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## **Editorial**

I am happy to share with you the 10<sup>th</sup> issue of International Journal of Community Pharmacy (IJCP). International Journal of Community Pharmacy (IJCP) is now one of the online indexed journals. IJCP is now officially indexed in Budapest Open Access Initiative and Directory of Open Access Journals. Hence we are happy that our journal will be accessed and will reach globally to professionals across the world.

Further, I am happy to announce that QIP program and Summer school training programs are coming up at Manipal College of pharmaceutical sciences in the month of June, 2011, which will be of great help to fellow pharmacist, faculties and students to keep them updated with the latest developments in our field. Details regarding the workshop are available at [www.manipal.edu](http://www.manipal.edu) website, also a news letter attached along with this issue.

**Regards**

**Prof N Udupa**

**Editor In Chief, IJCP**

## MESSAGE FROM ACPI

Dear Friends,

The health care has become critical in terms of quality, clinical outcomes and as well humanistic outcome. The patients demand for quality services is universal and is considered as patient right to know all the details regarding the health care services he is paying for it. The complexity, high costs and poor patient satisfaction has compelled the evaluations of quality of treatments and patient safety. The patient or the co payers of treatments are demanding the justification and optimization of money spent on health care. The future of treatments decisions will be largely based on pharmacoeconomics and out come research. There is no way that decisions in health care require evidence and as well justifications for every rupee spent on health care. Being aware of the changing scenario, The ISPOR has begin encouraging all health care professionals to evaluate all the treatments and outcomes so that the complexity of treatments becomes some what clear and appropriate decision can be taken. It is becoming increasingly pivotal to evaluate the pharmacy services and understand the areas of lacunae and lapses so that one can implement the correct approach and modernize the decisions. There is need for all of us look and evaluate the cost of therapies and how the patients outcomes regarding services of community pharmacy. The ACPI executive committee has successfully started in getting sanction of ISPOR Manipal chapter. Lot of things are expected from ISPOR Manipal and ACPI

Prof Anantha Naik Nagappa,

President,

ACPI

**National workshop on**

**“Community Pharmacist & Patient Health Care: An  
International Perspective”**

**To be held at Manipal on 11<sup>th</sup> June 2011**

**Venue**

**Manipal College of Pharmaceutical Sciences, Manipal  
University, Karnataka, India**

**Eligibility**

**Pharmacy teaching faculty, research Scholars and PG  
students of AICTE approved institutions**

**Registration fee Rs 300 only**

**No TA/DA will be provided to participants attending national  
workshop. However free accommodation at hostel and working  
lunch will be provided to registered participants**

**Registration form**

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# IDENTIFYING THE AGE AND DRUG USE PATTERN THROUGH PRESCRIPTION AUDIT AND SERVICES IN A COMMUNITY PHARMACY OF RURAL SET UP

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## Abstract:

The community (retail) pharmacy sector is the prime source of medicines for both ambulatory and hospitalized patients (minimum stock in many hospitals). The medicines manufactured by pharmaceutical companies are made available to the community pharmacy. Prescriptions are those which contain the medicines written by physicians or health care professionals, directing the pharmacist to dispense the medicines towards the prescription. **Aim:** The main aim of the study is to know the commonly used drugs among the different age groups and services given by the community pharmacist to the patients of rural population. **Methodology:** An observational study was carried out in a community pharmacy; a total number of 651 prescriptions were collected and evaluated. Anti diabetics (20.53%), antacids (13.77%) and anti-hypertensive's (13.7%) were the most commonly used drugs followed by NSIADS (12.85%). **Results and conclusion:** Drug use among males (52%) was found to be high, age group 66-75 prone to high use of medicines followed by 41-65 age groups. The services provided by the community pharmacy were found to be low and need to be trained and implementation of pharmaceutical care plan enhances the better patient care.

**Key words:** Pharmaceutical care, Post graduate students, Community pharmacy services

## Introduction:

The prescription of drugs is one of the most important factors in the rising costs of health services in both developed and developing countries.<sup>1</sup> According to a frequently quoted article on drug use<sup>2</sup>, the populations aged 65 years and older, who represent 12.4% of the population in the United States, take 31% of all prescription drugs. In Israel, a study that estimated the relative part of different age groups in the utilization of healthcare services found that the population 65 and over utilized 30% of the total expenditure on health of the health insurance funds.<sup>3</sup> In addition to the traditional manufacturing and dispensing of medicines, community pharmacy is expected to deliver value through these enhanced services (such as medication review) which stretch the boundaries of what community pharmacy has offered in the past.

Pharmaceutical care provides a more formalized relationship between the pharmacist and the patient and healthcare provider with the explicit purpose of improving patient outcomes. This increased engagement in the medication use process requires pharmacists to undertake the assessment and evaluation of medication regimens, monitor regimens to ensure desired outcomes are attained, counsel to ensure medications are being used optimally, communicate with healthcare providers, and document care.<sup>4</sup> Private pharmacies are often the first and only source of health care for a majority of patients in developing countries.<sup>5</sup>

Numerous studies have described the patterns and trends of drug utilization of the community-dwelling elderly population in the INDIA. To the best of our knowledge there were no studies on drug use pattern in a community pharmacy set up of this rural population.

### Materials and Methods:

Planning and preparation: Randomly a community pharmacy was selected for the study. Prior intimation of the study and permission from the community pharmacist was taken.

Conducting the audit:

Two post graduate students were involved in the audit process, where the data was collected from the patients who come in to the pharmacy with prescriptions for medicines.

Collecting and evaluating the audit data: One day complete audit was made and data was recorded and evaluated for age and drug use pattern.

Study design: This was a community pharmacy based observational study conducted in the month of 14 of March 2010. The variables studied were age, gender, number of Prescriptions, drug use pattern.

Study Population: A total of 651 prescriptions were analyzed.

### Results:

Table 1 shows the age wise pattern of which age group 66-75 constitutes maximum drug use and age group 41-65 constitutes the next highest use. The number of drugs per prescription shown in table 2 ranged from 1-6 drugs where 24.27% of prescriptions with single drug followed by 23.5% of prescriptions with 4 drugs. The pattern of prescription of drugs is shown in table 3 where the antidiabetics, antihypertensive and antacids were the most commonly prescribed drugs followed by NSAIDS. Out of 1198 drugs prescribed in 651 prescriptions males (52%) dominated the drug use than females (47.99%).

Table 1: Age wise pattern

Sl.No	Age.	Number of prescriptions.
1.	0-4	28
2.	5-10	24
3.	11-15	52
4.	16-40	76
5.	41-65	201
6.	66-75	225
7.	>76	45
Total number of prescription		651

Table 2: Number of Drugs per Patient

Number Of drugs per prescription	Number Of prescriptions	
	No	%
1	158	24.27
2	120	18.43
3	146	22.42
4	153	23.50
5	36	5.52
6	38	5.83
Total	651	

It is not uncommon for a person to have multiple prescriptions for different conditions, without any single prescriber knowing the entire set of drugs being used. Therefore, healthcare providers are not alerted to look for, and do not recognize signs of misuse or abuse. Often the elderly, their families, and their service providers are uninformed about the Potential for misuse and abuse of prescription drugs. This includes awareness of problems associated with taking multiple drugs and their potential interactions.

Table 3 Pattern of Drugs Prescribed in Prescriptions

Sl.No	Drug group	Total number of Prescriptions	Percentage (%)	Number Of Prescriptions	
				Males	Females
1	Antibiotics	38	3.17	25	13
2	NSAIDS	154	12.85	75	79
3	Antihistaminic	54	4.50	26	28
4	Antiasthmatics	87	7.26	30	57
5	Anthelmintics	12	1.00	8	4
6	Antitussives, Expectorants	54	4.50	36	18
7	Haematoincs	45	3.75	18	27
8	Topical preparations	32	2.67	12	20
9	Anti Diabetics	246	20.53	140	106
10	Anti hypertensive	159	13.7	94	65
11	Anti fertility agents	45	3.75	-	45
12	Anti convulsants	65	5.42	41	24
13	Antacids	165	13.77	87	78
14	Others	42	3.50	31	11
Total		1198		623(52%)	575(47.99)

### Discussion:

The number of drugs prescribed per patient(2.85) was comparable with the findings of the studies from C.M.C Vellore(2.4) and pune(2.8).<sup>6,7</sup> However in the study reported by A.B.Guvon et al<sup>8</sup> from Bangladesh, the mean number of drugs prescribed per patient was only 1.477. In the present study antidiabetics and anti hypertensive were the most commonly prescribed drugs followed by antacids, NSAIDS and antiasthmatics. A drug survey by krishnaswamy et al has listed nutritional products, sulfonamides, antibiotics, analgesics and anti-inflammatory drugs to be the most frequently prescribed drugs.<sup>8</sup>

In our study males (52%) were found to be the most commonly using drugs. This proportion was notably higher in age between 65-75, 41-65 and 16-40 where as in E. Fernandez-Liz et al<sup>6</sup> study females (51.15%) were most commonly used drugs followed by males and proportion was higher in 65–74, 75–84 and over 84 year age. The failure to register over-the-counter medication is also likely to mean that this study has underestimated the use of drugs available without prescription, particularly among women.<sup>9</sup> In addition, there is no information concerning how long the substance was used for, nor of the doses administered. Nevertheless, some of these limitations are common to other studies conducted in the General population.<sup>10, 11</sup> in practice, community pharmacists may be uniquely placed to help reduce the level of medication related morbidity in primary care by virtue of their accessibility and existing relationships.

**Conclusion:**

Despite many barriers, community pharmacy services are central to the safe and effective medicines management in advancing health. With rapidly occurring changes in the health care delivery and growing patient expectations, it is hoped that community pharmacy practice will change accordingly. The time spent on prescription handling was less and education regarding the drugs usage to the patients was comparatively low. If community pharmacy practice is to continue its evolution to patient-centered care, community pharmacist should be trained with regarding drug dose, route of administration, co-administration with other drugs, context of use, and expectations for better patient care.

**Acknowledgement:**

The authors are thank full to the community pharmacist of Bellur for giving opportunity for prescription auditing and also thank to the principal for his encouragement for the study.

**Future recommendations:**

Create awareness about the rational use of drugs and monitor the adverse drug reactions (PharmacoVigilance)

Training on rational drug use and pharmaceutical care plan

Establish drug information system

Conducting workshops and continuous education program

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Roe CM, McNamara AM, Motheral BR. Gender and age-related prescription drug use patterns. *Ann Pharmacotherapy* 2002; 36: 30-9.

# VITAMINS INDISPENSIBLE ELEMENTS: TODAY AND TOMORROW

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## Abstract

Nutritional deficiencies cause numerous conditions which affect the human organism and many of the lower species. This field of study has developed extensively during the last few decades, attaining great importance in the differential diagnosis and treatment of many conditions. Deficiency conditions, which were very difficult to treat a few years ago. These are now being successfully eliminated by the addition of the constituents namely vitamins, lacking in the diet of the individual. Each vitamin has specific jobs. Vitamin requirements differ according to dietary nutrient intake at each phase, and supplements must be tailored accordingly. In this article, we will review the nutritional uses, structures, dietary sources, human deficiency and toxicity of the various vitamins, as well as the potential roles of all vitamins in our life.

**Key words:** vitamins, deficiency, sources, toxicity, functions.

## Introduction:

Vitamins are accessory, indispensable food factors, non- energy producing organic compounds required as a nutrient in tiny amounts by an organism. In other words, an organic chemical compound (or related set of compounds) is called a vitamin when it cannot be synthesized in sufficient quantities by an organism, and must be obtained from the diet. There deficiency can result into diseased state<sup>1</sup>. The deficiency of various vitamins are shown by table no 2 and 3. Some have hormone-like functions as regulators of mineral metabolism (e.g., vitamin D), or regulators of cell and tissue growth and differentiation (e.g., some forms of vitamin A). Others function as antioxidants (e.g., vitamin E and sometimes vitamin C)<sup>1</sup>.

Classification of vitamins

They are classified as fat soluble (A, D, E, K) and water soluble (C and B group) vitamins as shown by figure no.1 and their structures are shown in figure no.2. The B-complex vitamins may be subdivided into energy releasing (B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, biotin etc.) and hematopoietic (folic acid and B<sub>12</sub>)<sup>2</sup>.

**Figure no.1: Classification of vitamins**

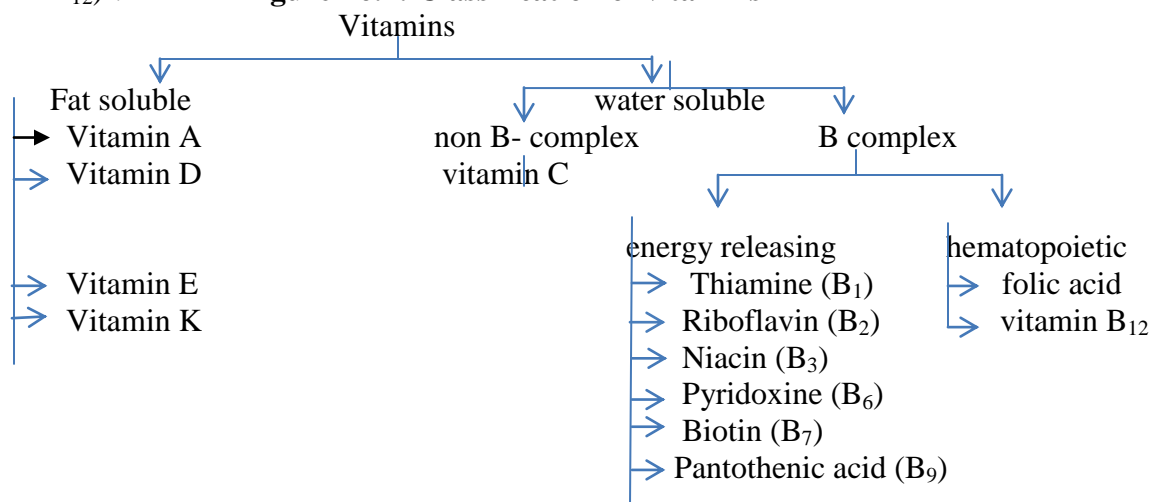
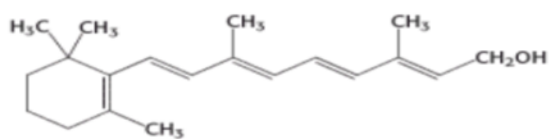


Table no. 2: Water soluble vitamins <sup>3</sup>

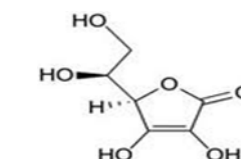
Vitamin	Consequences of deficiency
Thiamine (B <sub>1</sub> )	Beriberi (weight loss, heart problems, neurological dysfunction)
Riboflavin (B <sub>2</sub> )	Cheliosis and angular stomatitis (lesions of the mouth), dermatitis.
Pyridoxine (B <sub>6</sub> )	Depression, confusion, convulsions.
Nicotinic acid (niacin)	Pellagra (dermatitis, depression)
Pantothenic acid	Hypertension
Biotin	Rash about the eyebrows, muscle pain, fatigue (rare)
Folic acid	Anaemia
B <sub>12</sub>	Anaemia, pernicious anaemia
C (ascorbic acid)	Scurvy

Table no. 3: Fat soluble vitamins <sup>3</sup>

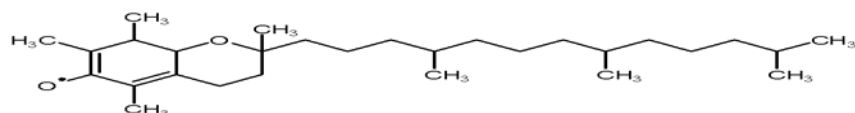
Vitamins	Function	Deficiency
A	Roles in vision, growth, reproduction	Night blindness, cornea damage, damage to respiratory and gastrointestinal tract
D	Regulation of calcium and phosphate metabolism	Rickets (children): skeletal deformities, impaired growth, Osteomalacia (adults): soft, bending bones
E	Antioxidant	Inhibition of sperm production; lesions in muscles and nerves (rare).
K	Blood coagulation	Subdermal haemorrhaging



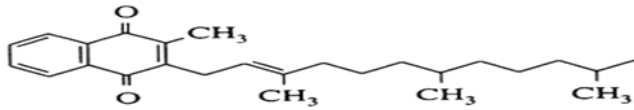
Vitamin A



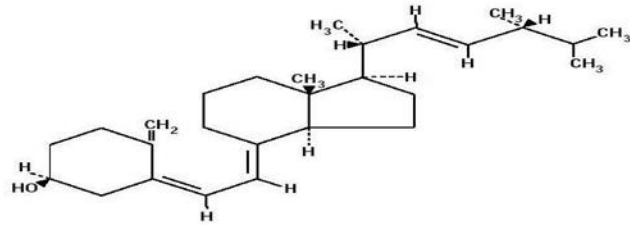
Vitamin C



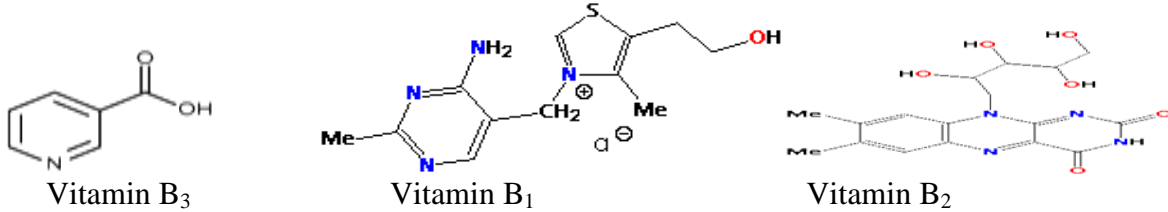
Vitamin E



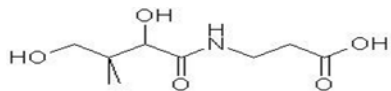
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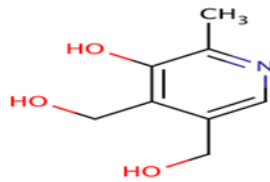
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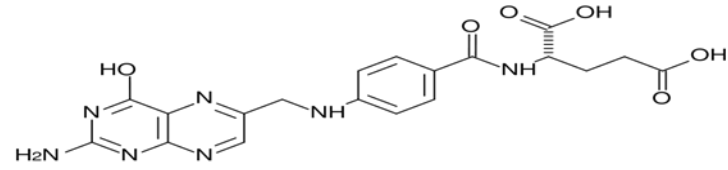
Vitamin B5



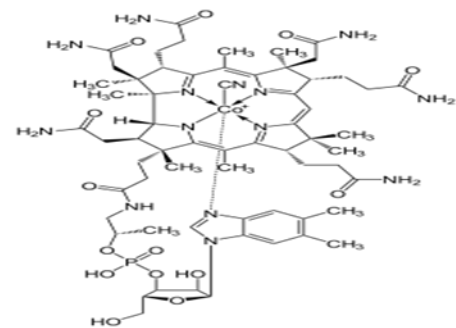
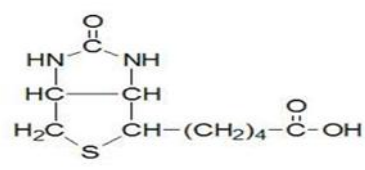
Vitamin B6



Vitamin B9



Biotin



Vitamin B<sub>12</sub>

Figure no 2: Structures of various vitamins

## **INDIVIDUAL VITAMINS:**

### **Vitamin A**

Vitamin A was the first fat-soluble vitamin to be discovered. A light yellow crystalline compound, vitamin A is also known as retinol, a name given in reference to the participation of this compound in the functions of the retina of the eye. Vitamin A has also been called the "anti-infective" vitamin due to its role in supporting the activities of the immune system.

### **Sources of Vitamin A**

Top sources of vitamin A include: Beef liver, Egg yolk, Cheddar cheese, Fortified milk

### **Functions**

While vitamin A is best known for its vital role in vision, this vitamin also participates in physiological activities related to the immune system, maintenance of epithelial and mucosal tissues, growth, reproduction, and bone development.

### **Other roles for vitamin A**

It is also known that vitamin A is essential for reproductive processes in both males and females and plays a role in normal bone metabolism. In addition, some of the most cutting-edge research in the field of genetics has been examining the role of vitamin A (in the form of retinoic acid) in regulating genetic events<sup>4,5</sup>.

### **Deficiency Symptoms**

Dietary deficiency of vitamin A is quite common in developing countries, and is associated with the high incidence of blindness, viral infections, and child mortality that occurs in impoverished populations. Vitamin A deficiency primarily affects the health of the skin, hair, eyes, and immune system, though loss of appetite, bone abnormalities, and growth retardation are also associated with inadequate intake of this vitamin. A tell-tale sign of vitamin A deficiency is hyperkeratosis, a goose bump-like appearance of the skin caused by excessive production of keratin (a protein found in skin) that blocks hair follicles.

Due to the important role of vitamin A in supporting the functions of the immune system, individuals with insufficient intake of this vitamin often experience increased susceptibility to viral infections, most notably measles, chicken pox, pneumonia, and respiratory syncytial virus (RSV).

Prolonged vitamin A deficiency can lead to night blindness, due to impaired production of rhodopsin, the compound in the retina responsible for detecting small amounts of light. Xerophthalmia, a condition characterized by changes to the conjunctiva and cornea of the eye, also results from prolonged vitamin A deficiency, and is a major cause of blindness in developing nations<sup>4</sup>.

Acute toxicity effects include headache, nausea, vomiting, drowsiness and destruction after 24 hours. Acute toxic dose – 25,000 international units. Chronic dose – 4000 international units every day for 6-15 months.

Chronic toxicity affects the skin in mucous membrane and musculoskeletal and neurologic systems. Skin and mucous membrane effects include erythema, eczema, pruritus, dry and scapped skin, conjunctivitis and alopecia. Musculoskeletal effects include pain and tenderness particularly in long bones of upper and lower extremities. Neurological effects include blurred vision and frontal headache. Findings also include hepatomegaly, ascites, erythematous dermatitis. Recent studies suggest that elevated levels of vitamin A may cause increased bone resorption and promote development of osteoporosis<sup>5</sup>.

## Vitamin E

Even though its name makes it sound like a single substance, vitamin E is actually a family of fat-soluble vitamins that are active throughout the body. Some members of the vitamin E family are called tocopherols. These members include alpha tocopherol, beta tocopherol, gamma tocopherol, and delta tocopherol<sup>6</sup>. Other members of the vitamin E family are called tocotrienols. These members include alpha, beta, gamma, and delta tocotrienol.

### Functions

Vitamin E acts as a powerful antioxidant by neutralizing free radicals in the body that cause tissue and cellular damage. Vitamin E also contributes to a healthy circulatory system and aids in proper blood clotting and improves wound healing. Other studies have shown that taking large doses of Vitamin E has decreased the risk of Coronary Artery Disease (CAD).

### Deficiency symptoms

Deficiency symptoms for vitamin E are difficult to pinpoint and controversial in the research literature. The area of broadest agreement involves malabsorption. In many research studies, low levels of vitamin E are associated with digestive system problems where nutrients are poorly absorbed from the digestive tract. These problems include pancreatic disease, gallbladder disease, liver disease, and celiac disease<sup>7</sup>. A second area of focus for vitamin E deficiency symptoms is called peripheral neuropathy. This area focuses on nervous system problems in the arms, hands, legs, and feet. Pain, tingling, and loss of sensation in these extremities have been associated with vitamin E deficiency. Although many healthcare practitioners report that skin problems appear closely linked to vitamin E deficiency, there are limited human research studies to support this view.

### Foods sources

Excellent sources of vitamin E include mustard greens, turnip greens, chard, and sunflower seeds, almonds, spinach, collard greens, parsley, kale, papaya, olives, bell pepper, brussels sprouts, kiwifruit, tomato, blueberries, and broccoli<sup>8</sup>.

## Vitamin K

Vitamin K is not a single chemical substance but rather a family of chemically related substances that go by the general name of "vitamin K." Over the past 20 years, no vitamin family has undergone a greater change in terms of our scientific understanding of its chemistry and function. In the past, members of the vitamin K family have traditionally been referred to as vitamin K1, vitamin K2, and vitamin K3. This terminology is largely being replaced by a different set of terms to describe what has now been determined to be a more complicated set of vitamin K compounds.

### Functions

Vitamin K is necessary for blood clotting. Without it, even a small cut would cause continuous bleeding in the body. Vitamin K also plays an important role in kidney function and bone growth and repair - some studies have even shown that it may help prevent osteoporosis<sup>9</sup>.

### Deficiency Symptoms

Persons deficient in vitamin K are first and foremost likely to have symptoms related to problematic blood clotting or bleeding. These symptoms can include heavy menstrual bleeding, gum bleeding, bleeding within the digestive tract, nose bleeding, easy bruising, blood in the urine, prolonged clotting times, haemorrhaging, and anaemia. A second set of vitamin K deficiency-related symptoms involves bone problems. These symptoms can include loss of bone (osteopenia), decrease in bone mineral density (osteoporosis), and fractures-including common

age-related fractures like that of the hips. Yet another set of vitamin K deficiency-related symptoms involves excess deposition of calcium in soft tissues. These calcification-based problems include hardening of the arteries or calcium-related problems with heart valve function<sup>10</sup>.

#### Foods sources

Excellent sources of vitamin K include: spinach, Brussels sprouts, Swiss chard, green beans, asparagus, broccoli, kale and mustard greens.

#### Toxicity

This particular toxicity is typically associated with formula pain in infants or those receiving vitamin K-3 (menadiol) injections. Because of its toxicity, menadiol is no longer used for the treatment of deficiency of vitamin K. effects may include jaundice in newborn<sup>11</sup>.

#### Vitamin D

Vitamin D is important in helping the body absorb and use calcium from food and supplements. It aids in bone and tooth formation and supports muscle and nerve function, and studies have shown that vitamin D helps to prevent osteoporosis<sup>12</sup>.

#### Functions

The hormonal functions of vitamin D include regulation of bone health, regulation of muscle health (including both skeletal and heart muscle), regulation of immune response, regulation of insulin and blood sugar, and regulation of calcium and phosphorus metabolism<sup>12</sup>.

#### Deficiency Symptoms

Bone pain, frequent bone fractures, and softening of the bones can all be symptoms of vitamin D deficiency. So can muscle aches and muscle weakness since vitamin D helps to regulate muscle composition and prevent too much fat accumulation alongside of muscle tissue. In this context, especially in older persons, frequent falls can point to deficiency of this vitamin. The key role of vitamin D in regulation of immune response means that lowered immunity can be a symptom of vitamin D deficiency, as can the presence of any autoimmune disorder. In older persons, cognitive problems (disturbances in thought processes) and depression can be symptomatic of vitamin D deficiency, and in children, stunted growth and severe asthma have also been shown to have vitamin D deficiency as potential causes<sup>13</sup>.

#### Foods sources

Excellent sources of vitamin D include salmon while very good sources include sardines, shrimp and vitamin-D fortified milk. Good food sources of vitamin D include cod and eggs.

#### Toxicity

Acute toxicity effects include nausea, headache, fatigue, bleeding. Inhibition of platelet aggregation, muscle weakness, keratin urea.

Chronic toxicity dose is more than 15,000 IU per day. effects include all of the above, suppression of other antioxidants and increase of the risk of haemorrhagic, stroke.

#### Vitamin C

Vitamin C also called ascorbic acid is a water-soluble nutrient that is easily excreted from the body when not needed. It's so critical to living creatures that almost all mammals can use their own cells to make it. Humans, gorillas, chimps, bats, guinea pigs and birds are some of the few animals that cannot make vitamin C inside of their own bodies<sup>14</sup>.

## Function

Vitamin C is required for the growth and repair of tissues in all parts of your body. It is necessary to form collagen, an important protein used to make skin, scar tissue, tendons, ligaments, and blood vessels. Vitamin C is essential for the healing of wounds, and for the repair and maintenance of cartilage, bones, and teeth <sup>14</sup>. Vitamin C is one of many antioxidants.

## Deficiency symptoms

Full-blown symptoms of the vitamin C deficiency disease called scurvy - including bleeding gums and skin discoloration due to ruptured blood vessels - are rare in the U.S. Poor wound healing, however, is not rare, and can be a symptom of vitamin C deficiency. Weak immune function, including susceptibility to colds and other infections, can also be a telltale sign of vitamin C deficiency. Since the lining of our respiratory tract also depend heavily on vitamin C for protection, respiratory infection and other lung-related conditions can also be symptomatic of vitamin C deficiency <sup>15</sup>.

## Food Sources

Excellent food sources of vitamin C include broccoli, bell peppers, kale, cauliflower, strawberries, lemons, mustard and turnip greens, brussels sprouts, papaya, chard, cabbage, spinach, kiwifruit, snow peas, cantaloupe, oranges, grapefruit, limes, tomatoes, zucchini, raspberries, asparagus, celery, pineapples, lettuce, watermelon, fennel, peppermint and parsley.

## Toxicity

Chronic toxic dose- more than 2mg per day. Acute toxic dose has not been determined.

Chronic toxic effects may be renal colic, diarrhoea, nausea, rebound scurvy in infants. Haemolysis, if G-6Pd deficiency present is possible. Other effects like dental decalcification and increased oestrogen levels. Findings may include rectal bleeding.

## Vitamin B<sub>1</sub> (thiamine)

Vitamin B<sub>1</sub>, also known as thiamine, helps fuel your body by converting blood sugar into energy. It keeps your mucous membranes healthy and is essential for nervous system, cardiovascular and muscular function.

## Deficiency

A lack of it can cause beriberi, a condition that involves confusion, muscle wasting, nerve problems and a rapid heartbeat. It's usually only seen in the United States in babies who are fed formula that isn't supplemented with Vitamin B1 or in people who drink large amounts of alcohol. People who drink heavily should talk to their doctors about how to quit drinking and whether they need vitamin B1 supplements <sup>16</sup>.

## Food sources

The best sources of Vitamin B1 are yeasts and liver. Pork, Whole-grain cereals, Rye and whole-wheat flour, Wheat germ, Navy beans and kidney beans.

## Vitamin B<sub>2</sub> (riboflavin)

Vitamin B<sub>2</sub>, also called riboflavin, works with other vitamins in the B complex to process calories from carbohydrates, protein and fat. Your body needs it for growth and red cell production, and adequate riboflavin intake promotes healthy skin and good vision <sup>17</sup>.

## Food sources

Riboflavin-enriched breads and cereals, Green, leafy vegetables and Dairy products.

## Toxicity

Vitamin B<sub>2</sub> turns the urine yellow orange. Vitamin B toxicity effects include tachycardia, hypotension, cardiac dysrhythmia, vasodilatation, weakness, convulsions, anaphylaxis. Acute toxicity is rare<sup>17</sup>.

#### Vitamin B<sub>3</sub> (niacin)

Vitamin B<sub>3</sub> is also called niacin. Like all the B-complex vitamins, it is important for converting calories from protein, fat and carbohydrates into energy. But it also helps the digestive system function and promotes a normal appetite and healthy skin and nerves.

#### Deficiency

The first signs of a vitamin B<sub>3</sub> deficiency are muscular weakness, inability to eat, and indigestion and skin problems. In its worst form, a deficiency results in pellagra, this is a serious disease with symptoms such as diarrhoea, mental confusion and skin problems<sup>18</sup>.

#### Food sources

Meat, poultry, fish, Peanuts, Yeasts, Milk and eggs contain small amounts, but are excellent sources of tryptophan.

#### Toxicity

Acute toxicity effects are prostaglandin mediated and include flushing, pruritus, wheezing, vasodilatation, headache, diarrhoea and vomiting. Chronic effects include jaundice and abnormally liver function tests.

#### Vitamin B<sub>5</sub> (Pantothenic acid)

The body uses pantothenic acid, also known as vitamin B<sub>5</sub>, to break down carbohydrates, proteins and fats for energy. Some claims have been made that pantothenic acid is effective for treatment of nerve damage, breathing problems, itching and other skin problems, but these claims have not been proven in clinical trials<sup>19</sup>.

#### Deficiency

Lack of pantothenic acid in the diet is rare, so there is no recommended daily intake for this vitamin. Often, pantothenic acid is included in B-complex multivitamins. Normal daily intake of pantothenic acid for adults is 4 to 7 milligrams<sup>19</sup>.

#### Food sources

Peas and beans (except green beans), Lean meat, poultry, fish, Whole-grain cereals etc.

#### Vitamin B<sub>6</sub> (pyridoxine)

Vitamin B<sub>6</sub>, also known as pyridoxine, helps brain function and helps the body convert protein to energy. Some research has shown that vitamin B<sub>6</sub> works with folic acid and B<sub>12</sub> to reduce levels of homocysteine (an amino acid) in the blood. Elevated homocysteine levels can increase a person's risk of heart attack<sup>20</sup>.

#### Food sources

Poultry, Pork, Fish, Eggs, Soybeans, Oats, Wholegrains, Bananas, Nuts and seeds.

#### Toxicity

Chronic effects include tachyphoea (high rate of breathing) and sensory neuropathies, such as burning pains, ataxia, clumpiness, paralysis. Findings range from normal CNS functions to progressive sensory ataxia, profound impairment of position and vibration sense and diminished tendon reflexes<sup>21</sup>.

### Vitamin B<sub>9</sub> (folic acid)

Folic acid, also known as folate, is important for the production and maintenance of new cells. This is especially necessary during both pregnancy and infancy when cell growth is extremely rapid<sup>22</sup>. Both adults and children need folic acid to make normal red blood cells and to prevent anaemia.

Having enough folic acid in early pregnancy can prevent birth defects, including problems with the spine (neural tube defects) and brain. Women who become pregnant and don't consume enough folate are also more likely to have babies who have low birth weight or are premature.

#### Deficiency

Folate deficiency can cause diarrhoea, anaemia, loss of appetite, weight loss, sore tongue and a variety of other symptoms. In a developing foetus, folic acid deficiency may cause birth defects<sup>23</sup>. People who drink large amounts of alcohol may need extra folic acid to prevent a deficiency. Sometimes, treatment of anaemia with folic acid will mask an anaemia caused by a vitamin B<sub>2</sub> deficiency. Always consult with your doctor before taking a large amount of any vitamin supplement<sup>23</sup>.

#### Food sources

Leafy greens such as spinach and turnip greens, Broccoli, Asparagus, Mushrooms, Liver, Dry beans and peas, Fortified cereals and grain products, Fortified juices.

### Biotin

Biotin is necessary for the formation of fatty acids and glucose, which are used as fuels by the body. Biotin also helps to break down amino acids and carbohydrates in the body<sup>24</sup>.

#### Food sources

Liver, Cauliflower, Salmon, Carrots, Bananas, Cereals and Yeast.

#### Deficiency

A lack of biotin in the body is rare, but certain skin conditions or genetic deficiencies may cause biotin deficiencies in infants. Biotin deficiency may cause skin rash, hair loss, high cholesterol levels and heart problems<sup>25</sup>.

### Vitamin B<sub>12</sub>

Vitamin B<sub>12</sub>, also called cobalamin, is a water soluble vitamin with a key role in the normal functioning of the brain and nervous system, and for the formation of blood. It is one of the eight B vitamins. It is normally involved in the metabolism of every cell of the human body, especially affecting DNA synthesis and regulation, but also fatty acid synthesis and energy production. As the largest and most structurally complicated vitamin, it can be produced industrially only through bacterial fermentation-synthesis<sup>26</sup>.

#### Functions

Vitamin B<sub>12</sub> is normally involved in the metabolism of every cell of the body, especially affecting the DNA synthesis and regulation but also fatty acid synthesis and energy production. However, many (though not all) of the effects of functions of B<sub>12</sub> can be replaced by sufficient quantities of folic acid (vitamin B<sub>9</sub>), since B<sub>12</sub> is used to regenerate folate in the body<sup>27</sup>.

#### Deficiency

Most vitamin B<sub>12</sub> deficiency symptoms are actually folate deficiency symptoms, since they include all the effects of pernicious anemia and megaloblastosis, which are due to poor synthesis of DNA when the body does not have a proper supply of folic acid for the production of thymine.

Food sources

Vitamin B<sub>12</sub> can be found in animal products, including fish, meat, poultry, eggs, milk, and milk products and fortified breakfast cereals.

### **Conclusion:**

The present review focused on all the therapeutic vitamins for which considerable knowledge and advances have been made concerning their roles. Among the essential factors present in the diet, we find a group of substances known as vitamins. These substances are very important for the tissues, as they are related to tissue respiration and other biologic processes. In the absence of some of these vitamins from the diet, deficiency states develop which show characteristic deformities in the oral tissues.

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Banerjee R. and Ragsdale S.W the many faces of vitamin B12: catalysis by cobalamin-dependent enzymes. *Annual review of biochemistry* 72: 209–47 (2003).

## A PROSPECTIVE STUDY ON THE PRESCRIBING PATTERN OF NSAIDS IN KOTTAYAM DISTRICT.

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### Abstract

**Objective:** The present prospective study was conducted in order to establish the prescribing trend of NSAIDs at three primary health centers of Kottayam Dist. Kerala. **Methods:** The study was done in July 2008. Data was collected from three different primary health centers. The prescription cards which included non-steroidal anti-inflammatory drugs (NSAIDs) for different disorders were monitored. WHO based prescription-auditing performa was used for data collection. **Results:** Demographic analysis of this prospective study revealed that use of NSAIDs was more prevalent in males (52.2%) than in females (47.8%). Pediatric patients in the age group 0-9 (70%). Most of the NSAIDs prescribed at primary health centers were individual and generic. Disease based analysis showed that NSAIDs were mostly prescribed for different types of pain (35.5% of the total NSAID prescribed). Patient care indicator analysis revealed certain lacunae in the prescribing habit. **Conclusion:** The present study represents the current prescribing trend of NSAIDs for different disorders and it also highlights certain shortcomings in prescribing and dispensing practice of newer NSAIDs. **Discussion:** A prescription based survey is considered to be one of the most effective methods to assess and evaluate the prescribing attitude of physician and dispensing practice of pharmacists. It is also important to consider the recommendations of different international bodies and audits to improve prescribing practice.

**Key words:** prescribing pattern, NSAIDs, prospective study

### Introduction

Painkillers are one of the commonly used drugs. Fever and pain is mostly associated with inflammatory diseases. The introduction of NSAIDs was a landmark event, and soon these drugs became the most widely used medication<sup>[1]</sup> not only for the relief of pain and fever but also for the anti-inflammatory effect.<sup>[2, 3]</sup> The NSAIDs which are available as 'over-the-counter' (OTC) drugs are one of the common cause of ADR reported to drug regulatory agencies as well as in many clinical and epidemiological studies<sup>[4,5]</sup>. Since there is no important difference among these drugs with regards to efficacy, the choice of NSAID treatment should be based on relative toxicity. Sporadic consumption of NSAIDs may subside the symptoms for time being, but the actual pathology may sometimes not only be hindered but may also be aggravated, complicate and eventually causes fatality. However, we do not have adequate information regarding the prescribing pattern of NSAIDs by the medical prescribers. The present study represents the current prescribing trends of NSAIDs.

### Methodology

**Setting:** Present prospective study was conducted at three Government Hospitals in Kottayam District, Kerala, after getting official consent from Medical Superintendent of each hospital. Data was collected in July 2008 with the help of a validated questionnaire and were analyzed to bring

out difference in NSAID prescribing pattern. The prospective study of prescribing pattern of NSAIDs was conducted in the following government hospitals in Kottayam district:

- 1) Taluk Headquarters Hospital, Kanjirapally
- 2) General Hospital, Palai
- 3) Taluk Headquarters Hospital, Pampady

These hospitals are located in the rural area and most of the patients visiting these hospitals were below poverty line. These are 500 bedded hospitals located at Kottayam district. At least 1000 patients visit the OPD daily.

#### Study Criteria:

##### Inclusion - exclusion criteria

The prescriptions were randomly collected from the OPD of these hospitals and prescription containing NSAIDs are selected. Eliminated prescriptions do not contain NSAIDs. Incomplete prescriptions were also excluded.

##### Source of data

Prescription from the OPD was collected and filled into a validated questionnaire.

##### Study Design

The study includes prescription survey of NSAID including patient details, past medical and medication history, present diagnosis etc. The demographic characteristics, drug related indicators and disease related indicators were also determined.

## Results

There is total number of 300 prescriptions, which were collected from 3 hospitals, and 47 of them are excluded as per exclusion criteria. The remaining 253 numbers were taken into account.

### 1) Demographic Analysis

(a) Demographic and clinical characteristics of 253 participating patients are shown in Table 1. Out of this 253 patients, 132 (52.2%) were male and 121 (47.8%) were female.

(b) Out 253 prescription, 70 were from the age group of 0-9 and this accounts for (27.66%) followed by 49 prescriptions (19.36%) for 50-59 age group, 41 prescriptions (16.20%) for 40-49, 23 prescriptions (9.09%) for 60-69, 22 prescriptions (8.69%) for 20-29, 20 prescriptions (7.9%) for 10-19, 15 prescriptions (5.92%) for 30-39 and 13 prescriptions (5.14%) for 80 and above.

### 2) Drug related indicators

A) Tablets are the most commonly prescribed dosage form, which accounts for 316 numbers, followed by 115 injections, 55 syrups and 10 ointments.

B) 253 prescriptions contain 1856 drugs, Out of which 496 (27.6%) were NSAIDs. Out of 496 NSAIDs, Paracetamol prescribed were 250 (50.4%), which includes 160 tablets, 48 injections and 42 syrups. Diclofenac prescribed were 95 (19.15%), which consists of 26 tablets, 59 injections and 10 ointments. The total number of Ibuprofen prescribed was 69 (13.91%), which consists of 58 tablets, 8 injections and 3 syrups. The total number of Mephenamic acid prescribed was 46 (9.27%), which consists of 36 tablets and 10 syrups. The total number of Naproxen prescribed were 11 (2.21%), in the form of tablets. Number of Nimesulide prescribed were 16 (3.22%) in tablet form and Aspirin prescribed were 9 (1.81%) in tablet form.

C) Out of 250 paracetamol prescribed, 227 were in the generic name and the rest in the trade name (calpol). Out of 95 diclofenac prescriptions 5 were in the trade name (voveran). Total numbers of prescriptions obtained for mephenamic acid is 46; out of this 20 were in the trade

name (meftal). 69 prescriptions were obtained for ibuprofen; out of this 9 were in the trade name (brufen).

D) Gastroprotective agents were given along with most of the NSAIDs. Out of the 253 prescriptions 154 contains gastroprotective agents, of which ranitidine constitutes about 135, 14 by omeprazole and 5 by rabeprazole.

E) Combination of NSAIDs can be seen in many of the prescriptions. Out of 253 prescriptions, 59 prescriptions were in combination of paracetamol and diclofenac. 8 prescriptions contain paracetamol and ibuprofen combination, 25 prescriptions contain paracetamol and mephenamic acid combination, 4 prescriptions contains paracetamol, diclofenac and naproxen combination and 8 contain paracetamol diclofenac and mephenamic acid combinations.

F) Out of 253 prescriptions 30 prescriptions contain vitamin B complex.

G) Out of 253 prescriptions, 72 prescriptions contain steroids. The most commonly prescribed steroid was Dexamethasone mainly for rheumatoid arthritis. Out of 72 prescriptions , 18 were prescribed for children, prednisolone is the commonly prescribed steroid for respiratory tract infection.

### 3) Disease related indicators

91 prescriptions of NSAIDs were for body pain, 87 prescriptions for fever, 40 prescriptions for headache, 14 prescriptions for arthritis, 12 prescriptions for dysmenorrhoea and 9 prescriptions for cardio vascular disorders.

Table 1. Gender distribution of patients undergoing NSAID treatment.

	Male N (%)	Female N (%)	Total Patients
Gender (%)	132 (52.2)	121 (47.8)	253

N=Number of patients

Table 2. Age groups in years

AGE GROUP	THQ Ppdy	THQ Kpally	GH Pala	Total
0-9	18	24	28	70 (27.66%)
10-19	4	4	12	20 (7.9%)
20-29	10	7	5	22 (8.69%)
30-39	6	3	6	15 (5.92%)
40-49	14	21	6	41 (16.20%)
50-59	22	15	12	49 (19.36%)
60-69	10	7	6	23 (9.09%)
Above 70	4	3	6	13 (5.14%)
Total	88	84	81	253

Table 3. Prescribing characteristics of different dosage forms of NSAIDs

DOSAGE FORMS	THQ Ppdy	THQ Kpally	GH Pala	Total
Tablets	98	140	78	316
Injections	82	17	16	115
Syrups	12	23	20	55
Ointments	4	6	-	10
Total	196	186	114	496

Table 4. Prescribing characteristics of different NSAIDs in different hospitals.

Drugs	THQ Ppdy			THQ Kpally			GH Pala			TOTAL
	T	I	O	T	I	O	T	I	O	
Paracetamol	50	24	8	65	12	14	45	12	20	250
Diclofenac	20	50	4	50	-	3	6	4	-	95
Ibuprofen	8	8	-	50	-	3	-	-	-	69
Mephenamic acid	8	-	4	10	-	6	18	-	-	46
Naproxen	6			3			2			11
Nimesulide	4			8			4			16
Aspirin	2			4			3			9
Total NSAIDS prescribed	196			186			114			496

T-Tablet, I-injection, O-Oral.

Table 5. Prescribing characteristics of different NSAIDs generic/trade name

Generic name	Trade name	Number of drugs in trade name	Number of drugs in Generic name	Total number of drugs prescribed
Paracetamol	Calpol	23	227	250
Diclofenac	Voveran	5	90	95
Mephenamic acid	Meftal	20	26	46
Ibuprofen	Brufen	9	60	69

Table 6. Prescribing characteristics of different NSAIDs with gastroprotective agents.

Gastroprotective agents	Number of prescriptions with gastro protective agents
Ranitidine	135
Omeprazole	14
Rabeprazole	5

Table 7. Prescribing characteristics of different NSAIDs in combination

Combinations	No. of prescriptions
paracetamol + diclofenac	59
paracetamol + ibuprofen	8
paracetamol +mephenamic acid	25
Paracetamol+diclofenac +naproxen	3
Paracetamol+ diclofenac + mephenamic acid.	8
Paracetamol +naproxen	12

Table 8. Prescribing characteristics of NSAIDs in combination with Steroids among different age groups

Age Category	Steroids
Pediatric	54
Adult	18

Table 9. Disease based analysis of the use of different NSAIDs

DISEASE	THQ Ppdy	THQ Kpally	GH Pala	Total
Body pain	32	27	32	91
Headache	14	16	10	40
Fever	30	26	31	87
Arthritis	6	5	3	14
Dysmenorrhoea	4	6	2	12
CVD	2	4	3	9
Total	88	84	81	253

### Discussion:

On the basis of prospective and observational study it was found that use of NSAIDs was more prevalent in Male (52.2 %) than in females (47.8%). Most of the patient who were prescribed with NSAIDs were in the age group of 0-9 (27.66%) followed by those in the age group of 50-59 (19.66%). The socioeconomic data shows that most of the patients lie below poverty line.

The disease based analysis of the data showed that maximum prescription having NSAIDs were those of body pain (35.98%) followed by fever (34.38%). The DU 90% has not been widely used as a tool of measuring qualitative and quantitative drug consumption of India. Despite certain limitations, this methodology has proved to be simple, inexpensive, rational, understandable and

easy to use. It provides useful information on the drug use pattern and could be widely used as a basis for preparing prescription guidelines<sup>[6]</sup>. It could also generally serve as a tool for monitoring adherence to evidence based recommendations. This is an important indicator for assessing the quality of drug prescribing. This is now being tested in primary health care and at hospital clinics in several places and in different countries <sup>[5]</sup>. The DU 90% segment has also been applied to look at, to what extent the evidence of relative toxicity with different drugs was implemented. In the present study Nimesulide, Paracetamol, Diclofenac, Ibuprofen makes the DU -90% segment.

On the basis of serious gastrointestinal complications and non-aspirin NSAIDs published between 1990 and 1999 researchers came up with the ranking of high risk (ketoprofen, piroxicam) and low risk (indomethacin, Diclofenac) NSAIDs <sup>[1,2,3]</sup>. Most of the NSAIDs prescribed at primary health centers of kottayam Dist. were in low risk group and the NSAIDs accounting for high risk does not make to DU 90%. Although it is quite clear that newer drugs, selective COX-2 inhibitors (Rofecoxib, Celecoxib) in the market are safer than traditional NSAIDs<sup>[1,6]</sup>, on account of their gastric tolerability, but these drugs because of their non-availability at the dispensing counter and high cost are not prescribed generally. Nimesulide prescribed is comparatively less (0.06%) and that too is only for 2 or 3 days. Moreover that, out 253 prescriptions 154 contains the gastro protective agents like Ranitidine, Rabeprazole, Omeprazole. 30 prescriptions contains vitamins. All these shows that the physicians are well aware of the adverse reactions related to the chronic use of NSAIDs and Nimesulide.

An another interesting prescribing pattern we have seen is, out of 250 paracetamol prescriptions 227 were in generic name, 90 out of 95 diclofenac prescriptions were in generic name 60 out 69 ibuprofen were in generic name . These also indicate that the physicians are not biased. A combination of NSAIDs was given in 59 prescriptions out of 253(23%).This also shows the physicians are not biased.

### **Conclusion:-**

On the basis of the present study there is still a considerable scope of improvement in the prescribing pattern such as under utilization of newer NSAIDs. It is also important to consider the recommendations of different international bodies and audits to improve prescribing practice of physician and dispensing habits of pharmacist and ultimately overall clinical standards. A continuous supervision is required through such kinds of systematic audit that provide feedback from the physician and help to promote rational use of drugs <sup>[11]</sup>. The present prospective study conducted at three primary health centre of Kottayam Dist., Kerala, was aimed to monitor the prescribing trends for conventional NSAIDs used in different disorders.

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## UNDERSTANDING AND IMPROVING PATIENT COMPLIANCE

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### Abstract

If true tragedy lies in the failure to achieve that which can be achieved, then non-compliance is a tragic flaw in our efforts to reap the benefits of treatments that work when they are taken. Despite wide recognition and documentation of its existence, patient non-compliance to prescribed medication regimens continues to be a prevalent problem. The purpose of this review is to examine the factors affecting compliance, forms, strategies intended to improve patient compliance with prescribed medications including compliance aids and to comment on these in light of the progress of knowledge and the future needs for research on this important topic. The pace of compliance research has slowed in the last few years but much work remains to be done.

**Keywords:** Patient, compliance, regimen, treatment.

### Introduction:

Low patient compliance with prescribed regimens is a distressingly common problem that sharply limits the success of medical care and undermines the execution and validity of clinical trials. Just as the practitioner must be aware of and deal with this problem in his or her practice, the clinical researcher must take compliance into account in the design, execution, and analysis of clinical trials<sup>1</sup>. Furthermore, the practitioner must be able to anticipate the influence of compliance on the outcome of clinical research if he or she is to interpret reports of therapeutic trials correctly. Medication compliance is defined as the extent to which a patient takes the medications as prescribed. There are multiple studies in the literature that report non-compliance rates of 30% to 50% or higher based on the class of agents and populations studies. When medication was to be taken over a long period, compliance rates dropped dramatically to approximately 50% for either prevention or cure. It can be defined as adherence to prescriber's instructions by the patient<sup>2</sup>.

Compliance can be calculated as follows:

$$\% \text{ compliance} = \frac{\text{NPD} - \text{NME}}{\text{NPD}} * 100$$

Where, NPD: no. of prescribed doses.

NME: no. of medication errors.

Factors affecting patient compliance<sup>3</sup>:

Route of administration: if the route of drug administration is painful or the patient finds any difficulty in swallowing some dosage form. So non-compliance is generally observed. Therefore the route of drug administration should be changed.

Type of therapy: chances of non-compliance are more in long term therapy and in multi-drug therapy. Patient may forget to take the medicine regularly or in time as prescribed.

Forgetfulness: if the frequency of administration is more, patients generally show non-compliance, because of forgetfulness.

Cost: as many expensive medicines are not in stock in various hospitals, some patients generally belonging to the lower economic strata may not buy such medicines and show non-compliance. It becomes an important factor for non-compliance, as a large section of Indian population is poor.

Poor instructions: since patients is generally anxious of his illness, he is therefore not in a proper position to receive the information that is being imparted by the physician. Physician and pharmacist should hence use simple language for compliance of therapy.

Side effects: as no drug is without side effects, patient may discontinue the treatment when nausea, vomiting, GI upset etc. are observed.

Poor standards of labelling: the labels on medication containers must be clear and specific, for eg. 'Take as required' or 'uses as directed' are not specific and clear instructions. Poor handwritten labels with bad handwriting are a major source of medication error.

Inappropriate packing: many elderly patients have difficulty in opening the container, especially if the size is too small or the cap is difficult to twist. The blister pack may be too rigid or the glass bottle may be fragile making handling difficult.

Complex therapeutic regimen: the degree of non-compliance is directly related to the complexity of the therapy. Patients that usually take 25-30 different drugs at varying time intervals during the day. Such dosage regimens are difficult to memorize and result in non-compliance

Nature of medication: preparations with an unpleasant taste colour or odour leads to non-compliance particularly in children. As large tablets are difficult to swallow, small tablets may give trouble because they are difficult to handle and identify. Liquid oral formulations may cause difficulty in transportation.

Forms of non-compliance

If we speak of non-compliance in the general sense, it means not taking a medication or treatment as directed by the treating clinician. This treatment failure can take at least four different forms: (1) failure to take the medication; (2) excessive medicating; (3) improper dose timing; and (4) taking the incorrect medication for the right reason or vice versa<sup>4</sup>.

Failure to take the medication includes missing doses or cessation of treatment altogether. Excessive medicating often happens because patients are not explicitly told to take a single drop and they adopt the 'more is better' strategy. This can also include those patients with poor instillation techniques who waste drops in an effort to get a dose in the eye. Improper timing of doses often happens because patients are not aware of the duration of their medication and instil drops when it is most convenient. This is especially prevalent with those medications requiring more frequent instillation. A study using an electronic medication monitor showed that patients tended to skip their noon dose and to space the other doses close together, apparently to make it easier to remember these doses. The last form of non-compliance mentioned above could include patients using their glaucoma medications to treat their red, itchy eyes or using up a bottle of gentamicin from a previous infection to treat their glaucoma before paying for their next prescription refill<sup>5</sup>.

Reasons for non-compliance

There are many reasons for non-compliance as shown in table no 1-4. Some are obvious while others are harder to grasp. It is important to realize that there is almost always a reason, legitimate or otherwise, for non-compliance and it is the doctor's duty to try to ascertain this reason and address it. Possible reasons for non-compliance:

1. Side effects.
2. Cost.

3. Increased frequency of doses.
4. Having multiple medical conditions.
5. Sex.
6. Increasing age.
7. Time in waiting room.
8. Poor patient understanding of severity of disease, goal of treatment, dosing, instillation technique.
9. Inconvenience<sup>6</sup>.

Difficulties encountered with the patient-physician relationship<sup>7</sup>

Patients misunderstand the clinician's instructions.

The treatment strategy selected is not explained sufficiently.

The realistic expected rate of improvement and potential treatment outcomes are not effectively conveyed to patients.

Treatment-related issues

Patients misunderstand the side-effects of treatment.

Patients misinterpret the risks and benefits of treatment.

Treatment regimen and instructions are too difficult to follow.

Patients forget to apply the medication.

Patients find that the therapy is intolerable.

Patients find that the cost of therapy is prohibitive.

Patients have difficulties storing the medication properly.

The medication has an unpleasant odour.

Lack of resources, related to the cost of medicines

Fear pertaining to side effects, safety, and efficacy

General anxiety of long-term illness.

Previous experiences and failure to recognize patterns of illness

Forgetting to take their medicines

Lack of understanding of their disease or medication

Differing educational and social levels; lack of family support

Lack of continuity of care and/or patients missing appointments

Use of alternative remedies

Size and/or number of pills per day, difficulty in swallowing pills, and dosing regimen

Poor communication/inadequate supervision

Religion, culture, and customs.

Table 1.Reasons for Noncompliance: Poor Physician–Patient Communication (Time, Quality, Rapport)<sup>8</sup>

Why does this occur?	How can this be improved?	Clinical practise and resource requirements
<p>-Post graduate education of physicians, especially communication skills.</p> <p>-Lack of integrated multidisciplinary teams, resulting in lack of continuity and poor information.</p> <p>-Use of medical jargon by health professionals.</p> <p>-Lack of time for clinicians to explain all the relevant information to patients.</p>	<p>-Establishment of multidisciplinary teams incorporating high quality patient information and care plans</p> <p>-Incorporating interpersonal skills into postgraduate education.</p> <p>-Investment of increased multidisciplinary time with newly diagnosed patients</p> <p>-Continuity of healthcare provider- building on previous consultation</p>	<p>-Physician communication- warmth, empathy, unconditional regard, trust.</p> <p>-Easily accessible, tailored patient information.</p> <p>-Manage clinic templates to allow longer consultations with patients who need more time.</p> <p>-Separate clinics for newly diagnosed, relapsing and routine follow up patients.</p>

Table 2.Reasons for Noncompliance: Fear—Side Effects, Safety, and Efficacy

Why does this occur?	How this can be improved?	Clinical practise and resource requirements
<p>-Patient misconceptions, eg. Equating increased frequency/ dosing to higher frequency of side effects.</p> <p>-Fear of adding to pre-existing symptoms with drug side effects.</p> <p>-Unclear communication about medicine- nature of prophylaxis</p>	<p>-Use of clear, balanced information about drugs, indications, effects and side effects.</p> <p>-Simplify wording on the package insert.</p> <p>-Anticipate patient fears, eg. Pregnancy, rectal preparations.</p> <p>-Better use of pharmacists.</p>	<p>-Clear information leaflets.</p> <p>-Simplified package insert.</p> <p>-Well-reasoned discussions relating to benefit- versus-safety concerns.</p>

Table 3.Reasons for Noncompliance: Size and Number of Tablets, Dosing Frequency

Why does this occur?	How can this be improved?	Clinical practise and resource requirements
-Large numbers of tablets. -Too frequent administration. -Large tablets. -Inconvenient, impractical administration, eg. enemas	-Minimum number of tablet/day. -Reduced dosing frequency. -Smaller tablets. -Alternative preparations.	-Patient participation in choice of preparation and administration. -More patient- friendly formulations. -Training to administer topical therapy.

Table 4.Reasons for Noncompliance: Patient in Remission, Feeling Well

Why does this occur?	How can this be improved?	Clinical practice and resource requirements
-Poor education about relapsing/ remitting nature of disease and value of prophylaxis. -Patients unaware of long – term therapy -Medication costs; patients stop treatment to save money, especially when drug costs are high.	-Better patient education; reduced relapse rates, possible reduction in colorectal cancer rates. -Positive reinforcement of link between remission and treatment. -Use of high risk questionnaires to identify patients at high risk of noncompliance and to target interventions.	-Motivation and reinforcement during clinical interactions. -Development and implementation of compliance risk questionnaires. -Exploration of patient expectation and role of clinician during remission

Strategies for improving compliance<sup>9</sup>:

Simplification of the therapeutic regimens:

Patient compliance may be obtained by minimising the complexity of regimen.

Physician must prescribe a minimum number of drugs with well-defined dosage schedules.

Sustained release, long acting oral preparations must be recommended for use. A single dose of drugs like phenytoin, propranolol may promote compliance by reducing side effects.

Some fixed drug combinations are prescribed in preferences to individual components for benefit like synergism eg. Levodopa and a decarboxylase inhibitor.

Improving standards of dispensing practise:

The container size should be selected to accommodate a label bearing dosage instructions which are precise, large, easily readable etc.

High quality rather than low cost container should be selected, if the medications are to be transferred from the original containers. For elderly, palm sized transparent bottle with a standard soft plastic screw cap is used.

Exact mode of administration and storage conditions should be written.

Pharmacist should write the ideal times of administration. In case of doubt, the label should be written in full after contacting the physician or patient. Instructions such as ‘take as required’

should always be accompanied by warning which specifies maximum number of doses that can be taken in 24 hour period.

Development of suitable medication packages<sup>10</sup>:

Pharmacist should select the system of presentation or packaging of medicines, which is most appropriate for the needs of individual patient.

Unit dose packaging and blister packs must be recommended. Like young women taking oral contraceptives.

A package system, in which all the different drugs to be taken at a specific time of the day are grouped together in one compartment of a compact unit. The medication box may be divided into sections according to the days of the week and the individual drugs are given in compartments corresponding to the times of administration. The advantage of using such a packaging container is that a pharmacist can accurately organize all drug therapy for an individual patient (on a weekly basis).

However, such memory aid packages may require regular and more frequent filling and supervision.

Supplementary & clear labelling:

It includes precautions or recommendations that enhance the advice of prescriber. The supplementary label should be concise, uncomplicated. It may be printed on the computer or a supply of common sticker should be kept with the pharmacist. Some of the suggestions for making these labels are<sup>11</sup>:

Description of the drug action may be given in lay terminology to reduce confusion and improve compliance. Symbols and graphics may be used to emphasize the correct times of administration. Details which are of interest of patient may be highlighted by keeping them in front of bottle, separate from the miscellaneous particulars (date of dispensing, name and address of pharmacy) which can be accommodated on the reverse.

A 'daily calendar' or a tablet identification card bearing details of the schedule may be given to improve compliance. Use an index to enable patients to locate their language quickly

Make the most of the extra printing space afforded by the multipage design. Use larger fonts to convey important information

Consider the information needs of the patient when writing label text – not just the minimum requirements of the regulators in a particular country

If a particular country is resistant to the use of booklet labels, place their language at an easy-to-find location (such as front or back page)

Patient counselling and education:

Using suitable verbal, written or audio-visual communication techniques and methods the pharmacist should inform, educate and counsel patients (or their representatives or guardians) about the following items for each medication in the patient's drug regimen.

Name, use, action, route, dosage form, special directions, precautions to be observed during administration, common side effects, selection of OTC drugs, prescription refill information.

Counselling can be done by<sup>12</sup>-

Verbal counselling

Printed information include:

Warning cards

Individualised medication instruction sheets.

Leaflets and booklets describing drugs and disease conditions.

Patient package inserts given by pharmaceutical manufacturer.

In – patient medication training programmes.

Compliance clinics.

During patient counselling information should be conveyed in a manner in which the patient can understand and speak common language.

Compliance aids:

Special medication containers, caps and systems: ‘MEDISET’ a 28 compartment container that contains four compartments for different time periods (i.e. morning, midday, evening, bedtime) for each day of the week. The “Med Light Tablet Organizer” also has 28 compartments as well as an alarm and flashing light.

Special designed caps, such as digital time piece that displays the time and day on which the last dose of medication was taken, and an alarm and flashing light when it is time to take next dose. Examples of such caps are prescript time cap, the pill timer and remind cap closures<sup>13</sup>.

For the patient with vision impairment or who otherwise have difficulty in reading products such as talking prescription, scrip talk and Aloud Talking Prescription labels have been developed to play a pre-recorded message when activated. Instructions for using the medication are recorded in a small electronic unit or microchip that is attached to the bottom of the container.

Blisters versus Bottles

Packaging in bottles offers significant financial and timeline advantages over blister packing. Unfortunately, this gain can be offset by the negative impact on patient compliance. Blisters provide the patient with a visual aid to taking their medication correctly. In addition, graphics and dosing instructions can be incorporated into the blister to further aid compliance. From a doctor’s perspective, it is far quicker and easier to assess compliance through the presence of unused medication present in a blister card than to start counting leftover tablets in a bottle. This makes the process of identifying, and acting on, poor compliance much easier.

New technologies- Smart Packaging<sup>14</sup>

The introduction of RFID-enabled computer chip technology has introduced the possibility of monitoring that a patient has taken medication, and when the medication was taken. Technological advances (for example, conductive inks) mean that these packs look the same as standard packaging to the patient, and can be produced using standard packaging equipment.

Smart Blister Packs

Examples of smaller blister packs include:

- Med-ic ECM (Information Mediary Corporation, Canada)
- Cypak (Sweden) and Cerepak (MeadWestvaco, US Licensee)
- Medicaid (Bang and Olufsen, Denmark)

While the exact mechanisms employed by the above packs vary slightly, they work on the principle that removing medication from a blister breaks the flow of current to a microprocessor. This break in the current is recorded as an event, and the date and time of each event is recorded by the microprocessor. When a patient returns their package to the physician, information from the microprocessor can be downloaded onto a PC using a wireless RFID reader. The physician can then make an instant assessment and, if necessary, work with the patient to improve compliance. Information can also be uploaded to a secure website where it can be used in subsequent data analysis by the CRO or study sponsor. Further enhancements to these systems include the addition of alarms to remind patients to take medication through the audible or visual

alerts, or even through digital means (SMS messages, emails). It is also possible to include an integral electronic diary/questionnaire pad that prompts the patient to enter information on adverse events or quality of life scores at the time of taking their medication.

#### **MEMS Caps**

This system is based around the inclusion of a microprocessor in a bottle cap. When the bottle is opened a mechanical spring mechanism is activated, completing an electronic circuit and recording an event. The cap records the time and date of each event. To minimise the number of these required for each trial, pharma companies often supply only a single cap/set-of caps per patient. These are re-used each time a patient is re-supplied during follow-up visits. As with smart blister packs, the MEMS system requires the use of appropriate software and readers<sup>14</sup>.

Information gained from this type of pack will give a clear picture of when the drug was removed from a package (but not necessarily when it was taken). As a result, they give a clearer picture of compliance than traditional methods, such as pill counting and paper diaries that do not record the time of dosing. This information is available to the physician, allowing them to target counselling and other measures specifically at non-compliers. It also allows poor compliers to be eliminated from the final trial analysis, removing the possibility that trial results will be compromised.

#### **Conclusion:**

It is evident that we have gained considerable knowledge during the last decade that can be harnessed to help patients follow medication regimens. As the number of efficacious regimens increases, this knowledge becomes all the more important. Unfortunately, the wind seems to have gone out of the sails of the compliance research enterprise when one considers that the majority of high quality studies were published during the earlier period, with good studies since then being few and far between. The flurry of studies in this recently by-gone era appear to have been stimulated mainly by the observation that disorder was treatable but frequently became inadequately treated disorder because of problems with patient compliance.

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