Offering corticosteroids in private pharmacies without medical prescription in Basra, Iraq.

بحث التخرج للمرحلة الخامسة

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Abstract

Introduction: Glucocorticoids, are known to be the most effective anti-inflammatory or immunosuppressive drugs, and have been used in the treatment of various intractable diseases. The present study was designed to evaluate and assess the % of pharmacies in Basra that offer oral and injectable GC without medical prescription in different diseases with precise information provided of different types of CS in different pharmacies locations in Basra city and to investigate the dispensing behavior of pharmacists in retail pharmacy practice and to assess their attitude toward dispensing of corticosteroid without prescription.

Method: A cross-sectional observation study involving 55 pharmacies in different regions in Basra city, Iraq.. We invites the pharmacists to fill a simple highly confidential questionnaire to record the level of the pharmacist education only; excluding any other personal information and the names of pharmacies and pharmacist director will not be disclosed for reasons of confidentiality and to encourage them to answer the questionnaire freely.

Results

About 89.1% of the total 55 surveyed pharmacies dispense CS without prescription for different skin diseases , 60% for drug allergy , 54.5% offer CS as appetite stimulant , 46.2% for insect bit , 45.3% in cases of asthma , 36.4% in cases of sever cough and only few percent of pharmacies dispense CS for arthritis. While regarding type of steroid offered varied depend on disease type and severity.

Conclusion: In conclusion, the majority of pharmacists are violating the pharmacy law without recognizing the potential harm they’re imposing the community in Iraq. Different types of corticosteroids offered in different diseases without any restriction and consequent side effects were very clear. Lack of OTC list could aggravate such proplem

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1.Introduction

Steroidal anti-inflammatory drugs, glucocorticoids, are known to be the most effective anti-inflammatory or immunosuppressive drugs, and have been used in the treatment of various intractable diseases.Since Edward Kendall isolated cortisone in the late 1930s and Philip Hench first used it to treat rheumatoid arthritis in 1948, More than 10 million new corticosteroid prescriptions are filled each year[**1**].GCs mainly exert their effects through intracellular glucocorticoid receptors. Large numbers of patients have been administered GCs . However, GCs frequently induce various side effects, which restrict their use like DM, osteoporosis, gastric ulcer, cataract, cushing syndrome, obesity and so on. So prescribing and dispensing GC required specific restriction and in different countries patient prescribed systemic corticosteroids for periods of more than three weeks should receive a steroid treatment card to advice patients about side effects and drug interactions in those patients**[2]** .

1.1.Indications[3]:

Corticosteroids are extensively used to treat many differentdisorders:

Allergic or hypersensitivity disorders, such as allergic reactions to drugs, serum and blood transfusions, and dermatoses with an allergic component.

Collagen disorders, such as systemic lupus erythematosus, scleroderma, and periarteritisnodosa.Collagenis the basic structural protein of connective tissue, tendons, cartilage, and bone, and it is therefore presentin almost all body tissues and organ systems.

Dermatologic disorders that may be treated with systemic corticosteroids include acute contact dermatitis,erythemamultiforme, herpes zoster (prophylaxis of postherpeticneuralgia), lichen planus, pemphigus, skinrashes caused by drugs, and toxic epidermal necrolysis.

Endocrine disorders, such as adrenocortical insufficiency and congenital adrenal hyperplasia.

Gastrointestinal disorders, such as ulcerative colitis and regional enteritis (Crohn’s disease)

Hematologic disorders, such as idiopathic thrombocytopenic purpura or acquired hemolytic anemia

Hepatic disorders characterized by edema, such as cirrhosis and ascites

Neoplastic disease, such as acute and chronic leukemias, Hodgkin’s disease, other lymphomas, and multiplemyeloma.

Neurologic conditions, such as cerebral edema, brain tumor, acute spinal cord injury, and myasthenia gravis

Ophthalmic disorders, such as optic neuritis, sympathetic ophthalmia, and chorioretinitis

Organ or tissue transplants and grafts (eg, kidney, heart, bone marrow). Corticosteroids suppress cellularandhumoral immune responses and help prevent rejection of transplanted tissue. Drug therapyis usually continued as long as the transplanted tissue is in place.

Other purposes:

1-Cerebral oedema: The mechanismby which steroids influence vasogenicoedema are thought to include the following **[4]** :

(1) stabilization of cerebral endothelium, (2) increase in lysosomal activity of cerebral capillaries; (3) inhibition of release of potentially toxic substances such as free radicals, (4) electrolyte shifts favoring transcapillary efflux of fluid; and (5) increase in local and global cerebral glucose use, leading to improved neuronal function.

2. Spinal cord injury: Asuggested protocol for traumatic cord injury includes the use of high dosemethylprednisolone[5]**.**

3. Steroids in surgery:High and long term steroids tend to produce adverse effects on GIT, woundhealing, and also cause increase in infection. However anti-inflammatory action of steroids havebeneficial role to play in surgery. Shimada et al in their retrospective study of patients undergoing resection of esophageal carcinoma,reported that those patients who received methylprednisolone 250mg prior and two days following surgery had low morbidity rates fromanastomotic leakage and liver dysfunction**[6].**

1.2 MECHANISTIC PHARMACOLOGY AND PHYSIOLOGY OF STEROIDS

The antiinflammatory properties of steroids have been attributed to their inhibitory effects on the action of phospholipase A2, an enzyme critical to the production of inflammatory compounds**.** Onesuch pathway is through their induction of the production of proteins called lipocortins. Glucocorticoidsstem the production of inflammatory mediators such as leukotrienes and prostaglandins and effectively halt the inflammatory cascade**[7,8].**

The ability of corticosteroids to act on different target tissues and exert biological responses depends in most cases on the presence of the glucocorticoid receptor (GR). The GR belongs to the large family of ligand-activated transcription factors, that includes receptors for the steroid hormones, thyroid hormone, retinoic acid, and vitamin D **[9].**It is an intracellular receptor, located in the cytoplasm. Binding of a ligand to the receptor initiates a series of cellular events involving synthesis of new proteins **[10].**Although there are two different

types of GR, currently available glucocorticoids predominantly bind to the type II receptor. Because of the ubiquitous nature of the GC receptor, corticosteroids act on a wide variety of cell types, which accounts for their many therapeutic indications, and also accounts for their negative side effects such as lymphopenia, hyperglycemia, osteoporosis, changes in bone-mineral density, growth retardation in children, cataracts, glaucoma, skin thinning, and suppression of the hypothalamus-pituitary-adrenal (HPA) axis due to a negative feedback mechanism **[11].**

1.3 Mechanism of action:

Exogenous CS drug molecules act at the cellular level by binding to glucocorticoid receptors in target tissues. The drugs are lipid soluble and easily diffuse through the cell membranes of target cells. Inside the cell, they bind with receptors in intracellular cytoplasm. The drug–receptor complex then moves to the cell nucleus, whereit interacts with DNA to stimulate or suppress gene transcription. Glucocorticoids increase or decrease transcription of many genes to alter the synthesis of proteins that regulate their many physiologic effects (eg, enzymes, transport proteins, structural proteins**(12**)

1.4.Action(13)

Inhibitingarachidonic acid metabolism.

Normally,when a body cell is injured or activated by various stimuli, the enzyme phospholipase A2 causes the phospholipids in cell membranes to release arachidonic acid. Free arachidonic acid is then metabolized to produce proinflammatoryprostaglandinsandleukotrienes. At sites of tissue injury or inflammation,corticosteroids induce the synthesis of proteins that suppress the activation of phospholipase A2. This action, in turn, decreases the release of arachidonic acid and the formation of prostaglandins and leukotrienes.

Strengthening or stabilizing biologic membranes.

Two biologic membranes are especially important in inflammatory processes. Stabilization of *cell membranes*inhibits the release of arachidonic acid and production of prostaglandins and leukotrienes, as described above. Stabilization of *lysosomal membranes* inhibits release of bradykinin, histamine, enzymes, and perhapsother substances from lysosomes. (Lysosomes are intracellular structures that contain inflammatory chemicalmediators and enzymes that destroy cellular debris and phagocytized pathogens.) This reduces capillary permeability and thus prevents leakage of fluid into the injured area and development of edema. It also reduces the chemicals that normally cause vasodilation and tissue irritation.

Others

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Inhibiting the production of interleukin-1, tumornecrosis factor, and other cytokines, impairing phagocytosis, impairing lymphocytes and inhibiting tissue repair.

1.5 Adverse effects:

Adverse Somatic Effects of Corticosteroid Therapy are wide and diverse and this reflect wide distribution of corticosteroid receptors in the body: Hypertension and Accelerated atherosclerosis are common **cardiovascular side** effect, acne, alopecia, hirsutism, Striae, skin atrophy and purpura are **dermatologic effect**. Regarding effect on **endocrine system** Obesity, Diabetes mellitus, Adrenal-pituitary axis suppression, Hyperlipidemia, Fluid and sodium retention, Loss of potassium, calcium, and nitrogen and delayed growth.

Others like Peptic ulcer disease, Pancreatitis and Fatty liver, Leukocytosis, Neutrophilia, Lymphopenia, oral candidiasis, Increased risk of systemic infection, osteoporosis, pseudotumorcerebri, cataracts and glaucoma**[14,15]**. Side effects of chronic use include bruising, muscle weakness, weight gain, skin changes, sleep disturbances, cataracts, and pathologic fractures**[16].** Glucocorticoid administration can also have psychiatric side effects: mood disorders, anxiety, delirium, and panic disorder. Psychotropic medication may be required to treat these symptoms, but the prognosis is favorable once the glucocorticoids are reduced or discontinued.[**17, 18].**adverse effects occur in up to 90% of patients who take glucocorticoids for >60 days . These side effects, including the more serious fractures and cataracts, occur even in patients taking low dosages**[16,19].** Glucocorticoids affect bone mineralization by inhibiting calcium absorption in the gastrointestinal tract and shifting signaling-molecule production to favor bone resorption .Recommendations for preventing glucocorticoid-induced osteopenia and its subsequent complications and comorbidities include supplementing calcium with vitamin D for glucocorticoid doses ‡5 mg/d and starting bisphosphonates when indicated by densiometric evaluation**[19].**In patients with preexisting diabetes, blood sugars should be measured more often than in patients without preexisting diabetes, and medications should be adjusted to maintainadequate control**[20].** Cushing syndrome and adrenal suppression have been observed in patients taking oral, intraarticular, epidural, inhaled, nasal, ocular, and topical glucocorticoid preparations .these side effects become more likely with longer durations of treatment and higher dosages, mineralocorticoid activity causes the retention of sodium and free water and the excretion of potassium**[20,21]**

Rapid reduction or abrupt withdrawal of corticosteroid therapy that has been prolonged or at high doses can cause three problems: secondary adrenal insufficiency (suppression of the HPA axis), steroid withdrawal or deprivation syndrome and relapse of the underlying disease for which the treatment had been prescribed **[22-24]**

What is the underlying disease for which the corticosteroids are being used?

The majority of patients who exhibit difficulties with withdrawal of corticosteroid therapy are suffering from severe hematological, inflammatory or immunological diseases. Therefore, the treating physician must beaware of which signs and symptoms indicate recrudescence of the subjacent disease, which in turn will provide information on speed of corticosteroid withdrawal, or even whether temporary dosageincreases will be necessary. If, on the other hand, there is no underlying disease to be treated, such as, for example, in situations where a corticosteroid was used to treat an allergic reaction which has already been resolved, the anti-inflammatory dosage can be abruptly reduced to a physiological dose without risk of adrenal insufficiency**[25,26]**.

What are the reasons for starting and discontinuing corticosteroid therapy?

The reasons for initiating treatment with corticosteroids vary greatly, due to the multiple therapeutic uses of this class of drugs. Withdrawal is considered when their use is no longer recommended or when significant side-effects appear. Exacerbation of herpetic keratitis is one of the rare contraindications to continuation of corticosteroid therapy**(26)**

Aim: The present study was designed to evaluate and assess the % of pharmacies in Basra that offer oral and injectable GC without medical prescription in different diseases with precise information provided of different types of CS in different pharmacies locations in Basara city and to investigate the dispensing behavior of pharmacists in retail pharmacy

Patients and methods

A cross-sectional observation study involving 55 pharmacies in Basra city, Iraq. This study was conducted from Nov-2015 to April- 2016. The sample was stratified randomly from different regions in Basra(Eastern, Western, Northern, Southern, Central) regardless of the pharmacy's size, deprivation and education levels of the area, such sample was intended to be representative of all Basra pharmacies(476). We invites the pharmacists to fill a simple highly confidential questionnaire to record the level of the pharmacist education only; excluding any other personal information and the names of pharmacies and pharmacist director will not be disclosed for reasons of confidentiality and to encourage them to answer the questionnaire freely ; only locations of pharmacies were documented for perfect pharmacies distribution in the samples area. There were no refusals to participate, so the response rate was 100% and a total of 55 pharmacies were surveyed.

The questionnaire used in the study was designed to be completed by asking community pharmacist directors, the pharmacists were explained the purpose of the study and instructed on how to answer questions in questionnaires and were asked to report the major corticosteroid dispensed in each clinical disease scenario presented in the study. The scenarios mentioned and discussed to pharmacist depend on general signs and symptoms of diseases and about advice giving to patients according to Questionnaire

Questionnaire

The location of the pharmacy	**Type of corticosteroid used**	**Dosage form**
Do you offer CS in the following		
Appetite stimulant (increase Wt.)		
Arthritis		
Drug allergy		
Sever Cough		
Asthma		
Skin diseases		
Insect bit		
If the patients insist inform individual the following(yes/No)		
Risk of CS		
diseases history		
Tapering on long term use		

Pregnancy &breast feeding	
Long term side effects	

Results:

We take 55 pharmacies in different regions in Basra-Iraq and we make a survey on dispensing of CS without prescription. About 89.1% of the total 55 surveyed pharmacies dispense CS without prescription for different skin diseases , 60% for drug allergy , 54.5% offer CS as appetite stimulant , 46.2% for insect bit , 45.3% in cases of asthma , 36.4% in cases of sever cough and only few percent of pharmacies dispense CS for arthritis as shown in figure (1).The most widely dispensed CS as appetite stimulant was Dexamethasone orally in about 32.7% in the total 55 pharmacy, 18.2% dispense Betamethasone orally and only 1.8% of pharmacies dispense Prednisolone as shown in figure (2).For arthritis 14.5% of pharmacies were dispense oral prednisolone, 12.7% dispense Betamethasone as injection, 7.3% dispense Methylprednisolone and 3.6% dispense Betamethasone oral as shown in figure (3).For asthmatic conditions, 27.3% of surveyed pharmacy dispense oral prednisolone, 18.2% dispense inhaled CS, 14.5% dispense oral hydrocortisone, 5.5% dispense oral Dexamethasone, 3.4% dispense oral hydrocortisone and 1.8% dispense oral Betamethasone as shown in figure (4).

In cases of drug allergy 55.2% of total 55surveyed pharmacy dispense hydrocortisone injection, 14.5% dispense Dexamethasone injection, 9.1% dispense Prednisolone oral, 1.8% dispense inhaled CS and 1.8% dispense topical CS as shown in figure (5).In cases of insect bit 27.3% of total 55 pharmacies dispense topical CS, 9.1% dispense hydrocortisone injection, 7.3% dispense oral Dexamethasone and 5.5% dispense Prednisolone oral as shown in figure (6).For sever cough 18.2% of total 55 pharmacies dispense Prednisolone oral, 7.3% dispense oral Dexamethasone, 3.6% dispense oral Betamethasone, 3.6% dispense hydrocortisone injection and 3.6% dispense Dexamethasone injection as shown in figure (7).

In cases of skin diseases. 54.5% of surveyed pharmacies dispense hydrocortisone topical, 21.8% dispense Betamethasone topical, 14.6% dispense triamcinolone topical, and 7.3% dispense Clob.topical and 7.3% dispense Mom.topical as shown in figure (8).

The percent of information's that provided by pharmacists when they dispense CS to the patients without prescription was 90.9% of pharmacists inform patients about the risk of using CS , 81.8% of pharmacists obtain the disease history from the patients , 74.5% of pharmacists provide information's on how to tapering of CS , 72.7% of pharmacists inform patients about the sideeffects of CS and 52.7% of pharmacists asking if the female patients were pregnant and breast feeding or not as shown in figure (9).

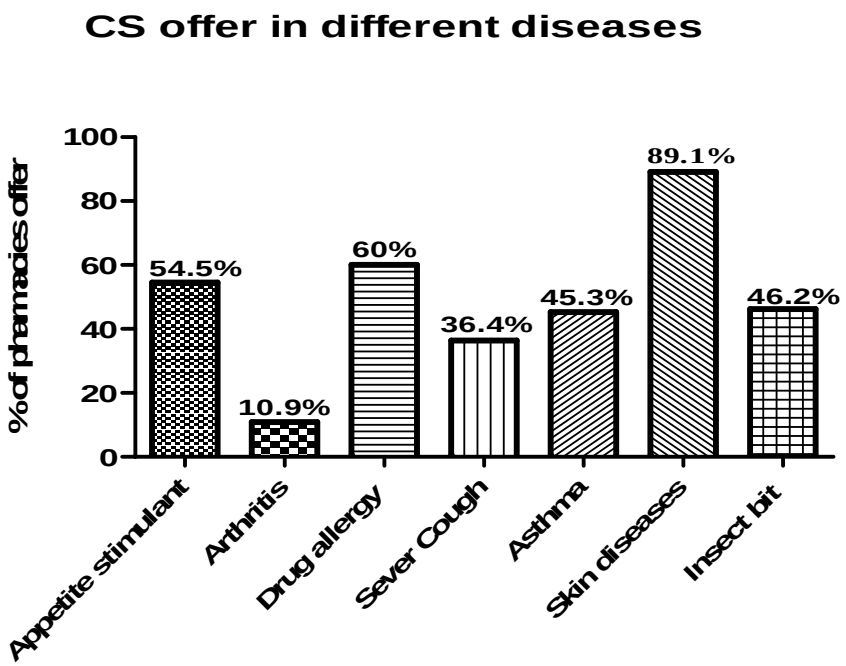

Fig (1): % of pharmacies offer CS without medical prescription in various diseases

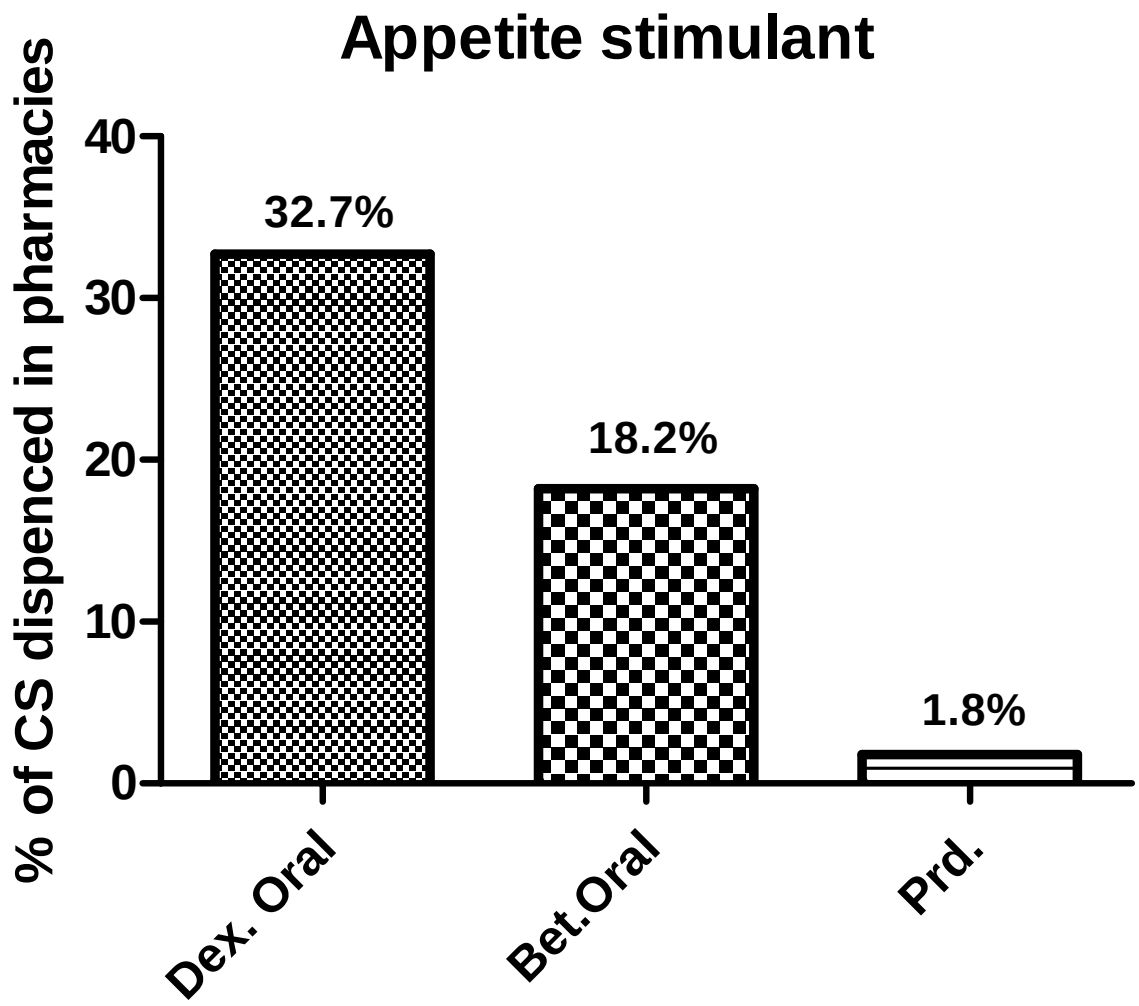

Fig (2): % of pharmacies offer different type of CS as appetite stimulant

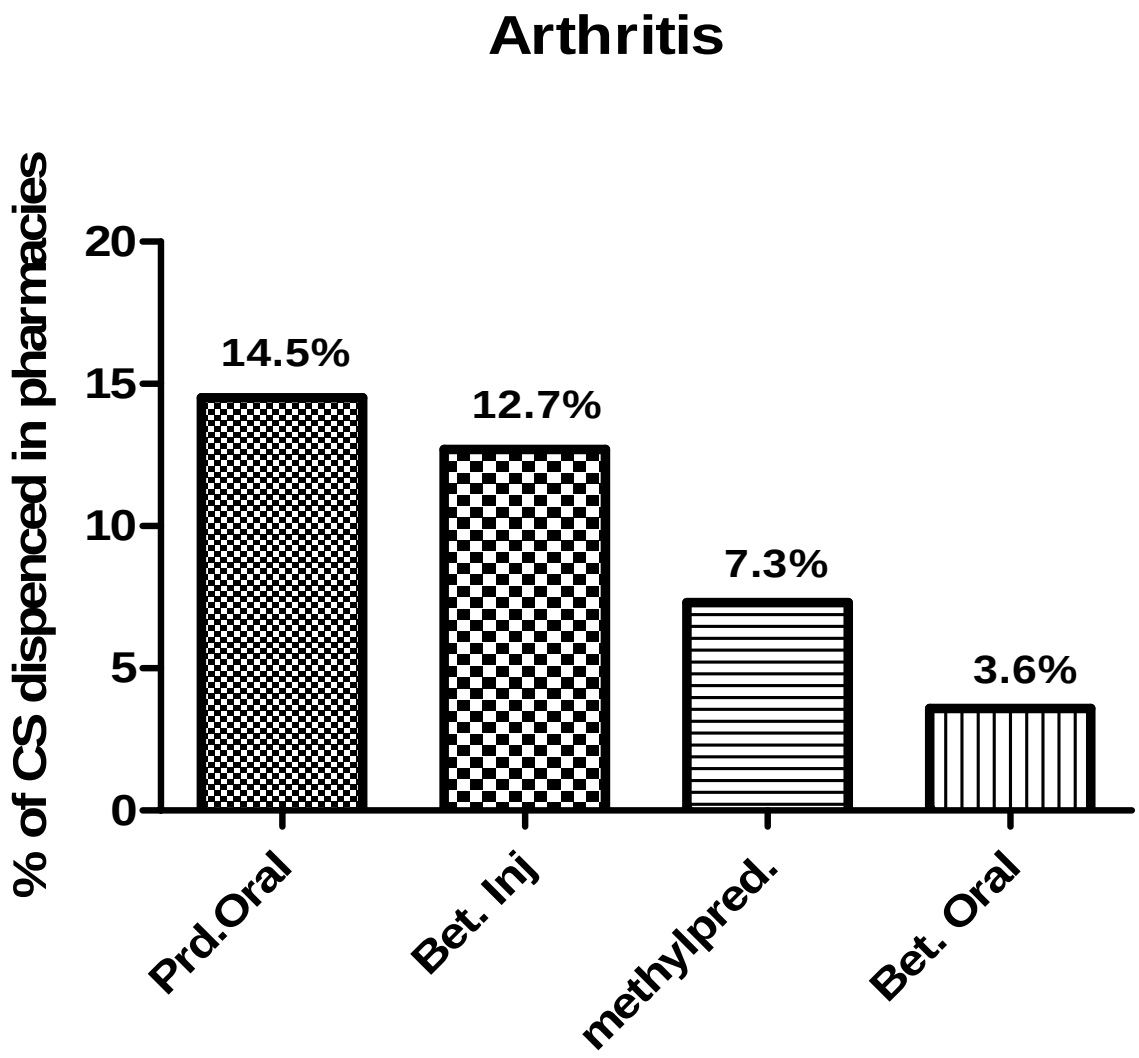

Fig (3): % of pharmacies offer different type of CS for treatment of arthritis

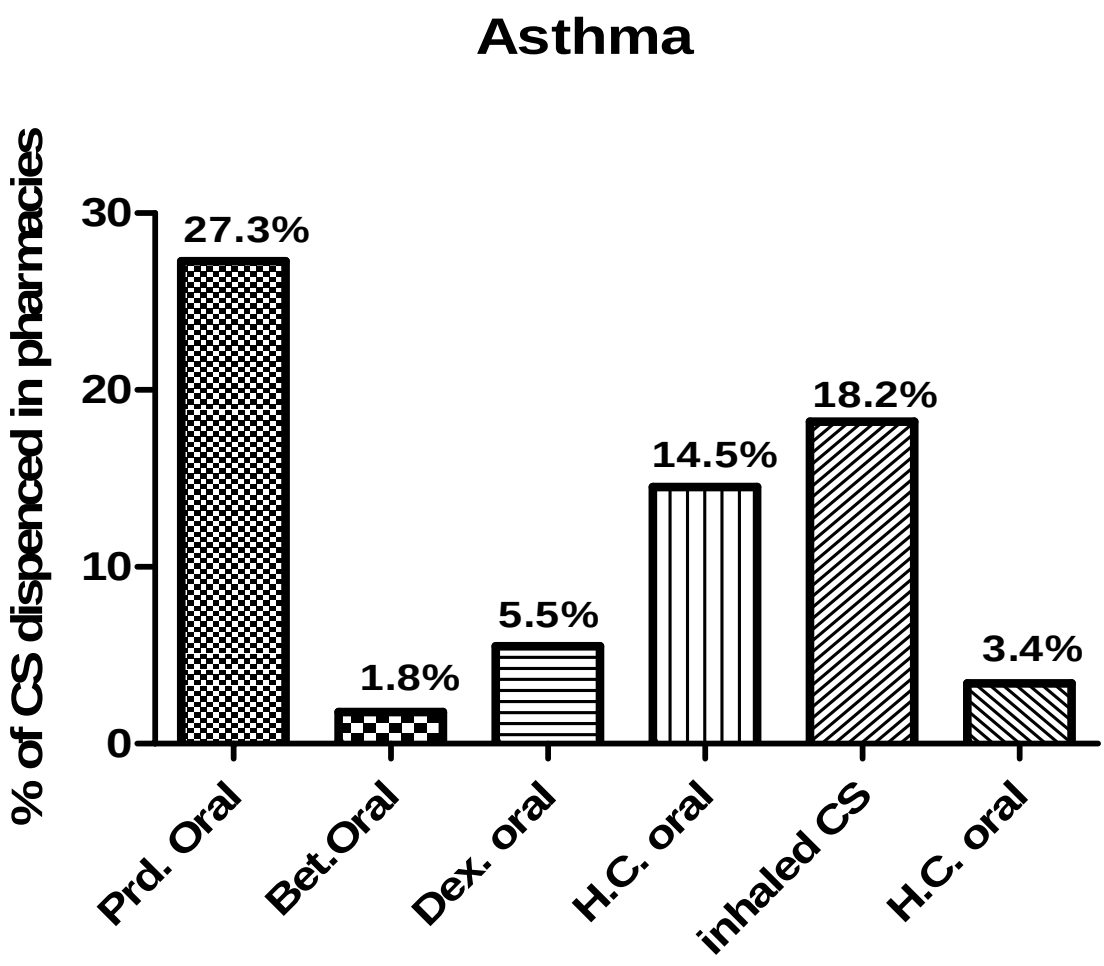

Fig (4): % of pharmacies offer different type of CS for treatment of asthma

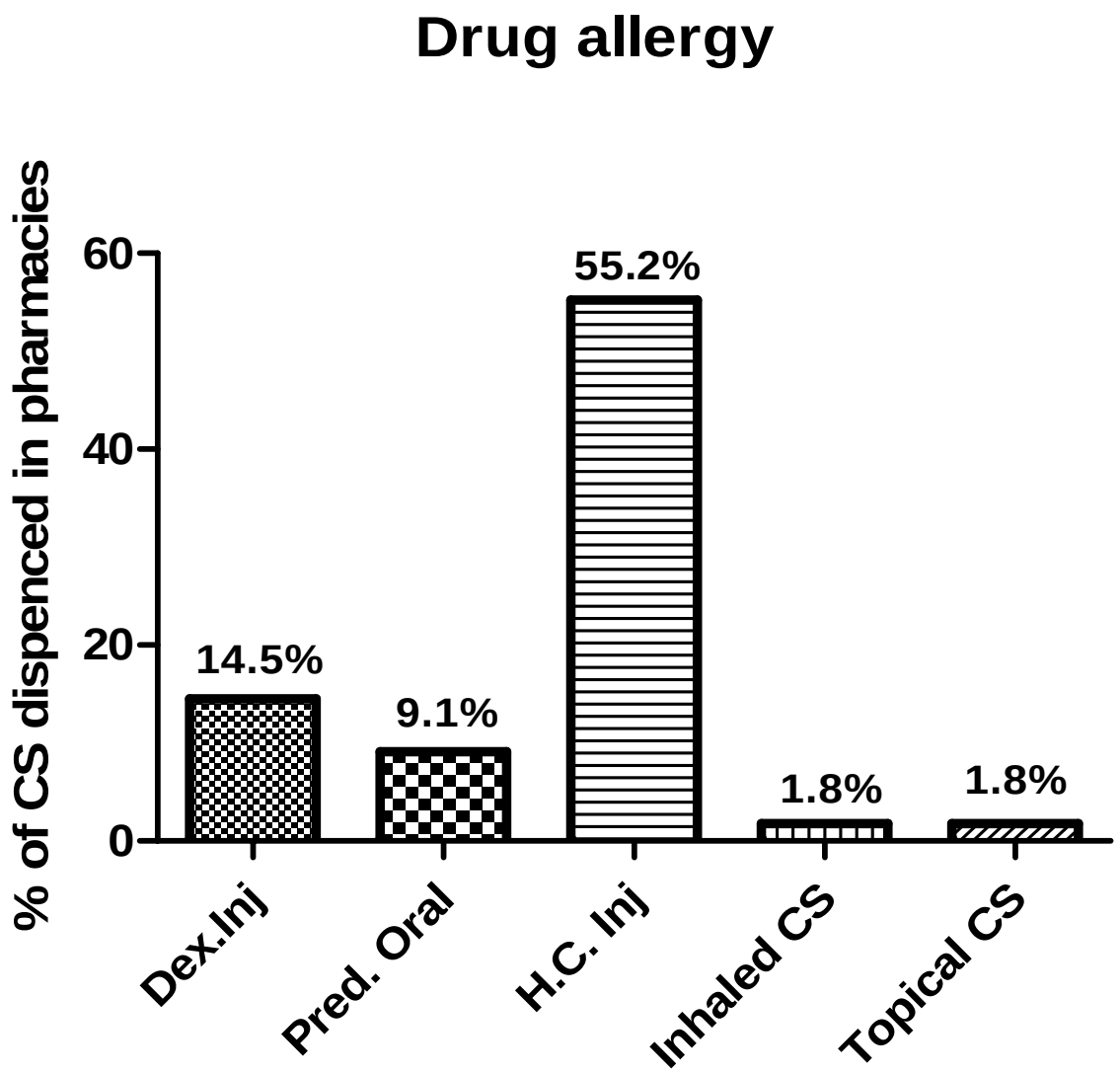

Fig (5): % of pharmacies offer different type of CS as anti allergic compounds

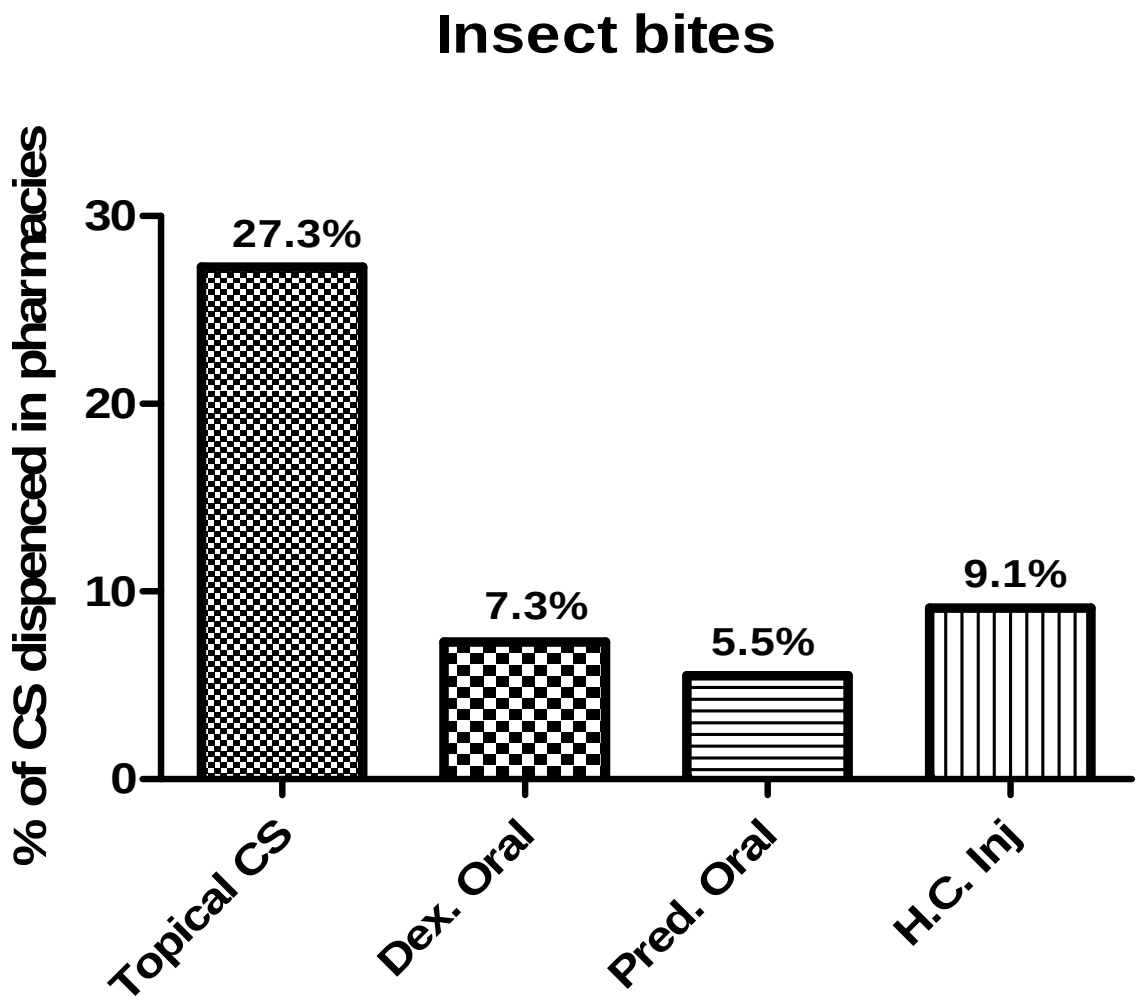

Fig (6) : % of pharmacies offer different type of CS for treatment of insect bite

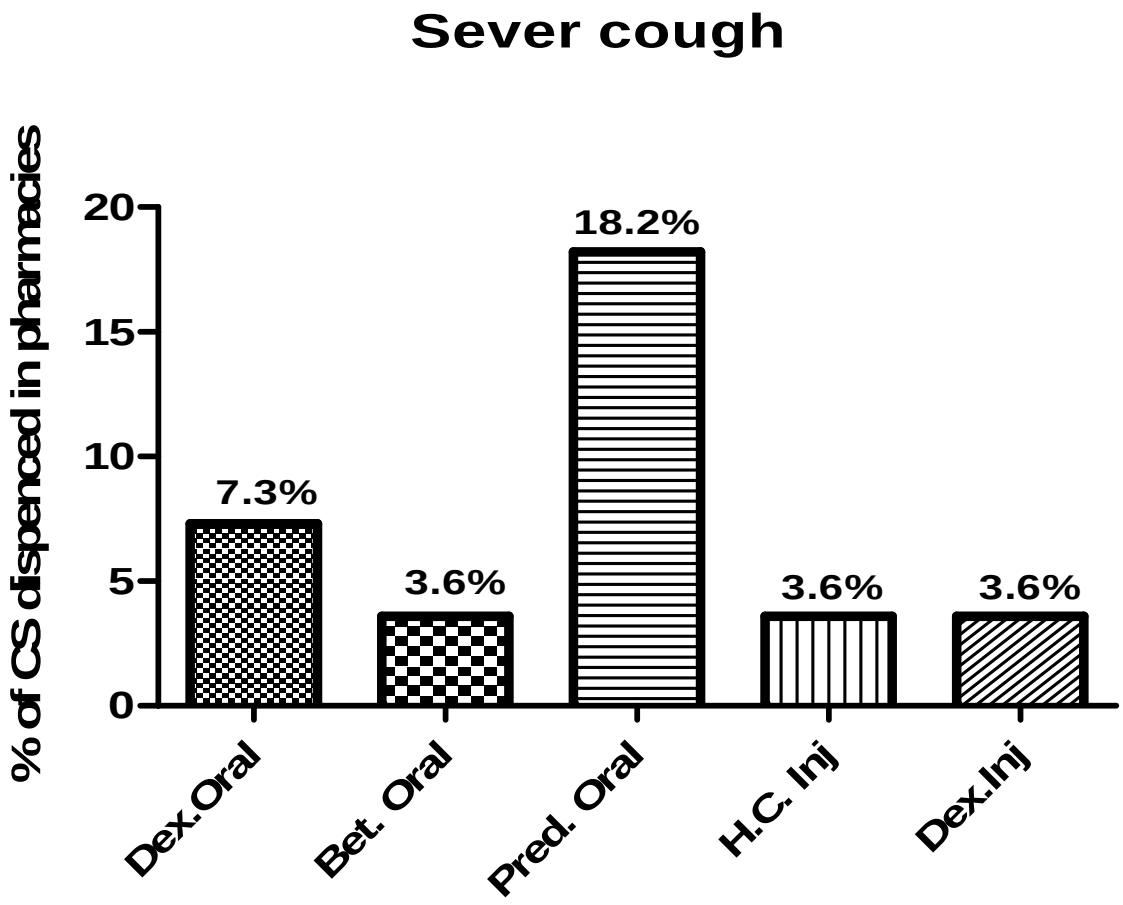

Fig (7): % of pharmacies offer different type of CS in sever cough

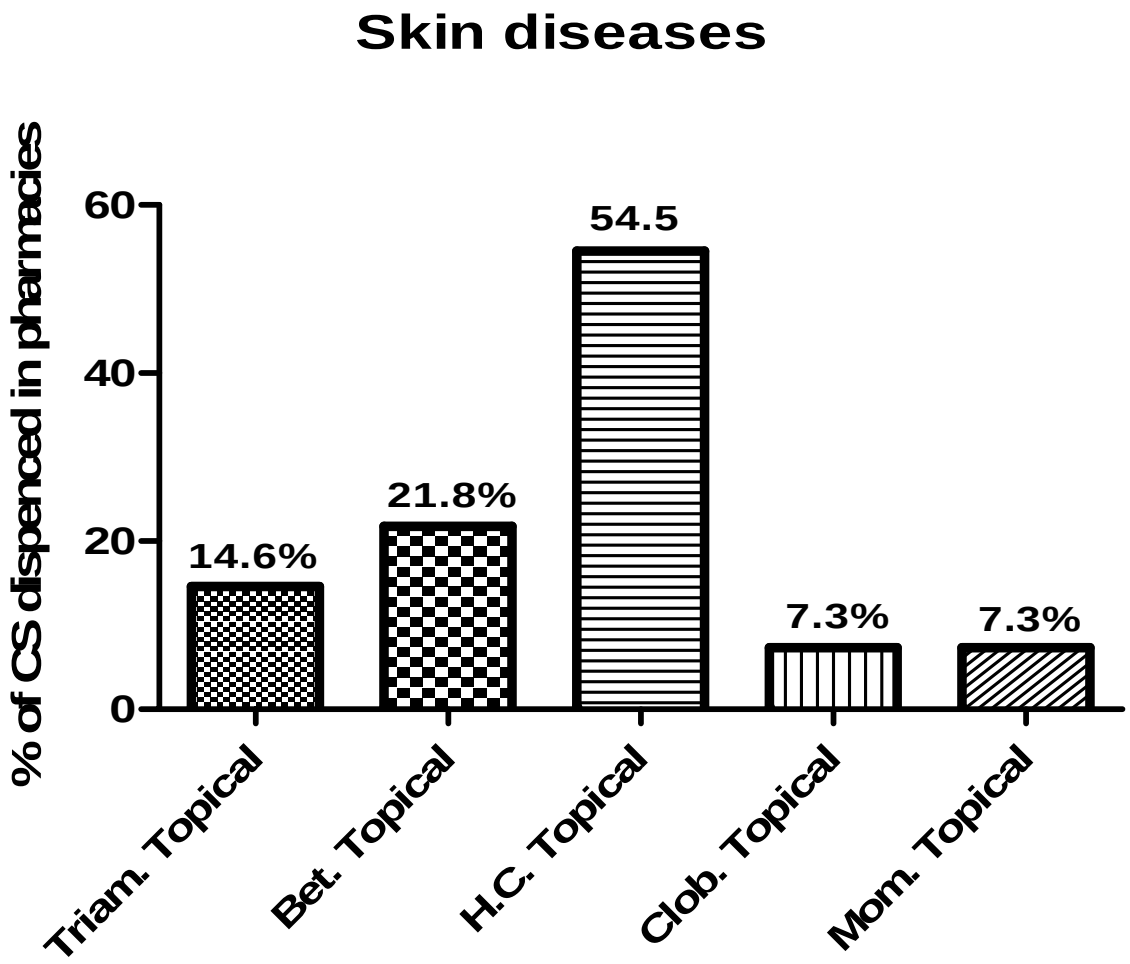

Fig (8): % of pharmacies offer different type of CS in skin diseases

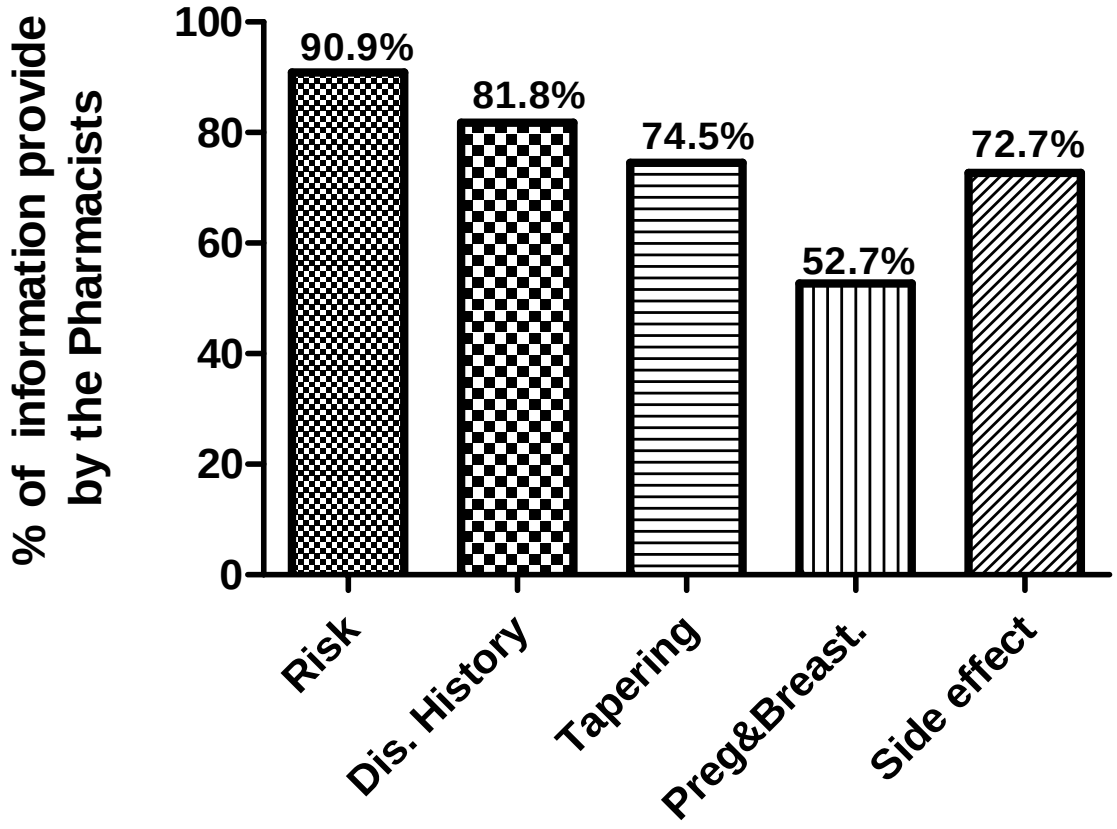

Fig (9): % of pharmacies provide information to the patients

Discussion

The resultsof this study indicate that any drug -despite its class- couldbe easily purchased in Iraq pharmacies without a prescription.Unfortunately, different types of CS offers without prescription in different countries. Corticosteroids were dispensed without prescription by most Pharmacies interviewed. As the number of pharmacies has grown dramatically in Basra competition has increased and profit margins decreased. Pharmacy staff may feel compelled to focus more on profit than on their Professional role[**27 ,28]**.Several studies have shown that prescription-only drugs are commonly dispensed without prescription in Vietnam and other Asian countries**[29 ,30]**. A decree regulating prescribing, stating that all corticosteroids are prescription-only drugs, has been in place since 1995.[**31]**clearly this shows that the regulations regarding prescriptions are generally not respected. Determinants such as customers' expectations, social acceptance, commercial pressures and profit needs may have more impact on actual practice compared to regulations and clinical [**32,33]**

The potential risk of not complying with the regulation might not be enoughof a deterrent, especially if economic margins are small. So the control needed to implement regulations has been lacking, due to weak and not clearly defined sanctions for violations as well as few incentives for officials and inspectors to focus on the issue this has also been described in other low-income countries [34,**35]**

This study does not underestimate the pharmacist's role in the society, but it rather gives a full image of the pharmacist's demographics, knowledge of non-OTC drugs and draws a clear image of their attitude toward dispensing. Reasons given were quite disreputable requiring an urgent reevaluation of who should be qualified to dispense CS, and what medications should be dispensed[**36]**.

Since their discovery, steroids have infiltrated nearly every branch of medicine and can be administered in nearly every route available. The effects of steroid use can vary widely, and the full spectrum of side effects can be present even in patients taking low doses. Practitioners must be aware that the drug can possibly exacerbate a preexisting condition or present a new medical condition. Knowledge of the clinical implications of prescribing these agents is critical

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