Methodology for surveillance of antimicrobials use among out-patients in Delhi

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**Background & objectives:** Determining antibiotic use in the population is problematic in India, as there are no population level databases on prescriptions and over-the-counter sales. This study attempts to establish a methodology for surveillance of antibiotic use in the community.

**Methods:** Antibiotic use was monitored in five municipal wards of Delhi, from January-December 2004. Thirty co-operative retail pharmacies were enrolled in Inderpuri (7), Karol Bagh (3), Patel Nagar (5), Rajinder Nagar (6) and Rajouri Garden (9); data on antibiotic use were collected in two ways. Firstly, bulk purchase data were collected by recording the quantities of all antibiotics purchased by these pharmacies every month over one year. Secondly, 15-25 ‘exit interviews’ were conducted with patients leaving the enrolled pharmacies every month. Antibiotic use from bulk purchase data was measured as defined daily dose (DDD)/1000 population and from exit interview data as DDD/1000 patients visiting the pharmacy during data collection and also as per cent patients receiving an antibiotic.

**Results:** Bulk purchase and exit interview data showed some similar patterns of antibiotic use with a growing peak in the consumption of most antibiotics classes in the months of February and March. Use of the fluoroquinolone group (J01MA) was much higher than other antibiotic classes by both methods. Exit interviews revealed that 21 per cent of persons who visited the pharmacies bought antibiotics. Both measures of use from exiting patient interviews showed the same trend over time.

**Interpretation & conclusions:** Both drug use methods can be used to measure antibiotic use in the private retail pharmacies and outpatient department of public facilities. Surveillance of antimicrobial drug use from private retail pharmacies in a municipal zone in Delhi indicated overuse of antimicrobial drugs, particularly fluoroquinolines.

**Key words** Antibiotics - antimicrobial surveillance - bulk purchase data - defined daily dose - private pharmacies

Antibiotic resistance in microorganism is a major public health problem worldwide. The increase in resistance is a result of several factors, but the major cause is the overall volume of antibiotic consumption, particularly for indications that do not require such therapy.

Until last decade, the major emphasis for study of bacterial resistance was confined to hospital-acquired microorganisms. However, increasing resistance has been observed in community-acquired microbes such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Escherichia coli* and group A Streptococci. The use
of antibiotics in the community is indiscriminate and its restriction is very difficult. Several studies have focused on the excessive use of antibiotics in general. Enhanced antimicrobial surveillance is one of the strategies to guide control of antimicrobial overuse or misuse. This is because the ability to study population-based pattern of antimicrobial use provides a more comprehensive understanding of how the physician and patient use these agents. Promoting appropriate use of antibiotics through various interventions will help stop unnecessary prescribing and misuse of antibiotics. For suitable interventions to be carried out in the community it is essential to know the extent of antimicrobial use and pattern of antimicrobials in the population. Countries such as Denmark and Spain have databases containing information on antimicrobials prescribed for all patients in the country. Prescription information for various populations (e.g., children versus adults) and between different provinces of the country are analysed to determine trends in antimicrobial use at the population level.

Data on the use of antimicrobial agent at the population level are lacking in India as we do not have any database for the consumption of antimicrobials in the community. This is mainly because, in India, unlike many developed countries, prescriptions are kept by the patient and not with the pharmacist and antibiotics may be obtained with or without a prescription. Therefore, determining antimicrobial use or antibiotic medicines (ABM) use is problematic, more so in the private sector, since there are no prescription records. Hence, there is an utmost need to develop a methodology that can measure consumption of antimicrobial use in the community.

This study was undertaken with the objective to develop a surveillance system for outpatient antimicrobial drug use in the community. Survey was conducted at private retail pharmacies as first step because establishing a surveillance method for private retail pharmacies is more difficult and a major source for antibiotic use than public sector.

**Material & Methods**

Surveillance of antimicrobials use was conducted in different residential areas that fall under five municipal wards of New Delhi. The study was carried out in conjunction with another study (not described here) to standardize the method to measure the antimicrobial resistance pattern for OPD patients of a private tertiary care hospital, Sir Ganga Ram Hospital located in Rajinder Nagar, West Delhi. Rajinder Nagar comes under Karol Bagh Zone of Municipal Corporation of Delhi. The localities (wards) that are under Karol Bagh zones are - East Patel Nagar, South Patel Nagar, Rajinder Nagar, Naraina in addition to Karol Bagh. So the data were collected from Patel Nagar (east, west, south), Rajinder Nagar, Naraina including Inderpuri and Karol Bagh. Rajouri Garden ward was also included because many patients from this locality visit the hospital where microbiology part of the study was carried out.

The study protocol was approved by the ethics committee of Sir Ganga Ram Hospital and the WHO. The study was done under the aegis of Delhi Society for Promotion of Rational Use of Drugs (DSPRUD) and clearance was obtained from the DSPRUD as well. Informed consent was obtained from all participants of the study.

Data on antimicrobial consumption were collected for one year from January to December 2004 so that all seasons of the year were covered. Antimicrobial data were collected from thirty well stocked licensed retail pharmacies located in the chosen five municipal wards (Table I).

Liaison was done with the associations of private pharmacists and meetings were held with the office bearers who helped in introducing various pharmacies of the area. Meeting and discussion on one-to-one basis were also held with all the pharmacists of enrolled private retail pharmacies for the study. The purpose and methodology to be used were discussed and all thirty pharmacy owners (pharmacists) co-operated for the entire period of the study. The rationale for enrolling 30 pharmacies (clarified below) was based on the recommendations on sample size suggested by the WHO.

**Data collection methodology:** Data was collected by the following two methods to measure the antimicrobial drug use in the population.

(i) Bulk purchase data - Purchase of antimicrobial drugs (sell-in data) by retail pharmacy was measured assuming that the same amount will be sold (sell-out) to patients and will be used in the population. Purchase data of all antimicrobials was recorded from the purchase bills (records) from the 30 enrolled pharmacies monthly over one year. A detailed proforma
was designed containing names of all antimicrobials and different strengths available for each. Two data collectors with pharmacy background were engaged for the study. After training of data collectors, a pilot survey was conducted before starting the actual survey. Data collectors visited all retail pharmacies (chemist shops) every 15 days and noted the quantity of all antimicrobials purchased by the pharmacy.

(ii) Exit patient interview data - Exit interviews were conducted at all 30 facilities. Patients/persons buying any antimicrobial drug for outpatients (OPD) were interviewed after they came out from the pharmacy shop after purchasing the medicines. Antibiotic purchased by any person whether with prescription, without prescription, or on the advice of chemist, was noted. A pre-designed proforma was used to collect data on the name of antimicrobial, dose and duration prescribed and how much purchased. The proforma was developed for the study and was field tested before the actual survey. Two trained data collectors visited the pharmacy. One counted all the patients visiting the pharmacy during the period of data collection and checked whether they received any antibiotic medicine (ABM). The other data collector interviewed the patients receiving an antibiotic as referred by his colleague.

The WHO manual recommends there should be 600 encounters (20 facilities and 30 patients/prescriptions per facility) for one survey. In this study 30 facilities and 20 prescriptions were adapted. Since the amount of time to get these interviews varied per shop 15-25 interviews per facility were conducted per month. Exit interviews of patients buying antimicrobial drug were conducted at each pharmacy per month for a period of one year. A total of 30,106 persons visited during the entire observation period and 6,633 patients (21.3%) bought antibiotics from these 30 enrolled pharmacies.

Outcome measures: A technical unit of measurement called the defined daily dose (DDD) was used in drug utilization studies. In the Anatomical Therapeutic Chemical (ATC) classification system, the drugs are divided into different groups according to the organ or system on which they act and on their chemical, pharmacological and therapeutic properties. DDD is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults. Consumption of antimicrobial drug was defined in terms of total number of DDDs using the WHO ATC/DDD system. Consumption for purchase data was expressed as DDD/1000 population/month and for exit interview as DDD/1000 patients attending the facility. From exit interviews, antibiotic use was also measured in terms of the percentage of patients receiving an antibiotic. The denominator for bulk purchase data was population (inhabitants) of the municipal ward, obtained from the Census Department of Delhi government. The denominator for exit interview data was the number of patients attending the facilities obtained by counting the number of patients attending the pharmacy during the time taken to do the target number of exit interviews.

Statistical analysis: A software programme was developed for entering the data and double entry was done to check for errors. The data obtained from purchase and exit interviews were analysed to show monthly patterns of use and consumption by various antibiotic groups or classes, using both data collection methodologies.

Results

Bulk purchase data was collected from 30 well stocked licensed pharmacies from five municipal wards. Details of the pharmacies in each area with their population are shown in Table I. A total of 31,106 persons visited during the entire observation period and 6,633 patients (21.3%) bought antibiotics from these 30 enrolled pharmacies.

Overall annual antibiotic consumption

Bulk purchase data: Consumption of fluoroquinolones, J01MA, was much higher than other classes of antibiotics followed by penicillins, J01C (mainly extended spectrum penicillins, ESP, J01CA, Fig. 1), cephalosporins, J01DA and macrolides, J01FA (Table II). Tetracyclines (J01A) were used to a lesser extent than the other groups and sulphonamides (trimethoprim group, J01E, and co-trimoxazole, J01EE01) were used the least. The number of DDDs/1000 population for fluoroquinolones (J01MA), penicillins (J01C), cephalosporins (J01DA), macrolides (J01FA) and tetracyclines (J01A) were 1347, 415, 381, 336, 258, respectively (Table II).

Exit patient interview data: Class-specific consumption of various antibiotic group followed exactly the same order as was seen from the bulk purchase data. Consumption of fluoroquinolones was highest than other classes of antibiotics, followed by penicillins, cephalosporins and macrolides. The DDDs/1000
patients attending the pharmacies for fluoroquinolone (J01MA), penicillins (J01C), cephalosporins (J01DA), macrolides (J01FA) and tetracyclines (J01A) were 32,805, 14,463, 12,888, 11,085, 4,699 respectively. As expected, the number of DDDs/1000 patients attending pharmacies from interview data was much higher than the number of DDDs/1000 population.

**Monthly trend of antimicrobial use**

*Bulk purchase data:* There were increases in consumption of various classes of antibiotics, viz., penicillins, cephalosporins, macrolides and tetracyclines in the months of February-March and August. Consumption of fluoroquinolones was much higher than other group of antibiotics throughout the year. Though there was an increase in the consumption of fluoroquinolones, J01MA, in the month of March, the maximum bulk purchase was seen in the month of June with a sharp dip in purchase in July (Fig 1).

*Exit patient interview data:* Figs 2 and 3 show month-wise analysis of consumption of different antibiotics from exit interviews (prescription data) for the two different measures used - DDDs/1000 patients attending pharmacies during data collection (Fig. 2) and per cent patients receiving an antibiotic (Fig. 3). The two measures viz., DDD/1000 patients and per cent patients receiving an antibiotic, showed virtually the same trends over time for all classes of antibiotics with much greater use of antibiotic occurring in February-April and with peak consumption in March. Consumption of fluoroquinolones was highest compared to other classes of antibiotics. There were some similarities with regard to patterns and trends in use between exit interview and bulk purchase data. For example, both methods showed much higher use of fluoroquinolones compared to other antibiotic classes - and slightly

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**Table I.** Number of private pharmacies and population of five areas surveyed in Delhi

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of pharmacies</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inderpuri (includes Naraina)</td>
<td>7</td>
<td>87,239</td>
</tr>
<tr>
<td>Karol Bagh</td>
<td>3</td>
<td>1,23,610</td>
</tr>
<tr>
<td>Patel Nagar</td>
<td>5</td>
<td>1,50,058</td>
</tr>
<tr>
<td>Rajinder Nagar</td>
<td>6</td>
<td>72,093</td>
</tr>
<tr>
<td>Rajouri Garden (includes Mayapuri)</td>
<td>9</td>
<td>4,69,963</td>
</tr>
</tbody>
</table>

**Table II.** Total consumption for one year of various classes of antibiotics in the five areas surveyed* in Delhi, India

<table>
<thead>
<tr>
<th>Antibiotic ATC Classification</th>
<th>DDD/1000 population (Bulk purchase)</th>
<th>DDD/1000 patients (Exit interview)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flouroquinolones (J01MA)</td>
<td>1346.76</td>
<td>32805.29</td>
</tr>
<tr>
<td>Penicillins (including ESP) (J01C)</td>
<td>415.11</td>
<td>14463.31</td>
</tr>
<tr>
<td>Cephalosporins (J01DA)</td>
<td>380.59</td>
<td>12888.31</td>
</tr>
<tr>
<td>Macrolides (J01FA)</td>
<td>335.97</td>
<td>11085.11</td>
</tr>
<tr>
<td>Tetracyclines (J01A)</td>
<td>258.08</td>
<td>4699.47</td>
</tr>
<tr>
<td>Co-trimoxazole (J01EE01)</td>
<td>39.48</td>
<td>95.49</td>
</tr>
<tr>
<td>Aminoglycosides (J01G)</td>
<td>5.99</td>
<td>55.21</td>
</tr>
</tbody>
</table>

*Data collected from 30 retail pharmacies which were located in the five surveyed areas; ESP, extended spectrum penicillins; ATC, anatomical therapeutic chemical; DDD, defined daily dose

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*Fig. 1. Monthly trends of consumption of different groups of antimicrobials by bulk purchase data collection from the retail pharmacies. Aminoglycoside (J01G); Cephalosporins (J01DA; Extended spectrum penicillins, ESP, J01CA; Macrolides (J01FA); Penicillins (J01C); Quinolones & fluoroquinolone (J01MA); Sulphonamide-trimethoprim (J01EE01; Tetracyclines (J01A)).

*Fig. 2. Monthly trends of consumption (use) of different groups of antimicrobials by conducting exit interviews at the retail pharmacies. Aminoglycoside (J01G); Cephalosporins (J01DA; Extended spectrum penicillins, ESP, J01CA; Macrolides (J01FA); Penicillins (J01C); Quinolones & fluoroquinolone (J01MA); Sulphonamide-trimethoprim (J01EE01; Tetracyclines (J01A).
higher consumption of other antibiotic during the winter months. Unlike bulk purchase data, exit interview data showed little increase in the consumption of various antibiotics - penicillins, cephalosporins, macrolides and tetracyclines during August and September (Figs 2, 3).

Discussion

Antimicrobial resistance is a global threat affecting industrialized and developing countries\(^{16,17}\). Reducing the excessive use of antibiotics is essential in both the community and hospital settings and the first step in this direction is to find out the consumption and pattern of various antibiotics used in the community. Most countries and studies\(^{18-20}\) choose ATC classification system and the DDD measurement unit, developed by the WHO\(^ {15}\). Monnet and colleagues\(^ {21}\) showed that the number of DDDs correctly indicate the number of antimicrobial prescription for outpatients at the national level. Thus the number of DDDs is an acceptable measurement unit to express outpatient antimicrobial use and to benchmark countries for their level of antimicrobial drug consumption. In this study an attempt was made to develop a surveillance system for antimicrobial use in the community in Indian context using standard measures.

Collecting data for a long period from private sector is difficult as it requires high level of co-operation from the private pharmacists. Moreover, in India 80 per cent of drug expenditure is out-of-pocket\(^ {22}\), meaning thereby 80 per cent of the population purchase medicines from private sector from their own savings. Therefore as a first step to establish a methodology for surveillance of antibiotic use in the community for out-patients, the survey was done in the private sector.

Purchase data from the pharmacy were collected instead of the sales data as it was difficult to get the sales data from pharmacies. It could not be ascertained whether all the purchase data bills shown by pharmacy owner were actually the total purchase and all the medicines purchased were sold. These are weaknesses of bulk purchase methodology. However, for surveillance, it should not matter provided the same degree of error was occurring each month. This is the reason that the trends over time and between classes found with bulk purchase data were cross-checked against trends found from exit interview data at the same facilities.

In the exiting patient interviews, two measures of consumption were used, again to see which outcome would be easier to measure and whether these would be equally good for surveillance. Thus, trends were compared using DDD/1000 patients attending pharmacies and per cent patients receiving an antibiotic class. The exact exposure of the population was captured by neither method, nor any of the three measures (DDDs/1000 population/month, DDDs/1000 patients, per cent patients receiving an antibiotic) of antibiotic use.

In this study some similarities of trends of antibiotic use were found in the community using bulk purchase data and exiting interviews, but also some differences particularly with regard to peak consumption of fluoroquinolones, possibly due to distortions in the market. Since bulk purchase data may not accurately reflect patient purchase, different from consumption observed by exit interview and did require data collection effort by the research team (not being collected by the retailers themselves), exit interviews may be a more accurate and sustainable method for surveillance. In theory, DDDs, which take into account dosage and duration, are a more accurate measure of exposure to antibiotics than % patients receiving an antibiotic. In the exit patient interviews, both measures were used and showed virtually the same patterns of use over time. Collection of data on dosage and duration requires more effort and is more subject to error than only collecting data on whether a patient receives an antibiotic or not. In this study it would seem that measurement of % patients receiving a class of antibiotics may be an easier more sustainable measure to use for long-term surveillance.

Both the methods identified a growing peak of antibiotic consumption in the months of February and March. This may be related to the change in season leading to more infections. Many reasons cited for antimicrobial overuse or misuse include defensive
prescribing, perceived or real pressure from patients and parents, inadequate knowledge of the proper indications, fee-for-service reimbursement. Some of the reasons might be contributing the overuse of antibiotics, particularly during the period of peak use, but an in-depth study would be required to confirm.

In conclusion, our study has shown that both the methodologies - bulk purchase data and exit interviews showed high use of antibiotics in the community, particularly fluoroquinolones. Since the collection of bulk purchase data relied on the prolonged goodwill of retailers, it might not be complete, and would not save time in terms of data collection. The exit patient interviews allowed the collection of additional information on patient perception, knowledge and prescribing behaviour, which may be useful to develop interventions to change behaviour.

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References