

Specially designed prescription form in duplicate were supplied to the prescribers. Each prescriber at general practice and primary health care levels was instructed to retain the duplicate after handing over the filled-in original to the patient. The investigator collected the duplicates from the prescriber at the end of the study period. The duplicates at St. John's Medical College Hospital were collected from the hospital pharmacy where all the hospital prescriptions are usually presented by patients for purchase.

At St. John's Medical College Hospital, four general disciplines [Medicine, Surgery, Paediatrics and Obstetrics and Gynecology (OBG)] and five speciality disciplines (Psychiatry, Dermatology, Orthopaedics, ENT and Ophthalmology) were chosen. Two prescribers in each of these specialities were supplied with 25 special prescription forms per person per day over a 10 day-period. The prescribers at the primary and urban general practice levels were supplied with a total of 100 prescription forms each.

The data on the duplicate prescription forms was stored on a computer database file with the following fields of entry for each form : patient identifying number, age and sex (patient information); drug (generic) name (drug information). Drugs were classified according to the ATC index (10) which was modified to facilitate data analysis. A customized software was developed to tabulate and analyze data. The number of drugs on each prescription provided the incidence of polypharmacy. Frequency of prescribing of individual drugs was analyzed in three categories, chosen because of common use, viz., nonsteroidal anti-inflammatory drugs (NSAIDs), antibacterial agents and drugs used in acid peptic disease (APD drugs).

The chi-square statistic was used to analyse the data.

RESULTS

The study sample included 1222 prescriptions for 2639 drugs, 296 prescriptions for 590 drugs and 292 prescriptions for 703

drugs from tertiary, primary and urban general practice levels respectively.

The proportion of drugs per prescription showed a significant difference across the three levels of health care (Table I). At the tertiary and primary levels, most prescriptions listed 1 or 2 drugs while at the general practice level most prescriptions listed 2 or 3 drugs. Only at the tertiary level was there any significant extent of prescriptions for 4 or more drugs.

TABLE I : Incidence of polypharmacy*.

Level of health care	Primary (n=296)	Tertiary (n=1222)	General practice (n=292)
No. of drugs per prescription			
1	68	405	33
2	169	437	130
3	52	229	108
4 or > 4	7	105	19
Mean \pm SD =	1.99 \pm 0.71	2.16 \pm 1.15	2.41 \pm 0.8

* $X^2 = 137$, $df = 6$, $P < 0.0001$

The frequency of prescribing of various drug groups is shown in Table II. Analysis of prescribing frequency of the four most frequently prescribed drug groups showed that the general practice level had a significantly high frequency of prescription of antibacterials ($X^2=91$, $df=2$, $P<0.0001$), NSAIDs ($X^2=90.09$, $df=2$, $P<0.0001$) and respiratory drugs ($X^2=8.882$, $df=2$, $P=0.01$). Prescribing frequency of vitamins and mineral supplements was significantly low at the general practice level ($X^2=6.66$, $df=2$, $P=0.04$). The relative proportions of prescribing frequency of these 4 drug groups, viz., NSAIDs, antibacterials, vitamins and respiratory drugs, also significantly differed among the three levels of health care ($X^2=59.83$, $df=6$, $P<0.0001$). The tertiary level prescribed vitamins and mineral supplements most, while the other two levels prescribed antibacterials most.

In NSAID, APD-drugs and antibacterial drug groups, the frequency of prescription of

TABLE II : Frequency of prescribing - Drug groups.

Level of health care	Primary	Tertiary	General practice
	(n=1222)	(n=296)	(n=292)
Drug groups	No. of prescriptions (percentage)		
Antibacterials	264 (21.60)	106 (36.30)	140 (47.30)
NSAIDs	245 (20.05)	102 (34.93)	133 (44.93)
Vitamins, mineral supp., etc.	296 (24.22)	77 (26.37)	52 (17.57)
Respiratory drugs & antihist.	214 (17.51)	43 (14.73)	69 (23.31)
Dermatologicals	158 (12.93)	27 (9.25)	15 (5.07)
GIT drugs (other)	54 (4.42)	19 (6.51)	40 (13.51)
Antiprotozoals	22 (1.80)	19 (6.51)	6 (2.03)
APD drugs	89 (7.28)	15 (5.14)	26 (8.78)
Gynaecologicals	41 (3.36)	15 (5.14)	11 (3.72)
Anti-anaemic agents	61 (4.99)	13 (4.45)	37 (12.50)
Antihelmintics	26 (2.13)	10 (3.43)	10 (3.38)
Antiasthmatics	109 (8.92)	10 (3.43)	16 (5.41)
CVS drugs	97 (7.94)	10 (3.43)	4 (1.35)
Vaccines	26 (2.13)	9 (3.08)	4 (1.35)
Urologicals	2 (0.16)	7 (2.40)	1 (0.34)
Ophthalmologicals & otologicals	46 (3.76)	6 (2.06)	1 (0.34)
Steroids for systemic use	67 (4.99)	3 (1.03)	1 (0.34)
Psycholeptic & psychoanaleptics	125 (10.23)	2 (0.69)	5 (1.69)
Others	82 (6.71)	4 (1.37)	1 (0.34)

"n" represents the total number of prescriptions and not of individual drugs or drug groups.

individual drugs which are commonly used and hence chosen for detailed analysis is shown in Table III. Statistical analysis of the two most frequently prescribed drugs in each category showed that the general practice level had a significantly high prescribing frequency of aminopenicillins (amoxycillin and ampicillin; $X^2=73.49$, $df=2$, $P<0.0001$) and ibuprofen ($X^2=26.2$, $df=2$, $P<0.0001$). Only in case of sulfonamides (sulfadiazine and co-trimoxazole) was the prescribing frequency significantly high at the primary health care level ($X^2=25.49$, $df=2$, $P<0.0001$).

An analysis of the relative proportions of the two drugs most prescribed from each group across the three levels showed that the proportionate prescribing frequency at the

general practice level of aminopenicillins to sulfonamides was significantly high ($3:1$, $X^2=14.79$, $df=2$, $P=0.0006$) and of paracetamol to ibuprofen also likewise significantly high ($2:1$, $X^2=7.78$, $df=2$, $P=0.002$).

TABLE III : Frequency of prescribing - individual drugs.

Level of health care	Primary	Tertiary	General practice
	(n=1222)	(n=296)	(n=292)
Drug groups	No. of prescriptions (percentage)		
Antibacterials			
Aminopenicillins	64 (05.24)	29 (09.8)	62 (21.00)
Sulphonamides	59 (04.83)	38 (13.00)	19 (06.42)
Pepicillin procaine	2 (00.16)	10 (03.42)	-
Cephalexin	25 (02.05)	2 (00.68)	14 (04.73)
Doxycycline	27 (09.25)	1 (00.34)	10 (03.44)
Erythromycin	21 (01.72)	1 (00.34)	4 (01.37)
Anti-TB drugs	34 (02.78)	-	-
APD drugs			
Antacids	56 (04.58)	14 (04.79)	18 (06.08)
Ranitidine	38 (03.11)	9 (03.08)	12 (03.05)
NSAIDs			
Ibuprofen	61 (04.99)	30 (10.27)	37 (12.50)
Paracetamol	55 (04.50)	22 (07.53)	63 (21.28)
Diclofenac	62 (05.07)	14 (04.79)	5 (01.71)
Piroxicam	22 (01.80)	1 (00.34)	1 (00.34)
Analgin	2 (00.68)	23 (07.88)	7 (02.40)
Imol (Ibuprofen + Paracetamol)	19 (01.56)	12 (04.11)	15 (05.14)
Robinaxol (Paracetamol + Methacarbamol)	24 (01.96)	-	-

"n" represents the total number of prescriptions and not of individual drugs or drug groups.

DISCUSSION

Incidence of polypharmacy: Average number of drugs per prescription (in a prescription audit) is an important index of the scope for review and educational intervention in prescribing practices. A community-based study on prescribing pattern conducted from retail outlets in India reported a mean number of 2 drugs per prescription (5), similar to our figures at the tertiary and primary levels. Hospital-based studies in India reported figures of 3-5 drugs per prescription (4). Bapna et al (7), in their

study of 2953 prescriptions at the primary health care level in Southern India, found that, on an average, each patient received 2.71 drugs. Our study showed a high proportion of 2- & 3-drug prescriptions as well as the highest mean number of drugs per prescription at the general practice level. While it may be practically difficult to keep the number of drugs per prescription to below two, practitioners ought to have good reasons to prescribe 3 or more drugs simultaneously because polypharmacy increases the risk of drug interactions, errors of prescribing and non-compliance.

Frequency of prescribing: If standard operating procedures such as ATC-DDD methodology (11) are employed by all researchers in drug utilization, results of prescription audit could be meaningfully compared. As suggested by Gaitonde (12) and later Hede et al (5) this study has attempted to compare prescribing pattern at different levels of our health care delivery system.

Drug group-wise, the most frequently prescribed drugs follow almost the same pattern as reported by other (4-7). The general practice and primary health care levels prescribed antibacterials most frequently, but, the choice of individual antibacterials most used at these levels (ampicillin, amoxycillin, sulfadiazine and co-trimoxazole) was justifiable as empirical first-line antibacterials prescribed in out-patient practice.

Individual drug-wise, our finding of sulfonamides as the most frequently prescribed among all antimicrobials at the primary health care level agrees with that of Bapna et al (7).

Obviously, the primary health care prescribing was dictated, and rightly so, by the availability of resources.

Since the most frequently prescribed groups of drugs followed almost the same pattern at all three levels of health care included in this study, it can be concluded that the broad morbidity pattern was also similar at all three levels.

Surprisingly, analgin and its combinations continue to be prescribed (tertiary 0.7%, primary 8% and general practice 2.4%), in spite of its toxic effects such as agranulocytosis, shock and cardiovascular reactions. It was declared a dangerous and irrational drug by the Drug Consultative Committee in 1980 (13).

The present study may serve as a pilot run to future researches in prescription audit with specific objectives at different settings. It is accepted that prescribers could have shown bias in selecting patients for use of the special prescription forms. Regrettably, this was a bias over which no control was feasible. Enough hypotheses on inappropriate prescribing could be generated and tested further on the basis of the results reported and used for educational interventions to improve prescribing pattern.

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Abstract: This study was undertaken to evaluate the level of glyoxysomes and malic acid in rat liver (R-2-ethylhexyl phosphate (DEHP)) in the diet for 24 weeks. Protein-bound hexose, hexosamine and malic acid were measured in plasma and liver of rats treated with DEHP, whereas the glyoxysome distribution was a reduction following DEHP administration. Evaluation of glyoxysomes as a marker of the carcinogenic process, it is suggested that enhanced malic acid in membrane components observed in the present study may be related to the carcinogenic potential of DEHP.

Key words: DEHP-ethylhexyl phosphate, glyoxysomes, malic acid, protein-bound hexose

INTRODUCTION

Many properties of mammalian cells are mediated through the cell surface. Glycoproteins and malic acid, major constituents of cell membrane which play an important role in maintaining the integrity of cell membrane show variations during neoplastic transformation (1). Mammalian glycoproteins are responsible for cell recognition and various immunological processes like autoimmune diseases and cancer. Malic acid, a membrane constituent involved in cell contact phenomena, growth control and cellular invasiveness has been demonstrated to be increased at the surface of cancer cells in humans (2).

Phenolic esters such as di (2-ethylhexyl) phthalate (DEHP) are extensively used as plasticizers in the manufacture of polymeric materials. DEHP has been demonstrated to induce neoplastic proliferation and hepatocellular carcinomas in rodents (3). Reddy and Lalwani (4) proposed an increase in the synthesis of H₂O₂ generating peroxisomal oxidation system which causes prolonged metabolic oxidative stress and initiation of genetic neoplasia.

Glyoxysomes are known to cause profound alterations in the cell membrane. Although hepatic effects of DEHP have been extensively documented, studies on DEHP-induced changes in cell surface components in rodents and glyoxysomes in particular are limited. Previous studies from this laboratory have shown morphological changes and alterations in membrane associated enzymes and components in rats following chronic DEHP administration (5, 6). This preliminary report evaluates levels of protein bound hexose, hexosamine and malic acid in liver, plasma and erythrocyte membrane of rats following DEHP administration.

METHODS

Wistar male rats weighing 100-120g were housed in polypropylene cages in a temperature and humidity controlled environment with a 12-h light/dark cycle. Standard pellets were obtained from M/s. Nestle Feed Ltd, Mysore. The animals had free access to food and water. Rats were fed 2% DEHP in the diet for 24 weeks and sex matched animals were used as controls. Biochemical assays: Blood was collected in heparinized tubes. The plasma was separated