever is among the most commonly consulted pediatric symptoms but there is a lack of consensus in the guidance available to parents on the optimal way to manage it.²⁹⁻³³ Thus, appropriate counseling of parents on fever, and the proper use of oral antipyretic analgesic medications to manage it, should be encouraged.

The majority of parents (58%) re-used medications previously prescribed for their child for another illness without medical consultation. This has been shown to be a major contributing factor for ADRs.^{34,35} Although we cannot be certain of any link between reported ADRs and the medicines under investigation, it is clear that the children's parents have made such a link to oral antipyretic analgesic medications. Educating the public on the importance of correctly disposing of unused medicines, as well as consulting physicians before the re-use of any medicines, is crucial.³¹ Schemes to dispose of unused medication have been successfully carried out in some countries.^{34,35} Previous studies found similar results about parental lack of knowledge regarding ADRs associated with medicines.³⁶⁻³⁸

It is important for physicians to describe in appropriately measured language the correct use of antipyretic analgesic agents to parents whether or not they have previously been counseled on using similar medication. Additionally, there is a major role to be played by pharmacists because they can provide appropriate advice on the management of fever and pain. Although ibuprofen and acetaminophen are generally regarded as well tolerated and effective when used appropriately for the management of fever and pain in children, they should be used cautiously to minimize the risk of ADRs.³⁴⁻³⁸

A limitation of this study is the possibility of recall bias in parents' experience of oral antipyretic analgesic agents with their children that could affect the results. Also, it should be noted that some questionnaires were filled in by parents in outpatient clinics attending because of concerns about their child's health that could again have influenced their answers. With some parents identifying as illiterate, the administration of the survey by a researcher rather than self-completion may have introduced some inconsistency. A further limitation was not asking specifically whether the child was admitted to hospital as a consequence of any potential ADRs.

Conclusions

Not unexpectedly, parental experiences of potential ADRs related to their oral administration of antipyretic analgesic agents to

their children in Saudi Arabia were varied. Although the majority of parentally reported (but not proven) ADRs were mild, a significant number of severe ADRs were reported. Future research should consider whether there is a role for physicians and pharmacists in educating parents in Saudi Arabia, and perhaps more widely, about the optimal use of oral antipyretic and analgesic medications in children.

Declaration of Competing Interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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M. Tobaigy conceived the study and, together with K. MacLure, M. Radwi, A. M. Almalki, A. H. Alhasan, M. Tannoury, and Z. Attieh, designed the questionnaire and performed the study. The manuscript was written by all authors.

References

- Titchen T, Cranswick N, Beggs S. Adverse drug reactions to non-steroidal anti-inflammatory drugs, COX-2 inhibitors and acetaminophen in a paediatric hospital. *Br J Clin Pharmacol*. 2005;59:718–723.
- Maison P, Guillemot D, Vauzelle-Kervroedan F. Trends in aspirin, acetaminophen and non-steroidal anti-inflammatory drug use in children between 1981 and 1992 in France. *Eur J Clin Pharmacol*. 1998;54:659–664.
- Hay A, Costelloe C, Redmond N, Montgomery A, Fletcher M, Hollinghurst S, et al. Acetaminophen plus ibuprofen for the treatment of fever in children (PITCH): randomized controlled trial. *BMJ*. 2009;339:b3295.
- Kanabar D. A clinical and safety review of acetaminophen and ibuprofen in children. *Inflammopharmacology*. 2017;25(1):1–9.
- Khan T, Ibrahim Y. A qualitative exploration of the non-prescription sale of drugs and incidence of adverse events in community pharmacy settings in the Eastern Province of the Kingdom of Saudi Arabia. *Eur J Hosp Pharm Sci Pract*. 2012;20:26–31.
- De S, Tong A, Isaacs D, Craig JC. Parental perspectives on evaluation and management of fever in young infants: an interview study. *Arch Dis Child*. 2014;99(8):717–723.
- The Medicines and Healthcare products Regulatory Agency. <https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency>. Last accessed on 15/01/2020.
- Clavenna A, Bonati M. Adverse drug reactions in childhood: a review of prospective studies and safety alerts. *Arch Dis Child*. 2009;94:724–728.
- Kozer E, Greenberg R, Zimmerman DR, Berkovitch M. Repeated supratherapeutic doses of paracetamol in children—a literature review and suggested clinical approach. *Acta Paediatr*. 2006;95(10):1165–1171. doi:10.1080/08035250600580503.
- Torissi L, Soulaymani A, Mokhtari A., Soulaymani R. Cases of Adverse Drug Events in Pediatrics: Prospective Study at a Hospital in Rabat (Morocco). 2018;10(3):362–366.
- Elzagallaai AA, Greff M, Rieder MJ. Adverse Drug Reactions in Children: The Double-Edged Sword of Therapeutics. *Clin Pharmacol Ther*. 2017;101(6):725–735. doi:10.1002/cpt.677.
- Sutherland A, Phipps DL, Tomlin S, Ashcroft DM. Mapping the prevalence and nature of drug related problems among hospitalised children in the United Kingdom: a systematic review. *BMC Pediatr*. 2019 Dec 11;19(1):486. doi:10.1186/s12887-019-1875-y.
- Hawcutt DB, Mainie P, Riordan A, Smyth RL, Pirmohamed M. Reported paediatric adverse drug reactions in the UK 2000–2009. *Br J Clin Pharmacol*. 2012 Mar;73(3):437–446. doi:10.1111/j.1365-2125.2011.04113.x.
- Jimenez R, Smith A, Carleton B. New Ways of Detecting ADRs in Neonates and Children. *Current Pharmaceutical Design*. 2015;21:5643. <https://doi.org/10.2174/1381612821666150901105555>.
- Li C, Martin B. Trends in emergency department visits attributable to acetaminophen overdoses in the United States: 1993–2007. *Pharmacoepidemiol Drug Saf*. 2011;20(8):810–818.
- Buck M. Preventing Acetaminophen Overdosage. *The Annals of Pharmacotherapy*. 2000;34(32–4).
- Ghaleb MA, Barber N, Franklin BD, Yeung VW, Khaki ZF, Wong IC. Systematic review of medication errors in pediatric patients. *Ann Pharmacother*. 2006;40(10):1766–1776. doi:10.1345/aph.1G717.
- Al-Jaser N, Epi M, Awofeso N. *Current topics in public health*. Epidemiology of patients diagnosed with prescription and non-prescription drug overdose at the Riyadh Security Forces Hospital between January 2007 and December 2011. In-Tech; 2013.
- Ozanne-Smith J, Routley V, Scott I, Scott G. *Pharmaceutical Poisoning to 0-19 Year Olds: National Public Health Partnership Public Health Planning and Practice Framework Trial*. Melbourne, Australia: Monash University Accident Research Centre; 2002.
- Abou-Auda H. An economic assessment of the extent of medication use and wastage among families in Saudi Arabia and Arabian Gulf countries. *Clin Ther*. 2003;25(4):1276–1292.
- Tobaigy M, Radwi M, Alhasan AH, et al. General public's perspectives of issues relating to misuse of medicines: a cross-sectional survey in Jeddah. *Int J Clin Pharm*. 2019;41:1148–1151. doi:10.1007/s11096-019-00893-5.
- Tobaigy M, Stewart D, Helms PJ, Williams J, Crum J, Steer C, McIay J. Parental reporting of adverse drug reactions associated with attention-deficit hyperactivity disorder (ADHD) medications in children attending specialist paediatric clinics in the UK. *Drug Saf*. 2011 Mar 1;34(3):211–219.
- Jara MD, Montero AP, Bara MTG, Cabrerizo S, Zapatero L, Molero MIM. Allergic reactions due to ibuprofen in children. *Pediatr Dermatol*. 2001;18:66–67.
- Wolfe MM, Lichtenstein DR, Singh G. Gastrointestinal toxicity of nonsteroidal anti-inflammatory drugs. *N Engl J Med*. 1999;340:1888–1899.
- Grimaldi-Bensouda L, Abenhaim L, Michaud L, Mouterde O, Jonville-Béra AP, Girardeau B, David B, Autret-Leca E. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society of Pediatric Gastroenterology. *Eur J Clin Pharmacol*. 2010;66(8):831–837.
- Wolf M, Davis T, Tilson H, Bass P, Parker R. Misunderstanding of prescription drug warning labels among patients with low literacy. *Am J Health Syst Pharm*. 2006;63(11):1048–1055.
- Babakor S, Ghamdi M. Prevalence and Determinants of Over-the-Counter Analgesics Usage among Patients attending Primary Health Care Centers in Jeddah, Saudi Arabia. *J Young Pharm*. 2018;10(1):91–97.
- Apa Li SF, Lacher B, Crain E. Acetaminophen and ibuprofen dosing by parents. *Pediatr Emerg Care*. 2000;16(6):394–397.
- Eskerud J, Laerum E, Fagerthun H, Lunde P, Naess A. Fever in general practice I. Frequency and diagnoses. *Fam Pract*. 1992;9:263–269.
- Impicciatore P, Pandolfini C, Casella N, Bonati M. Reliability of health information for the public on the World Wide Web: systematic survey of advice on managing fever in children at home. *BMJ*. 1997 Jun 28;314(7098):1875.
- Meremikwu MM, Oyo-Ita A. Physical methods versus drug placebo or no treatment for managing fever in children. *Cochrane Database of Systematic Reviews*. 2003(2).
- Fallis D, Frick M. Indicators of accuracy of consumer health information on the Internet: a study of indicators relating to information for managing fever in children in the home. *Journal of the American Medical Informatics Association*. 2002 Jan 1;9(1):73–79.
- Greisman L, Mackowiak P. Fever: beneficial and detrimental effects of antipyretics. *Curr Opin Infect Dis*. 2002;15(3):241–245.
- Smolen A. Role of the Pharmacist in Proper Medication Disposal. *US Pharm*. 2011;36(7):52–55.
- O'Driscoll D, Ryan J, Brogan C, Henman M. The DUMP Campaign. *Irish Pharmacist*. 2009;11(5):19–22.
- Lokker N, Sanders L, Perrin E, Kumar D, Finkle J, Franco V, et al. Parental misinterpretations of over-the-counter pediatric cough and cold medication labels. *Pediatrics*. 2009;123(6):1464–1471.
- McD Taylor D, Robinson J, MacLeod D, MacBean CE, Braitberg G. Therapeutic errors among children in the community setting: nature, causes and outcomes. *J Paediatr Child Health*. 2009;45(5):304–309.
- Tzimenatos L, Bond GR. Severe injury or death in young children from therapeutic errors: a summary of 238 cases from the American Association of Poison Control Centers. *Clin Toxicol*. 2009;47(4):348–354.