DOI:10.1111/j.1365-2125.2007.02865.x

Attitudes and experiences of community pharmacists towards paediatric off-label prescribing: a prospective survey

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What is already known about this subject

- There are increasing concerns about the safety and efficacy of paediatric off-label medicines.
- In the UK, each year 26% of children receive an off-label prescription from their general practitioner.
- The community pharmacist is the final and key professional in the chain, with the responsibility to ensure that medicines are both prescribed and dispensed appropriately.

What this study adds

- The majority of community pharmacists are aware of off-label prescribing, but through work experience rather than undergraduate or postgraduate training or professional development.
- Community pharmacists, like UK general practitioners, underestimate the levels of paediatric off-label prescribing, and appear unclear as to the most common reasons for a prescription being off label.
- Most community pharmacists stated that they should inform the prescriber that a medicine was off label; however, when given specific practical examples, less than half would actually appear to do so.
- The majority of community pharmacists have been asked by the public to sell over-the-counter medicines for paediatric off-label use.

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Keywords
attitudes, community pharmacy, off-label prescribing, paediatrics, questionnaire, survey

Received
30 August 2006
Accepted
24 October 2006
Published *OnlineEarly*
23 February 2007

Aim
To identify community pharmacist experiences of, and attitudes towards paediatric off-label prescribing.

Methods
A prospective questionnaire-based study, with a 21-item questionnaire issued to 1500 randomly selected community pharmacies throughout the UK during 2005 on three separate occasions.

Results
Four hundred and eighty-two (32.1%) completed questionnaires were returned. Over 70% of respondents were familiar with the concept of off-label prescribing, primarily through dispensing experience rather than education, although only 40% were aware of having dispensed a paediatric off-label prescription within the previous month. The reasons given for a prescription being off label were younger age than recommended (84.6%, 297/351), primarily for antihistamines, analgesics and β_2-agonists, and higher (73.9%, 229/310) or lower than (41%, 103/258) recommended dose, primarily antibiotics and analgesics. Over 60% of respondents had been asked by the public to sell paediatric over-the-counter medicines, such as antihistamines, analgesics and steroid preparations for off-label use. The majority of respondents used the British National Formulary or the Pack Insert rather than specialist formularies or guidelines as a source of specialist paediatric information. Although 78% of respondents believed they had a responsibility to inform the prescriber that a medicine was off label, only 66% believed that they had a similar responsibility to inform parents.

Conclusion
The community pharmacists who responded to this questionnaire appear to be aware of and concerned by the issues which surround paediatric off-label prescribing. Despite this, most gained relevant knowledge through work experience rather than undergraduate or postgraduate training or professional development.

Introduction

The launch in 2004 of the UK government's National Service Framework (NSF) for children coincided with growing concerns about the safety and efficacy of paediatric medicines use, particularly off-label prescribing [1]. Specific standards were outlined in the NSF to promote the safe and effective use of children's medicines, aimed at both doctors and pharmacists. The paediatric use of unlicensed and off-label medicines is widespread throughout both primary and secondary care, where on average 5–10% of medicines prescribed in the community and 40% prescribed in hospital are off label or unlicensed [2–9]. Although the level of off-label prescribing in primary care is less than that in hospital, in absolute terms such prescribing by general practitioners (GPs) affects at least 26% of all 0–16-year-olds [5]. Despite these high levels of off-label prescribing, only 40% of GPs admit to prescribing in this way or to being aware of the issues surrounding such prescribing [8]. The high levels of off-label prescribing in the community, together with a lack of medical awareness, and the increasing number of paediatric medicines available over the counter (OTC), serves to highlight the growing importance of the community pharmacist in ensuring appropriate paediatric medicines use.

The concerns about paediatric off-label and unlicensed medicines revolve around an increased frequency and severity of adverse drug reactions (ADRs), the potential for treatment failure and a general lack of long-term safety and efficacy data [10–14]. Despite these concerns, widespread use of off-label and unlicensed medicines is inevitable since, for ethical and practical reasons, appropriate paediatric clinical trials have not been conducted to date. However, this situation is changing with the introduction of new legislation in the USA such as the 1997 Food and Drug Administration Modernization Act, the 1998 'Paediatric Rule', the 2002 Best Pharmaceuticals for Children Act and the 2003 Paediatric Research Equity Act. These Acts not only ensure appropriate reward for those pharmaceutical companies willing to undertake paediatric studies, but also that the appropriate legislative framework and funding are available to ensure the assessment of both on-patent and off-patent medicines for paediatric use [14, 15]. The rate of change in the EU has been less rapid, although new legislation is due to be implemented in late 2006 [16–18].

Community pharmacists in the UK are responsible for overseeing the supply of prescription and nonprescription medicines for use in children and this public health function places them as the 'gatekeepers' ensuring that all medicines, including those prescribed off label, are prescribed and dispensed appropriately [19, 20]. To this end, continuing professional development and access to the best available evidence is essential to permit the pharmacist to make informed decisions about paediatric off-label prescriptions. As little is known about the community pharmacy aspects of paediatric off-label prescribing, the aims of this study were to assess the attitudes, concerns and experiences of UK community pharmacists towards paediatric off-label prescribing and dispensing.

Methods

During 2005 a postal questionnaire comprising 21 questions with a combination of tick-box responses or 5–6 point scale questions, two of which also allowed written comment, was sent to 1500 randomly selected community pharmacies throughout the UK (approximately 12.5% of the total registered premises) obtained from the Royal Pharmaceutical Society of Great Britain (RPSGB). Prior to the full study, the questionnaire was piloted in 15 pharmacies and amended according to response. Baseline demographic data included details of respondent's length of registration as a pharmacist, type of community pharmacy, hours of direct patient contact and annual hours of continuing education. Questions specifically addressing dispensing practice and attitudes included knowledge of and reasons for paediatric off-label prescribing, classes of drugs dispensed off label, most common reasons for concern when dispensing off label, sources of information for dispensing to children, and transfer of information to parents and prescriber. Prior to asking these questions, the following brief statement defining off-label prescribing was provided: 'Many medicines prescribed for children, both in general practice and hospital, are used outwith the terms of their product licence ('off label'), e.g. at a lower or higher dose than recommended, for a younger age group than recommended, a different formulation, or for a different indication than recommended'. If a response had not been returned within 4 weeks, a further questionnaire was sent out; this procedure was performed on two separate occasions at 4-weekly intervals. Grampian Research Ethics Committee advised that this study did not require formal review by a National Health Service ethics committee.

Statistics

All data was entered on to an Excel database and analysed using the SPSS statistics package (SPSS Inc., Chicago, IL, USA). Where appropriate, percentage and the absolute number of respondents out of the total number to answer that question (denominator) are

included. Because the number of pharmacists to answer each question varied, so does the denominator.

Results

Demographics (Table 1)

Questionnaires were distributed to 1500 randomly selected community-based pharmacies throughout the UK. After three repeat postings starting in June 2005 and ending in August 2005, 482 (32.1%) completed questionnaires were returned. The majority of respondents were female (52%) and worked for large multiple pharmacies (>30 pharmacies) (54.3%), had been registered for >15 years (53%), reported >30 h of direct patient contact a week (82%) and completion of >20 h continuing education in the last 12 months (73%). The majority of respondents (75%) reported that paediatric prescriptions (0–12 years) formed <20% of their dispensing workload.

Off-label dispensing

None of the responses regarding paediatric off-label prescribing were affected significantly by gender, length of time since qualification, length of registration or work place.

The majority of respondents (73%, 344/473) admitted to being familiar with the concept of off-label prescribing. When asked how they became familiar, 64% (134/212) of respondents who answered this question said they had gained their knowledge through dispensing experience rather than undergraduate (16%) or postgraduate (2%) courses/lectures. During the preceding month 40% of respondents (186/465) admitted to knowingly dispensing off-label prescriptions to children (0–12 years), while 47% denied any such dispensing and 13% were unsure. Of those who recognized that they had dispensed off-label medicines, in the majority of cases no more than three prescriptions were dispensed during this time (median 2, interquartile range 2, range 1–6). The most common reasons given by respondents for a dispensed prescription being off label were younger age than recommended (84.6%, 297/351), primarily for antihistamines, analgesics and both oral and dry powder inhaled β_2-agonists, and higher than (73.9%, 229/310) or lower than (41%, 103/258) recommended dose, primarily antibiotics and analgesics. As expected, different route of administration (8.5%, $n = 18/211$) and different formulation (21.3%, 43/220) were the least common reasons for a paediatric medicine being off label. Lack of dosage data (60%, 232/386), risk of side-effect (36%, 134/372) and lack of clinical trials data (32%, 117/371) were recognized as major areas of concern for pharmacists when dispensing paediatric off-label medicines. Less than one-fifth of respondents believed that a lack of appropriate formulations or lack of efficacy data were of concern. When asked about specific examples of paediatric off-label prescribing, approximately 90% of respondents considered prescribing of inhaled steroids (88%, 360/411), β_2-agonists (84%, 346/414) or paracetamol (93%, 393/421) at higher than the recommended dose to be of concern. Despite these high levels of concern, only 39% of respondents said that they would always contact the prescriber if a child were prescribed high-dose steroids or β_2-agonists, although 74% would contact the prescriber in the case of high-dose paracetamol. Of least concern were antibiotics prescribed at less than the recommended dose. When questioned about OTC medicine sales, 61% (284/468) of respondents had been asked to sell OTC medicine for children for situations outside the product licence. The most common reasons given were younger age than recommended (90%, 261/290, predominantly antihistamines, analgesics and steroid

Table 1
Demographic data

Gender	$N = 474$	Male 48%						
Length of registration (years)	$N = 473$	<5, 22%	5–9, 13%	10–14, 12%	15–19, 11%	>19, 42%		
Patient contact per week (h)	$N = 474$	<10, 2%	10–19, 5%	20–29, 11%	30–39, 35%	>39, 47%		
Continuing education (h year^{-1})	$N = 470$	<5, 4%	5–9, 6%	10–14, 7%	15–19, 10%	20–24, 9%	25–29, 11%	>29, 53%
Paediatric dispensing workload, %	$N = 464$	<10, 41%	10–19, 34%	20+, 12%	Don't know 13%			

N, The total number of respondents.

creams), higher than recommended dose (66%, 129/195, predominantly analgesics and antihistamines) and different indication (37%, 71/190, primarily antihistamines requested for use as sedatives).

The most important sources of information used by community pharmacists to evaluate paediatric prescriptions were the British National Formulary (BNF) (88% of respondents, 411/470) and the package insert (64% of respondents, 289/449). Less frequently used information sources included the manufacturer's summary of product characteristics (23%, 108/466), Monthly Index of Medical Specialities (15%, 68/463), National Guidelines (12%, 57/462) and the local formularies (7%, 33/457). When asked about their own role in the process of paediatric off-label prescribing, the majority of respondents (78%, 363/462) agreed or strongly agreed that the pharmacist has a responsibility to inform the prescriber that they are prescribing off-label medicines for children, while 66% (309/465) agreed or strongly agreed that the pharmacist also has a responsibility to inform the parents that the medicines prescribed for their children are off label.

Discussion

With the expanding role of the community pharmacist in ensuring public health and safe medicines use, an understanding of the issues surrounding off-label prescribing is essential. This is the first study to assess the levels of awareness and experiences of paediatric off-label prescribing of UK community pharmacists. This information is essential to ensure the design of appropriate education strategies, fundamental to training and policy organization. Fifteen hundred randomly selected community pharmacists throughout the UK were sent a questionnaire survey; however, despite three separate postings over a 12-week period, the level of return was poor, with less than one-third of those approached responding. Such a low response rate is not uncommon for questionnaire-based studies; however, as a group, pharmacists have been particularly vocal in their support for greater involvement in patient pathways to facilitate the provision of an optimum 'gatekeeper' service [19, 20].

Although the majority of respondents were familiar with the concept of off-label prescribing, most admitted to having gained their knowledge through dispensing experience rather than any formal undergraduate or postgraduate training, a similar situation to that reported by GPs [8]. This response, which was unaffected by the length of registration, together with almost a quarter of respondents being unfamiliar with the concept of off-label prescribing, highlights a significant deficiency in current pharmacy undergraduate and postgraduate education.

The most frequently used sources of information for paediatric dispensing were the BNF and the pack insert; the least commonly used were local specialist formularies and national formularies/guidelines. Despite the wide availability of specialized paediatric reference sources, including the 2001 and 2003 editions of *Medicines for Children* published by the Royal College of Paediatrics and Child Health (the precursor of the BNF for children), only one respondent admitted to using them. However, this situation is likely to improve with the distribution of the BNF for children to all community pharmacies free of charge. Although paediatric off-label prescribing is common in primary care, affecting 26% of children, only 40% of respondents admitted to having knowingly dispensed such medicines in the previous month, suggesting a possible failure to recognize off-label prescribing when it occurs. It is interesting to note that in a recent survey of GPs, although 74% were aware of off-label prescribing, only 40% admitted to prescribing medicines off label [8]. The most common reasons given by pharmacists for off-label prescribing were: younger age than recommended and higher than recommended dose, responses similar to those given by Scottish GPs [8], but not actually consistent with the results of previous community-based studies in the UK, where lower dose than recommended was reported to be the most frequent, and younger age than recommended one of the least frequent reasons for off-label prescribing [5]. However respondents did correctly identify antibiotics, analgesics (primarily high-dose paracetamol) and antihistamines, as those drugs most frequently prescribed off label [5]. The major areas for concern cited by respondents when dispensing off-label medicines for children were the lack of dosage information, the risk of side-effects and the lack of clinical trials data, findings in agreement with previous studies of hospital-based paediatricians and primary care physicians [8, 21]. Surprisingly, only 20% of respondents believed that a lack of appropriate formulations was a significant issue, a finding similar to that reported for hospital paediatricians [21]. However, for community pharmacists, such low levels of concern possibly reflect a lack of extemporaneous paediatric dispensing experience, and an unawareness of the current situation, where hospital pharmacists overcome the lack of appropriate formulations by buying in unlicensed specials, importing products from abroad or by supplying extemporaneous preparations.

Except for low-dose antibiotics, almost all respondents expressed appropriate levels of concern when

given specific examples of potentially harmful off-label prescribing such as high-dose inhaled steroids, β_2-agonists or paracetamol. Considering the potential risk of undertreatment or the development of bacterial resistance, it is not clear why a prescription for a low-dose antibiotic failed to generate concern. More importantly, despite high levels of concern for other forms of off-label prescribing, only a third of respondents said that they would always contact the prescriber to check on the dose. Why community pharmacists do not contact the prescriber is unclear; however, this may indicate a need for improvement in communication systems. Almost three-quarters of respondents believed they had a role to play in informing the parents that a child's medicine was off label, an action which, in light of the policy statement made by the Royal College of Paediatrics and Child Health [22], could confuse the parent and potentially place both the pharmacist and prescriber in an awkward situation.

The NSF states that 'children and young people should receive medicines that are safe and effective, that are dispensed and administered by professionals who are well-trained, informed and competent to work with children'. The RPSGB subsequently distributed informal guidance to pharmacists encouraging them to 'play their part by developing and providing high quality information to children and carers, particularly for unlicensed and off label medicines and to promote concordance by involving children and carers in their medicines and giving them a choice wherever possible'. Achieving the goal of appropriate paediatric prescribing requires good communication between prescriber and pharmacist, and in the present study almost 70–80% of pharmacists agreed that they had a responsibility to inform the parents and prescriber that medicines were off label. However, without standard agreed protocols, either party may see the other as questioning their competence, a situation which may in part be resolved by the availability of the BNF for children, now in its second edition, the recent provision of pharmacist-oriented child-based learning packages available [23, 24] and the establishment of the UK Medicines for Children Research Network, which has been tasked with addressing the issues surrounding paediatric medicines use. However, the first step in the education process is widespread recognition and awareness of current deficiencies, without which the availability of suitable information becomes almost academic.

Study limitations

Postal 'self-report' questionnaires are a limited instrument for assessing prescribing and dispensing practice accurately and it is difficult to conclude confidently that the responses elicited accurately represent the attitudes and behaviour of the respondents. However, it is to be hoped that the anonymity of the questionnaire will have encouraged honesty. There may also be potential for recall bias, which should have been minimized by limiting the period of recall to 1 month. A further concern is the low level of response despite three reminders, which could give rise to selection bias. However, the demographics of respondents in this study were essentially similar to those for the UK pharmacy workforce, suggesting that any selection bias should be limited.

Conclusion

While all licensed medicines used to treat children have been rigorously tested before their general use, not all are specifically licensed for use in children. Until this situation is rectified, the pharmacist should aspire to being competent and confident in recognizing and dealing with appropriate off-label and unlicensed prescribing. However, to fulfil this role greater emphasis should be placed on both undergraduate and postgraduate education, together with evidence-based information, and training in the use of off-label drugs.

Competing interests: None declared.

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