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# DRUG UTILIZATION STUDY IN INDOOR ADULT ORGANOPHOSPHORUS POISONING PATIENTS AT A TERTIARY CARE HOSPITAL IN CENTRAL INDIA

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**ABSTRACT**

**Background:** Organophosphorous poisoning is a common medical emergency. Due to few drug utilization studies on OP poisoning this study was carried out to evaluate the consumption pattern of commonly used drugs, according to PDD, DDD/100 bed days and PDD/DDD ratio in patients treated for organophosphorus poisoning.
**Material and Methods:** A prospective observational study was carried out in a tertiary care hospital over four months period from May to August 2018. Data was analysed using SPSS Software version 16.
**Result:** Total 64 organophosphorus poisoning cases were recorded, out of which 37(57.81 %) were males whereas females were 27(42.18%). The majority of cases were from 21-30 years age group followed by 31-40 years age group. Most of the cases 53 (82.82%) were from rural areas. PDD/DDD ratio values for Atropine and Cefotaxime were >1 suggesting overdosing of antidotes and antimicrobials in our MICU and medicine wards.
**Conclusion:** OPP is an important health concern where issues of antibiotic misuse and overuse are practiced.ATC/DDD system is a tool for presenting drug utilization research in order to improve quality of drug use and is recommended by WHO as international standard for drug utilization studies. Therefore, resident doctors and interns should be given appropriate knowledge of ATC/DDD system for rational use of drugs. Improved adherence to infection control practices, optimum utilisation of laboratory tests and antimicrobial stewardship programmes are very essential to curb resistance and improve health benefit in OPP.

## INTRODUCTION:

In India the majority of the population is employed in agriculture. Due to more uses of pesticides and agrochemical products, organophosphorous poisoning is more common according to Ramesha, K. N., Rao, K. B., & Kumar, G. S., (2009) study. [1]

Consumption pattern of drugs in any set up can be known by carrying out drug utilization research which is defined as the "marketing, distribution, prescription and use of drugs in a society with special emphasis on resulting medical, social and economic consequences".[2] It help us to evaluate the pattern of drug use and early detection of irrational drug prescriptions. As there is no enough information available, rational discussion about the desirable level of consumption is hindered. The fundamental measurement of consumption should be made available to clinicians, policy makersand researchers so that it would be easier for them to detect variation in consumption of drug use annually in health care system The Anatomical Therapeutic Chemical classification (ATC) / Defined Daily Dose (DDD) system is a tool for presenting drug utilization research in order to improve quality of drug use and is recommended by the WHO as the international standard for drug utilization studies.**[2]** The Norwegian Medicinal Depot initiated the ATC system in the year 1970, and is now co-ordinated by the WHO Collaborating Centre for Drug Statistics Methodology, established in Oslo in 1982. Drugs are divided in different groups based on organ or system on which they act and their therapeutic and chemical characteristics. Each drug is assigned at least one ATC code, which are classified into groups at five different levels. (Hutchinson, J. M., Patrick, D. M., Marra, F., Ng, H., Bowie, W. R., Heule, L., & Monnet, D. L., 2004) [3].

The DDD is an artificially and arbitrarily created statistical measurement used for research purposes when comparing the utilization of drugs. The formal definition of the DDD is 'the *assumed* average maintenance dose per day for a drug used for its main indication in adults.' DDD are assigned only to drugs that have already been provided with an ATC code.

The DDD methodology was developed in response to the need for converting and harmonizing readily available volume data (bulk costs and prescriptions) from supply statistics of pharmacy inventory data into medically meaningful units; it allows us to make crude estimates of the number of persons exposed to a particular drug or class of drugs [4–6].

In view of limited data on drug utilization study in OP Poisoning in indoor patients, we proposed to study the consumption pattern of commonly used drugs in this condition of tertiary care teaching hospital in Central India.

## MATERIAL AND METHODS:

A prospective observational study was conducted, after permission from the institutional ethics committee (Letter No./ GMCA/ EC/ Patho/ 451A/ 2018 Dated 21-05-2018) in the Medical ICU and wards of 540 bedded tertiary care teaching hospital. Indoor case papers of the organophosphorous poisoning diagnosed patients admitted in the ICU and medicine wards were studied. Total 64 patients were enrolled in the study. The study was carried out for a period of four months (May 2018 to August 2018)

**Inclusion criteria:**

1. Patients ≥ 18 years age.
2. Patients willing to give written consent.
3. Patients diagnosed by the clinician as organophos phorous poisoning

**Exclusion criteria:**

1. Patients < 18 years age.
2. Critically ill patients.
3. Patients discharged against medical advice.

Following parameters were collected in predesigned format: age, sex, residence, average duration of treatment. Detailed information on drug schedule including name of drugs, dose, frequency and duration of treatment was recorded from patient's case records. Data was entered in Microsoft excel and descriptive statistics was applied and was analysed in the department of Pharmacology. Drugs were classified according to the anatomical therapeutic classification (ATC) system based on their chemical, pharmacological and therapeutic properties. The drug consumption was measured using parameters such as DDD/100 bed-days, PDD and PDD / DDD ratio.

DDD/100 bed days were calculated using the following equation:

$$\text{DDD/100 bed days} = \frac{\text{Total dose in mg during study period x 100}}{\text{DDD of drug x study duration (days) x bed strength x Average bed occupancy rate}}$$

The number of DDD/100 bed days is utilized to analyse the consumption variation in the prescribed drugs.

$$\text{Average bed occupancy rate} = \frac{\text{Total in patient service days for a period x 100}}{\text{Total in patient bed count x number of days in the period}}$$

PDD is the average daily amount of a drug that is actually prescribed.

$$\text{PDD} = \frac{\text{Total Amount of Drug Prescribed}}{\text{Number of Days the Drug was prescribed}}$$

The PDD to DDD ratio was then calculated. Antibiotic use was calculated in percentage and as well as in DDD/100 bed days unit.[7]

**Drug usage in DDDs was calculated by the formula:**

$$\text{Drug usage (in DDDs)} = \frac{\text{Items issued x Amount of Drug per Item}}{\text{DDD}}$$

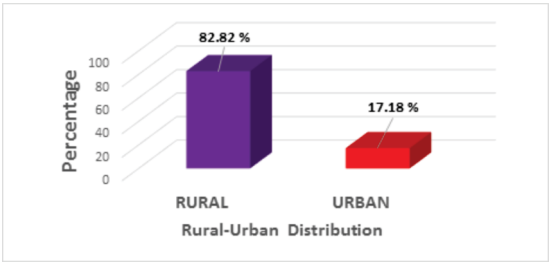
**RESULTS:**

**Table No.1 Distribution of demographic pattern:**

| Sex | Number Of Cases | Percentage |
|---|---|---|
| Male | 37 | 57.81 |
| Female | 27 | 42.18 |
| Total | 64 | 100 |
| **Age Group ( In Years )** | **Number Of Cases** | **Percentage** |
| < 20 | 10 | 15.62 % |
| 21-30 | 24 | 37.50 % |
| 31-40 | 16 | 25 % |
| 41-50 | 5 | 7.81 % |
| 51-60 | 6 | 9.37 % |
| 61-70 | 3 | 4.68 % |
| **Total** | 64 | 100 % |

A total of 64 patients diagnosed with organophosphate poisoning were enrolled in the study. Out of 64 OP poisoning cases 37(57.82 %) were male whereas females were27(42.18%). Maximum number of patients were 37.50 % in the age group of 21-30 years followed by 25 % in age group 31- 40, 15.62 % in age group of < 20, whereas minimum were in age group of 61-70(4.68 %). (Table No. 1)

**Figure 1. Rural-urban distribution of cases**




Most of the cases of OP poisoning were from rural areas 53 (82.82%) followed by 11(17.18%) from urban areas. (Figure 1)

**Table No.2: Commonly utilised drugs, their ATC code and DDD/100 bed days in OP poisoning.**

| Sr. No. | Drugs | ATC code | PDD (mg) | WHO DDD | PDD/ DDD Ratio | PDD/ DDD Ratio | DDD / 100 bed-days |
|---|---|---|---|---|---|---|---|
| 1 | Atropine | A03BA01 | 28.53 | 1.5 mg(P) | 19.02 | > 1 | 0.13 |
| 2 | Cefotaxime | J01DD01 | 6517.6 | 4 gm(P) | 1.63 | > 1 | 0.01 |
| 3 | Ranitidine | A02BA02 | 325.9 | 0.3gm(P) | 1.08 | > 1 | 0.01 |
| 4 | Ciprofloxacin | J01MA02 | 800 | 0.8gm(P) | 1 | 1 | 0.0004 |
| 5 | Paracetamol | N02BE01 | 600 | 3gm(P) | 0.2 | < 1 | 0.00006 |
| 6 | Ondansetron | A04AA01 | 8 | 16 mg(P) | 0.5 | < 1 | 0.0002 |
| 7 | Haloperidol | N05AD01 | 5 | 8 mg(P) | 0.6 | < 1 | 0.0002 |
| 8 | Calcium Gluconate | A12AA03 | 100 | 3 gm(P) | 0.03 | < 1 | 0.00002 |
| 9 | Hydrocortisone | H02AB | 200 | 30 mg(P) | 6.66 | > 1 | 0.002 |
| 10 | Lasix | C03CA01 | 80 | 40 mg(P) | 2 | > 1 | 0.0006 |
| 11 | Vitamin K | B02BA01 | 10 | 20 mg(P) | 0.5 | < 1 | 0.0002 |
| 12 | Thiamine | A11DA01 | 100 | 50 mg(P) | 2 | > 1 | 0.0013 |
| 13 | Magnesium Sulphate | A06AD04 | 500 | 7 gm(P) | 0.07 | < 1 | 0.000022 |
| 14 | Ursodeoxycholic Acid | A05AA02 | 600 | 0.75gm(O) | 0.8 | < 1 | 0.0025 |

P= Parenteral; O= Oral
< 1 - Under Dose, > 1 - Over Dose, = 1 – Adequate Dose
ATC- Anatomical Therapeutic Chemical classification system,

PDD- prescribed daily dose, DDD- defined daily dose
Utilization pattern of various drugs including DDD / 100 bed days, PDD, DDD, PDD/DDD ratio has been summarised as in Table 2.

PDD gives the average daily amount of drug that is actually prescribed. The ratio of PDD to DDD was calculated. It is used to indicate adequacy of dosing. The ratio of more than one (>1) suggest overdosing, less than one (<1) suggests under dosing and equal to 1 (=1) suggest adequate dosing ( Lahon K, Shetty HM, Paramel A, Sharma G , 2011).[8]

Table No. 2 shows values of PDD/DDD ratio >1 for Atropine, Cefotaxime, Ranitidine, Hydrocortisone, Lasix and Thiamine suggesting overdosing of these drugs in our MICU and medicine wards. For Ciprofloxacin the ratio is 1 suggesting adequate dosing. PDD/DDD ratio is <1 for Paracetamol,

Ondensetron, Haloperidol, Calcium Gluconate, Vitamin K, Magnesium Sulphate, Ursodeoxycholic acid.

**Table No. 3: Distribution of class of drugs prescribed**

| Sr. No. | Drugs | Number of patients | Percentage |
|---|---|---|---|
| 1 | (Antidote) Atropine | 61 | 22.67 |
| 2 | (Antidote) Pralidoxime | 61 | 22.67 |
| 3 | Antimicrobials | 64 | 23.79 |
| 4 | H2 Blockers | 59 | 21.95 |
| 5 | Antiemetic | 01 | 0.37 |
| 6 | Others | 23 | 8.55 |
| | Total | 269 | 100 |

In this study maximum number 64 (23.79 %) of cases received drugs from antimicrobial class followed by Atropine and Pralidoxime (antidotes) 61 (21.67 %) each whereas minimum number 01 (0.37 %) of cases received drugs from antiemetic class of drug as shown in Table No.3

**Table No. 4. Frequency of Antimicrobial Prescription**

| Sr. No. | Frequency of Antimicrobial Prescription | No. of patients | Percentage |
|---|---|---|---|
| 1 | Single | 59 | 92.18 |
| 2 | Multiple | 05 | 07.82 |
| **Total** | | 64 | 100 |

In this study single antimicrobial treatment was maximum 59 (92.18%) of prescriptions and rest were with multiple antibiotics i.e. 5 (7.82%) is shown in Table No.4.

**Table No. 5. Route of Administration of drug**

| Sr.No. | Drug | Route of Administration | Number of Patients | Percentage |
|---|---|---|---|---|
| **1** | Cefotaxime | IV | 59 | 92.18 |
| **2** | Ciprofloxacin | IV | 01 | 1.56 |
| **3** | Metronidazole | IV | 02 | 3.13 |
| **4** | Pipzo | IV | 02 | 3.13 |
| **Total** | | | 64 | 100 |

The route of administration of antimicrobials was intravenous for 100% and oral for 0 % cases as shown in Table No.5.

**Table No.6. Comparative drug consumption in DDDs of some drugs**

| Name of Drug | Drug consumption (in DDDs) | | | | Total |
|---|---|---|---|---|---|
| | May | June | July | August | |
| **Atropine** | 165 | 661 | 549 | 240 | 1615 |
| **Cefotaxime** | 75 | 520 | 540 | 250 | 1385 |
| **Ranitidine** | 5 | 35 | 36 | 17 | 93 |

Total consumption of Atropine was 1615 DDDs , 1385 DDDs of Cefotaxime and 93 DDDs of Ranitidine. Usage of Atropine in terms of DDDs was highest in the month of June (661 DDDs). Use of Cefotaxime was highest in the month of July (540 DDDs) and that of Ranitidine was highest in the month of July (36 DDDs) Table no. 6.

## DISCUSSION

This study addresses one of the common but important clinical problems in developing nations and the lacunae in management guidelines. OP Poisoning either in the form of self poisoning or accidental consumption requiring intensive care in the hospital is an important concern in developing nations.

In Emergency Departments of hospitals arrival of Poisoning cases are very common in India. The research shows that per month on an average 38 cases are reported and this is due to occupational exposures mainly ones involved in agriculture, easy availability of toxic agents and no awareness particularly in rural areas ( Singh NP, Kaur G., 2012) [9]

In this study, a male predominance 57.82% was observed which shows similar pattern by other studies in India by Mittal, N., Shafiq, N., Bhalla, A., Pandhi, P., & Malhotra, S. (2013)[10] , Gupta, P., Kumar, A., Singh, S. P., Prakash, M., Gupta, M., & Kumar, P. (2016)[11] and Ramesh, V., Chavan, V. R., Arshad, M., & Raghunandan, M. (2016) study.[12]

In our study we found that young adults (21-30 years) are more prone to poisoning. Bari M. S., Chakraborty S. R., Alam M. M. J., Qayyum J. A., Hassan N., & Chowdhury F. R. (2014) also found that adolescents and young adults were more prone to poisoning due to economical stress, work pressure after marriage quarrel with family, and other life settlement issues.[13]

In this study, the most common poisoning agents were pesticides. Maharani B., & Vijayakumari N. (2013) study similarly reported pesticides as the most common poisoning agent in Tamil Nadu, Southern India.[14]

We found that the systemic prophylactic antibiotic was used in all patients with OPP. While there is lack of substantial evidence to recommend the use of prophylactic antibiotics in these patients, we propose the urgent need to study the prescription practices among intensivists in resource limited nations. An antibiotic resistance poses a serious threat to humans and subverts global economy. It is unaccountable that high usage of antibiotics exists in a poisoning ward. Various clinical trials did not prove any benefit of antibiotic therapy for acute poisonings especially in organophosphate poisoning (Priyendu A., Vandana K. E., Varma M., Prabhu N., Rahim A. A., & Nagappa A. N. (2017).[15]

In this study 59 (92.18%) cases were prescribed single antimicrobial while multiple antimicrobials were prescribed in 5 (7.82%) cases; whereas in Suraj R., Gopinath R., Rajakannan T., Mohanta G. P., & Kuruvilla A. (2008) study 49.82 % cases were prescribed Single antimicrobial.[16]. The route of administration of antimicrobials was intravenous for 100% and oral for 0 % of the prescriptions whereas 43% was the intravenous route of administration and 57% was oral route of administration of antimicrobials in R. Suraj et al.'s (2008) study.[16].In this study the empirical use of Cefotaxime IV in maximum no. of patients (92.18%) in tertiary care and not following antibiotic stewardship programme is not cost effective and institutional antibiotic policy to be strictly followed. Number of encounters with parenteral Cefotaxime was higher (92.18%) in this study which seems inevitable to achieve immediate drug action in treatment of poisoning cases. To reduce the consumption of the antibiotics in OP Poisoning restricted parenteral antibiotics usage policy should be followed ( Tiwari S. A., Ghongane B. B., Daswani B. R., & Dabhade S. S. (2017).[17]

In this study, average no. of drugs per prescription were 4.4 which is higher than the WHO reference value of 1.6–1.8. Different studies in India observed higher values of average drugs per prescription e.g. 3.6 by Mittal, N., Mittal, R., Singh, I., Shafiq, N., & Malhotra, S. (2014).[18] and 13.54 by Patel M.K., Barvaliya M.J., Patel T.K., and Tripathi C.B., (2013) [19]

However use of multiple drugs in ICU setting especially to treat OP Poisoning is inevitable and thus cannot be considered irrational polypharmacy. In this study of 4 months duration total consumption of Atropine was 1615 DDDs, followed by 1385 DDDs of Cefotaxime and 93 DDDs of Ranitidine. However, Atropine consumption was found to be 661 DDDs in month of June, as there were maximum cases of OP Poisoning in this month.

Drug utilization studies with ATC /DDD metric system to further comment on consumption pattern of drugs used in O P poisoning in this geographical region is need of the hour.

## LIMITATIONS:

It was a single centered study having a narrow regional focus. Ideally a multicenteric study including various geographical regions would provide more concrete evidence in this area. Further research with larger sample size should be taken up in this field to establish guidelines regarding the use of antibiotics in OPP cases.

## CONCLUSION:

OPP is an important public health concern in monsoon season where issues of antibiotic misuse and overuse are practiced. In the present study younger age males with rural background involved in agricultural work were found to be more prone for organ ophosphorous poisoning.

The empirical use of antibiotics in poisoning patients can be addressed by availability of culture sensitivity test and strictly following institutional antibiotic policy if available and optimum utilization of laboratory tests. Regular training should be imparted in ATC /DDD methodology among interns and resident doctors to rationalise the prescribing behaviour of doctors working in public health hospital.

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