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RESEARCH ARTICLE

A prospective observational study on the attitude and experience of community pharmacists towards off-label and unlicensed prescriptions for the pediatric population

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ABSTRACT:
Off-label is defined as any drug use outside the terms of product license; while the unlicensed use refers to using a drug in children when it has not received marketing authorization for use in them. The objective of the study was to determine the attitude and experience of community pharmacists towards off-label and unlicensed prescriptions for the pediatric population. This study was carried out as a prospective observational study for a period of six months at the community pharmacies in and around Chennai. Validated questionnaire to assess the attitude and experience of community pharmacists towards unlicensed and off-label prescriptions for the paediatric population was given to those community Pharmacists who have registered in the State Pharmacy Council as Pharmacist. Questionnaires issued were self administered by the community pharmacists and the answers recorded by them were collected and then assessed. Over 70% of respondents were familiar with the concept of off-label prescribing, primarily through dispensing experience rather than education. 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. Most common off-label drug was paracetamol being 32% (BNFC) of all prescribed in this manner. Most common information sources was British national formulary for children (BNFC), Current index medical specialities(CIMS) and local formularies. The majority of respondents (74%) admitted to being familiar with the concept of off-label prescribing .The majority of respondents, 88% agreed or strongly agreed that the pharmacist has a responsibility to inform the prescriber that they are prescribing off-label medicines for children, and 32% unsure that pharmacist also has a responsibility to inform the parents that the medicines prescribed for their children are off-label. Dispensing labeled and licensed drugs in pediatric patients should be promoted among the community pharmacist as well as pediatricians in order to avoid exposing children to unnecessary risk. Participation in Continuing Medical Education should be encouraged among community pharmacist to keep their knowledge updated.

KEYWORDS: Off-label, Unlicensed, Community Pharmacy, Pediatrics, Questionnaire, Attitude

INTRODUCTION:
Off-label is defined as any drug use outside the terms of product license; while the unlicensed use refers to using a drug in children when it has not received marketing authorization for use in them[1].

Many drugs used to treat children in hospital are either not licensed for use in children or prescribed outside the terms of their product license. Drugs are subject to licensing procedures to ensure their safety, quality and effectiveness. The age bands are as follows:

- Term newborn babies - age 0 to 27days
- Infants and toddlers - age 28days to 23months
- Children – age 2 to 11yrs
- Adolescents - age 12 to 17 yrs

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Childhood diseases and disorders may be qualitatively and quantitatively different from their adult equivalent [2].The high level of off-label prescribing in the community, together with a lack of medical awareness and an increasing number of over the counter drugs, shows to highlight the growing importance of the community pharmacist in ensuring the appropriate pediatric medicines use. Children and young people should receive medicines that are safe and effective which is dispensed by professionals. The commonly prescribed off label drugs are Paracetamol, Amoxicillin, Salbutamol, Promethazine, Monteleukast, cetrizine, ranitidine and Vitamins. The list of approved drugs differs between countries and drugs that are approved in one country may not be approved in another. However, non-approved drug may be less well documented than the approved ones uses off-label [2-4].

Once a drug is marketed, the medicines control agency (MCA) closely tracks the product's unwanted effects in a process that relieves heavily on spontaneous reporting by prescribers (as with the yellow card system) and on data collected in post marketing surveillance by the manufacturer. Therefore, we intended to evaluate the extent of off-label or unlicensed drugs dispensed by community pharmacists and types of off-label use of medicines in pediatric populations and experiences towards it. British National Formulary for Children (BNFC) is a pharmaceutical reference book that contains a wide spectrum of information and advice on prescribing and pharmacology, along with specific facts and details about many medicines available on National Health Services (NHS). National Formulary of India (NFI) contains lists of medicines that are approved for prescription, which throughout the country, indicating products are interchangeable[4-6].

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 pediatric medicines use, particularly off-label prescribing[7]. 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 pediatric 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% of prescribed in hospital are off-label or unlicensed. Widespread use of off-label and unlicensed is inevitable since, for ethical and practical reasons, appropriate pediatric clinical trials have not been conducted to date[8-12]. 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 'Pediatric Rule' the 2002 Best pharmaceuticals for children Act. These Acts not only ensure appropriate reward for those pharmaceutical companies willing to undertake pediatric 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 pediatric use[6,13]. Community pharmacists are responsible for the supply of prescription and non-prescription 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. In order to reduce off-label prescribing primary care, physicians need to be aware of the situation and acknowledge their role in providing optimal treatment for children[14-15].

MATERIALS AND METHODS:

The study proposal was approved by the institutional ethics committee (IEC/DOPV/2015/04). It was carried out as a prospective observational study for a period of six months at the community pharmacies in and around Chennai. Validated questionnaire to assess the attitude and experience of community pharmacists towards unlicensed and off-label prescriptions for the paediatric population was given to those community Pharmacists who have registered in the State Pharmacy Council as Pharmacist. Questionnaires issued were self administered by the community pharmacists and the answers recorded by them were collected and then assessed. The questionnaire was given to the pharmacist, and about 3days of time was given to answer the questionnaire. Then, it was collected on the third day and analyzed.

RESULTS:

Questionnaires were distributed to 100 community pharmacies and all questionnaires, were answered and on the third day returned. The majority of respondents were male (85%) fig1 and worked for small independent (1-4pharmacies) (79%) had been registered for >10-15years (81%), reported >10hrs of patient direct contact a week (69%) and completion of 10-14hrs continuing education in the last 12months (65%). The majority of respondents (74%) reported that pediatric prescriptions (0-12yrs) formed <20% of their dispensing work load.

The majority of respondents (74%) admitted to being familiar with the concept of off-label prescribing. When asked how they became familiar, (74%) of respondents who answered this question said they had gained their knowledge through dispensing experience (44%) rather than undergraduate (24.8%).Postgraduate (14.8%), journal article (10%) and conferences (6%) fig2. During the preceding month, 64% of respondents admitted to knowingly dispensing off-label prescriptions and (0-12yrs), while 30% denied any such dispensing and 6%

were unsure. Of those who recognized that they had dispensed off-label medicines, in the majority of cases, no more than two prescriptions were dispensed during this time. The most common reason given by respondents for a dispensed prescription being off label was younger age than recommended (74%), primarily antihistamines, NSAID and higher than (6%) or lower than (6%) recommended dose, primarily antibiotics and analgesics. Lack of dosage information (60%), risk of side effects (15%) and lack of clinical trials data (15%) were major areas of concern of pharmacists when dispensing pediatric off-label medicines. Less than10 respondents believed that a lack of appropriate formulations or lack of efficacy data was concerned.

When asked about specific examples of pediatric off-label prescribing, approximately 80% of respondents considered prescribing of inhaled steroids (58%), ß2agonists (12%), paracetamol (30%) at higher than the recommended dose to be of concern. Only 79% of respondents said that they would always contact the prescriber if a child were prescribed high dose steroids or ß2agonists, although 83% would contact the prescriber in the case of high dose of paracetamol. When questioned about OTC medicine sales, 69% of respondents had been asked to sell OTC medicine for children for situations outside the product license. The most common reasons given were higher than recommended dose (83%), predominantly antihistamines, analgesics and younger age than recommended (13%), predominant steroids, analgesics. The most important sources of information used by community pharmacists to evaluate pediatric prescription were the British national formulary (BNF) (10.3%), and current index of medical specialists (CIMS) (28.4%), package insert (21.1%) and local formulary (25.2%). Less frequent or moderately used information sources included the national guidelines (14%) monthly index of medical specialities (MIMS) (1%). When asked about their own role in the process of pediatric off-label prescribing, the majority of respondents, 88% agreed or strongly agreed that the pharmacist has a responsibility to inform the prescriber that they are prescribing off-label medicines for children, while (68%) of the respondents, agreed or strongly agreed and 32% unsure that pharmacist also has a responsibility to inform the parents that the medicines prescribed for their children are off-label.

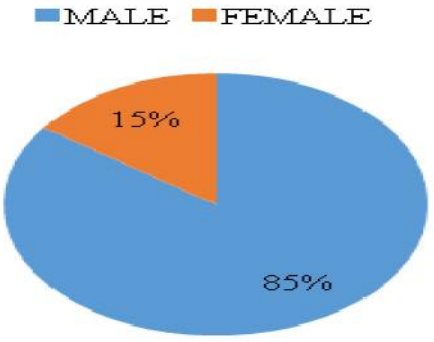

Fig1: Gender distribution of community pharmacists

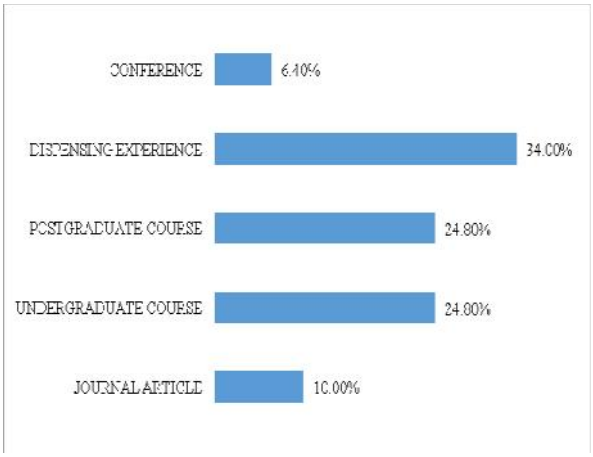

Fig 2:Various resources used to be aware of off-label prescribing

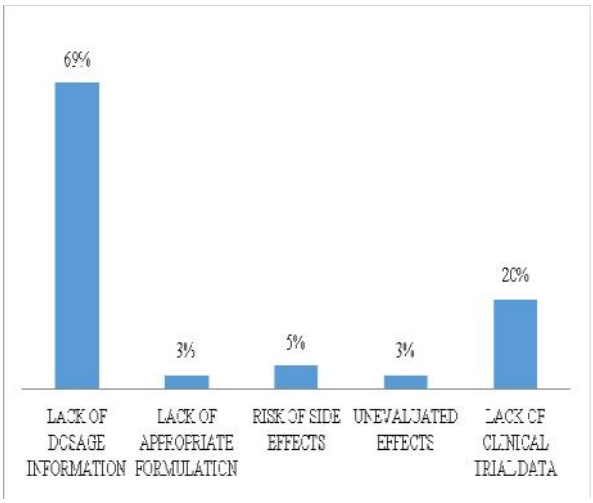

Fig 3: Resources of concern to pharmacist when dispensing off-label medicines for children

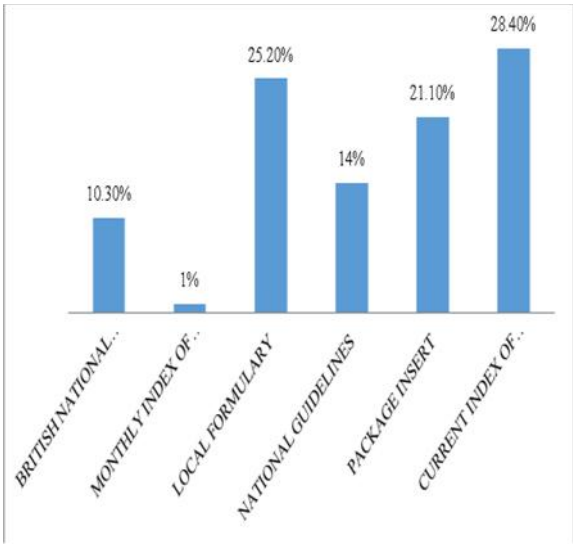

Fig 4: Utilization of information resources usein relation to prescribed pediatric medicines

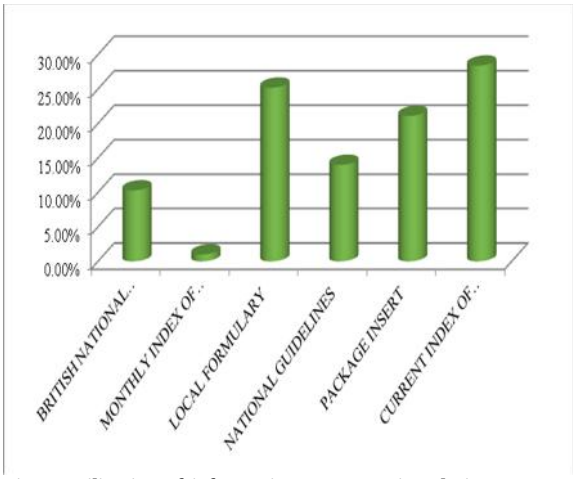

Fig 5: Utilization of information resources in relation to over the counter pediatric medicines

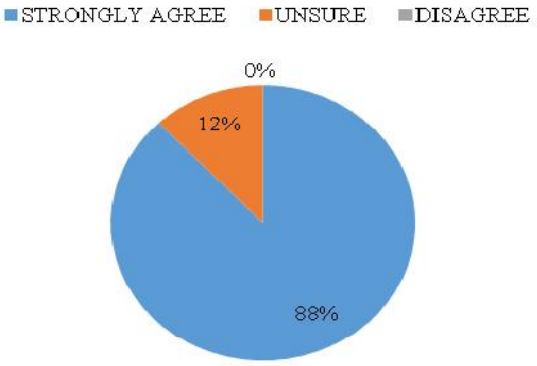

Fig 6: Responsibility of pharmacist in informing parents that prescribed medicines are off-label

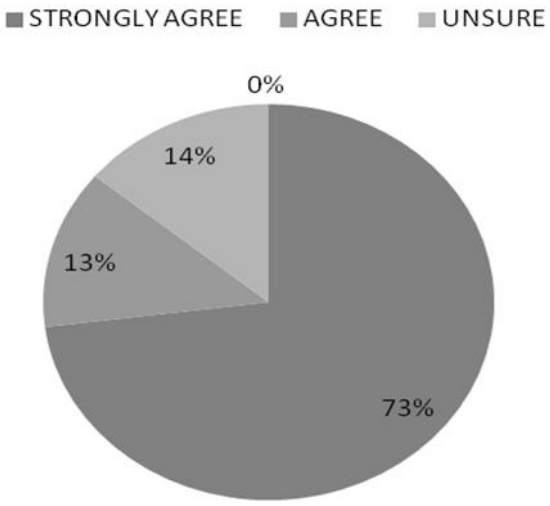

Fig 7: Responsibility of pharmacist in informing prescriber that prescribed medicines are off-label

TABLE 1: Awareness of licensing restrictions concerning otc medicines

S.NO	LICENSING RESTRICTIONS DRUGS	YES	NO
1.	IBUPROFEN increases at 3years and again at 8years	 97 97	 03 03
2.	CHLORPHENIRAMINE MALEATE tablets not recommended under 6years	83	17
3.	CHLORPHENIRAMINE syrup is not recommended under 1 yrs	100	0
4.	EURAX CREAM is not recommended for children under 3yrs	32	68

Table 2: Awarenesas of licensing restrictions concerning prescribed paediatric medicines

S.NO	LICENSING RESTRICTIONS DRUGS	YES	NO
1.	ERYTHROMYCIN increases at 2years and again at 8years	 97 97	 03 03
2.	PENICILLIN V increases at 1years and again at 6years	 83 66	 17 34
3.	CO-AMOXICLAV increases at 1years and again at 6years	 73 73	 27 27
4.	Salbutamol syrup is not licensed for use in chidren under 2years of age	93	07
5.	Terbutaline tablet is not licensed for use in chidren under 7years of age	45	55
6.	Cetrizine tablet is not licensed for use in chidren under 2years of age	100	00
7.	Loratidine tablet is not licensed for use in chidren under 2years of age	82	18

Table 3: Whether pharmacist would contact the prescriber if drug was off-label

S.NO	DRUGS	ALWAYS	SOMETIMES	NEVER
1.	ß2 agonist for asthma at higher than recommended dose	89	11	-
2.	Inhaled steroids prescribed at higher than recommended dose	79	21	-
3.	Paracetamol prescribed at a younger than recommended dose	65	23	12
4.	Oral salbutamol prescribed to children under 2yrs	93	07	-

DISCUSSION:

With the expanding role of the community pharmacists in ensuuring public health and safe medicines use, and understanding of the issues related to off-label prescribing is essential. This information is essential to ensure the design of appropriate education strategies and fundamental to training. The level of return was good, with morethan two third of those approached responding. Although the majority of respondents were familiar with the concept of off-label prescribing, most of them gained knowledge through dispensing experience rather than undergraduate and post graduate training, a similar situation is reported by general physicians (GPs)[16]. This response, which was unaffected by the length of registration, together with almost a three fourth of respondents being unfamiliar with the concept of off-label prescribing.

The most frequently used sources of information for the paediatric dispensing were CIMS and package insert; and least commonly used sources were BNF, National formulary guidelines. But in the prospective study, frequently used sources of information were BNF and package insert which was reported in the UK. Providing a BNF for children to all the community pharmacists as complement, can help to improve from the current scenario. Although paediatric off-label prescribing is common in primary care, only 39% of respondents admitted to having knowingly dispensed such medicines in the previous month, which alarms that the off-label prescribing was not recognized by 61% of the respondents when it occurred. On the other hand, it is interesting to note that in a recent survey of GPs, even though 74% were aware of off-label precribing, only 40% admitted that they were prescribing off-label medicines[17].

The most common reasons given by pharmacists for off-label precribing were eighther lower or higher dose than the recommended dose which is in line to the UK prospective study[18]. Lower than recommended dose waas reported to be the most frequent reason for off-label prescribing[19].The major areas of concern cited by respondents when dispensing off-label medicines for children were the lack of dosge information, the risk of side effects and lack of clinical trial data,findins in agreement with previous studies of hospital based paediatricians and primary care physicians[17]. Only 20% of respondents believed that lack of appropriate formulation was a significant issue to be reported to hospital paediatricians[16]. So community as well as hospital pharmacist should overcome from lack of appropriate formulations by buying in unlicensed specials, importing products from abroad or by supplying extemporaneous preparations. While the high level of concern for other forms of off-label precribing was studied, only one-third of respondents said they would always contact the prescriber to check on the dose. This may indicate that need for improvement in communication system. Almost three-quarters of respondents believed they had a role to play in informing the parents that a child's medicine was off-label.

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 work with children'. Achieving the goal of appropriate paediatric prescribing requires good rapport between the prescriber and pharmacist.

CONCLUSION:

Dispensing labeled/ licensed drugs in pediatric patients should be promoted among the community pharmacist as well as pediatricians in order to avoid exposing children to unnecessary risk. Participation in Continuing Medical Education should be encouraged among community pharmacist to keep their knowledge updated clinical trials is in process.

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REFERENCES:

1. Turner S, Longworth A, Nunn AJ and Choonara I. Unlicensed and off label drug use in paediatric wards: prospective study. BMJ. 316(7128); 1998:343–5.
2. Impicciatore P. Incidence of adverse drug reactions in paediatric in/out-patients: a systematic review and meta-analysis of prospective studies. Lancet. 359;2002: 1373–8.
3. Wong I, Sweis D, Cope J and Florence A. Paediatric medicines research in the UK: how to move forward? Drug Safety 26; 2003:529–37.
4. Choonara I and Conroy S. Unlicensed and off label drug use in children: implications for safety. Drug Safety. 25; 2002: 1–5.

5. Turner S, Nunn AJ, Fielding K and Choonara I. Adverse drug reactions to unlicensed and off label drugs on paediatric wards: a prospective study. Acta Paediatr. 88; 1999: 965–8.
6. Horen B, Montastruc JL, Lapeyre and Mestre M. Adverse drug reactions and off label drug use in paediatric outpatients. Br J Clin Pharmacol. 54; 2002: 665–70.
7. National Service Frame Work Documents for Children, Young People and Maternity Services, Part 2. Available at http://www.dh.gov.uk.
8. Conroy S, Choonara I, Impicciatore P, Mohn A, Arnell H, Rane A et al. Survey of unlicensed and off label drug use in paediatric wards in European countries. BMJ. 320; 2000: 79–82.
9. Turner S, Longworth A, Nunn AJ and Choonara I. Unlicensed drug use on paediatric wards. BMJ. 316; 1998: 342–5.
10. Turner S, Nunn AJ and Choonara I. Unlicensed drug use in children in the UK. Paed Perinatal Drug Ther. 1; 1997: 152–5.
11. Daukes ES, Simpson C, Helms PJ, Taylor MW and McLay JS. Paediatric off label prescribing in general practice. Eur J Clin Pharmacol. 60; 2004: 349–53.
12. Turner S, Longworth A, Nunn A and Choonara I. Unlicensed and off label drug use in paediatric wards: prospective study. BMJ. 316; 1998: 343–5.
13. Spielberg S. Paediatric therapeutics in the USA and internationally: an unparalleled opportunity. Paediatric Perinatal Drug Ther. 4; 2000: 71–4.
14. NHS Scotland. Pharmacy for Health: The Way Forward for Pharmaceutical Public Health in Scotland. Glasgow: Public Health Institute for Scotland 2002.
15. Dot Pharmacy. Issue CPG Launches Gatekeeper Initiative. 1996. Last accessed: 26 June 2006. Chemist and Druggist Online, CMP Information Ltd. 20.
16. McLay JS, Tanaka M, Daukes ES and Helms PJ. A prospective questionnaire assessment of attitudes, and experiences of off label prescribing amongst hospital based paediatricians. ArchDis Child. 91; 2006: 584–7.
17. Daukes ES, Taylor M, Helms PJ and McLay JS. Off label prescribing to children: attitudes and experience of general practitioners. Br J Clin Pharm. 60; 2005: 145–9.
18. Stewart D, Rouf A, Snaith A, Elliott K, Helms PJ & James S. McLayAttitudes and experiences of community pharmacists towards paediatric off-label prescribing: a prospective survey. Br J Clin Pharmacol. 64;2007:190–5.
19. Daukes ES, Simpson C, Helms PJ, Taylor MW and McLay JS. Paediatric off label prescribing in general practice. Eur J Clin Pharmacol. 60; 2004: 349–53.