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Research Article

STUDY ON ANTI-INFLAMMATORY THERAPY IN CHRONIC DISEASES, ITS HOPES AND CHALLENGES IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Introduction: According to the U.S Centres for Disease Control and Prevention, together the chronic diseases account for 63% of all deaths worldwide. The chief causes of these diseases are through the induction of inflammation that is by the changes in diet and lifestyle. Wide heterogeneous group of drugs called anti-inflammatories are used to suppress the innate inflammatory pathway and thus prevents persistent or recurrent inflammation.

Objectives: To assess the benefits of anti-inflammatory drugs in chronic diseases, to evaluate the challenges that result in a poor therapeutic outcome, to assess the developing co-morbidities in patients on the anti-inflammatory drug(s) and to assess the betterment of patient concerning the pain-related quality of life.

Materials and methods: A prospective observational study enrolled 100 patients. Anti-inflammatory prescriptions were assessed, evaluated and questionnaire provided to patients is assessed for the benefits and challenges of the anti-inflammatories for 6 months.

Results: In a sample of 100 patients, 41were men, 59 were women. According to the visual analogue scale, on admission, moderate pain was in 52% and severe pain in 46%. After treatment during discharge, 4% were with no pain, 8% moderate and 88% minor pain. This shows that the pain severity dropped in every patient during their discharge i.e., the benefit is attained. An average of 18.17% improvement due to anti-inflammatory use was established in the patient's pain-related QOL. The factors like suspected ADR (11.61%), DDIs (36.61%), drug choice problems (11.61%), no tapering of dose (38.73%) and comorbidities (1.4%) were the major challenges for incomplete recovery. The co-morbidities identified – pneumonia (0.02%) oral candidiasis (0.01%) anaemia (0.01%).

Conclusion: Though these anti-inflammatories are of great help in arresting inflammation and pain, their use must be tempered according to the need with the realization that they can cause potential harm.

INTRODUCTION

According to the definition of the US National Centre for Health Statistics, chronic disease is one lasting three months or more. These diseases can neither be prevented by vaccines nor cured by medication, nor do they just disappear. That is, it's a condition that can be controlled with treatment for months.

According to the U.S Centres for Disease Control and Prevention, together these chronic diseases account for 63% of all deaths worldwide. The chief causes of these diseases are through the induction of inflammation that is by the changes in diet and lifestyle (infections, obesity, alcohol, tobacco, radiation, environmental pollutants) brought about by industrialization, economic development, urbanization, and market globalization, all of which have accelerated over the past 10 years.[2]

In chronic diseases, the exact identity of the inflammatory stimulus is unknown and, if known, is difficult to remove. Thus, there is an interest in therapeutically targeting the inflammatory response. There has been a success to arrest the inflammation triggered by primary inflammatory dysregulation or autoimmunity in chronic diseases with anti-inflammatory therapy, but, there are considerable limitations.[1]

There is a strong association between chronic inflammatory conditions and chronic diseases. Chronic inflammation damages the cells of the brain, heart, arterial walls, and other anatomic structures; this damage leads to various inflammatory

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chronic diseases. Studies on inflammation at the molecular level showed that various biomarkers are involved in the process of inflammation.

Many of these biomarkers are transcription factors such as NF-κB and STAT3; inflammatory cytokines and chemokines such as tumour necrosis factor-alpha (TNF)-α, interleukin (IL)-1, IL-6, IL-8, and MCP-1; inflammatory enzymes such as cyclooxygenase (COX)-2, 5- lipoxygenase (LOX), 12-LOX, and matrix metalloproteinases (MMPs); and other factors such as prostate-specific antigen (PSA), C-reactive protein (CRP), adhesion molecules, vascular endothelial growth factor (VEGF), and TWIST are found common in most chronic diseases.[3]

The studies listed below indicate mounting evidence of a stronger association between inflammation and chronic diseases

1. Several cytokines/chemokines such as IL-2, IL-12, IL-18, IFN-γ, and TNF-α and their receptors have shown to be up-regulated in patients with IBD.[5,6]
2. CRP, an acute-phase protein produced by the liver during bacterial infections and inflammation, was found to be a common marker for detecting cardiovascular and atherosclerotic diseases.[7]
3. Inflammation is also a cause of autoimmune diseases such as rheumatoid arthritis, in which excess levels of cytokines such as TNF-α, IL-6, IL-1β, and IL-8 are often found.[8]
4. Elevated levels of other cytokines such as IL-1α, IL-2, IL-4, IL-6, IL-10, IFN-γ, TGF-β1, TGF- β2, and TNF-α have also been found in frozen sections of central nervous system tissue from multiple sclerosis patients.[10]
5. Similarly, cerebrospinal fluid samples from patients with Alzheimer disease, Parkinson disease, amyotrophic lateral sclerosis, multiple sclerosis, and schizophrenia have been shown to exhibit the overexpression of cytokines and NF-κB.[11]
6. Likewise, in patients with diabetes, high levels of CRP, IL-6, IL-1, and TNF-α—along with the abnormal expression of NF-κB—have been observed.[12]

Anti-inflammatory medications

Anti-inflammatory drugs are wide heterogeneous group of drugs that are used to suppress the innate inflammatory pathway and this prevents persistent or recurrent inflammation.[13] Broadly, they consist of corticosteroids, cyclooxygenase-2 inhibitors, antimetabolite drugs such as methotrexate and azathioprine, and anti-cytokine agents.[13] Mycophenolate is another immune-modulating drug.

Glucocorticoids

Glucocorticoid reduces inflammation by decreasing the activation of neutrophils, macrophages, and T-helper cells. They also down-regulate the production of multiple cytokines, including IL-1, IL-2, IL-6 and TNF-alpha, through the inhibition of gene transcription. Besides, glucocorticoids inhibit the production of prostanoids through decreased expression of COX-2 and are partly responsible for the up-regulation of anti-inflammatory factors, including IL-10 and annexin-1.[13]

Cyclooxygenase-2 inhibitor

Inhibition of COX-2 isoenzyme, downregulates the production of regulatory cytokines (e.g. IL-1ß, TNF-alpha) and B- and T-cell proliferation is reduced.

Colchicine

The anti-inflammatory effect of colchicine is mediated primarily through the inhibition of microtubule assembly. This inhibits inflammasome activation, cell chemotaxis, and the production of leukotrienes and cytokines thus inhibiting inflammation. By inhibiting the inflammasome, colchicine inhibits IL-1ß activation from its precursor, pro-IL-1ß, thus limiting the inflammatory response. Colchicine is also responsible for inhibiting the expression of IL-1ß, IL-6 and TNF-alpha through the reduced activation of macrophages.[13]

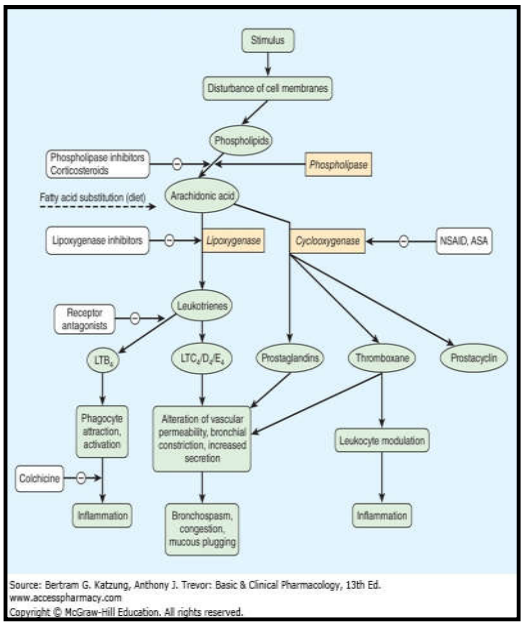
Antimetabolites

Different antimetabolite drugs have different mechanisms of action. Methotrexate, an antifolate drug that interferes with DNA replication, exerts its anti-inflammatory action through the inhibition of cytokines. Methotrexate is also believed to inhibit lymphocyte proliferation through the inhibition of purine synthesis. Azathioprine, a purine analogue that also inhibits DNA synthesis, inhibits T-cell proliferation through complex genetic interactions leading to a depressed immune response.

Anticytokine drugs

This is a class of recombinant engineered antibodies that interact with the immune system. Within this broad class of immunomodulating agents, different agents target different cytokines involved in the inflammatory pathway. The main targets are TNF-alpha (infliximab, adalimumab), IL-1 antagonism (canakinumab, anakinra) and IL-2 antagonism (daclizumab).[13]

Pictorial presentation of the birth of inflammatory & painmediators and their arrestors



The drugs like COX-2 inhibitors, glucocorticoids and other biologic and non-biologic anti-inflammatory can help in

reducing the inflammation thereby they successfully arrest the further worsening of conditions, which is due to inflammation. As these are the drugs, there are many unwanted effects associated with them, which may spoil the condition of the patients with the weak genome, co-morbidities or in patients with polypharmacy. The challenges in targeting inflammation in any chronic inflammatory disease lie in 3 properties, which are characteristic of processes that are critical for evolutionary survival: redundancy, compensation, and necessity.[1]

The main aim of the study is to assess the benefits associated with anti-inflammatory therapy that is the reduction of inflammation and relieving the pain and erythematic immobility associated with it and thus realising the benefits of these drugs concerning the pain-related quality of life.

Certain harms may, however, be associated with the use of anti-inflammatory agents. Impeding anti-inflammatory medications will also affect the overall immune system, leaving recipients of these drugs vulnerable to infection, in particular, opportunistic infections, such as systemic fungal infections, and those caused by Mycobacterium and other atypical organisms. These infections can be potentially life-threatening.

Some anti-inflammatory drugs, such as methotrexate and cyclophosphamide can lead to myelosuppression causing a decrease in white cell count and suppression of the immune system. NSAIDs, COX-2 inhibitors and steroids have also been shown to increased risk of gastrointestinal mucosal injury through the inhibition of prostaglandins and many more renal and hepatic damages.

The need of study lies in analyzing these challenges and overcoming them by tempering the drug need with the realisation that they can cause potential adverse reactions and also with careful attention to dose, duration of therapy concomitant risk factors and combined use of more specific drug to reduce disease activities and to prevent the birth of new co-morbidities.

Objectives of the Study

Primary Objectives

- To assess the necessity and benefits of anti-inflammatory drugs in chronic diseases.
- To evaluate the challenges that result in poor therapeutic outcome.
- To assess the developing co-morbidities in patients on the anti-inflammatory drug(s) and also in the patients with the history of anti-inflammatory use.
- To assess the betterment of patient concerning the pain-related quality of life.

Secondary Objectives

- To identify the most commonly used anti-inflammatories.
- Identifying the measures to overcome the challenges faced in this therapy.

METHODOLOGY

Study site: Shamanur Shivashankarapa Institute of Medical Sciences and Research Centre (SSIMS & RC), Davangere, Karnataka.

Study duration: The study was conducted for six months.

Study design: The study was a prospective, observational study.

Sample size: 100 patients

Study criteria: The study was carried out by considering the following inclusion and exclusion criteria.

Inclusion Criteria

- All the inpatients with chronic disease(s) above 18yrs of age, irrespective of gender.
- Patients with at least one anti-inflammatory drug in current medication chart and with or without medication history of anti-inflammatory drug use.

Exclusion Criteria

- The cases with dosing errors which includes overdose or the sub-therapeutic dose of the prescribed anti-inflammatories.
- Pregnant mothers and TB patients.
- Patients in ICU.
- Patients who are not willing to participate in the study
- Patients with insufficient data in their records.

Source of Data

The data about patients were collected from the case sheets and treatment chart of all inpatients on anti-inflammatory therapy from the department of general medicine and orthopaedics.

Ethical Approval

Ethical approval was obtained from the Institutional Ethical Committee of Bapuji Pharmacy College, Davangere.

Study Procedure

- A prospective observational study was conducted in the chronic diseased in patients with the use of anti-inflammatories in SSIMS & RC, Davangere.
- The data required for the study was collected from the patient case sheets.
- Inpatients in general medicine and orthopaedics meeting the inclusion criteria were enrolled in the study.
- The demographic details, number of drugs prescribed, dose and frequency both during admission and discharge were recorded in a properly designed data collection form.

Materials Used

- Informed consent form
- Patient case sheet
- Treatment chart
- Data collection form

- Questionnaire to assess the pain-related quality of life in patients with chronic disease(s) (according to domains and facets set by world health organization)
- Pain Scale (Standford pain scale – information on chronic pain)
- Micromedex (Drug information software).

RESULTS

Distribution of patients based on gender

A total of 100 cases were collected, out of which 59 (59%) were females and 41 (41%) were males.

Table 1 Distribution of patients based on gender (N = 100)

Gender	Number of patients	Percentage (%)
Male	41	41
Female	59	59

Distribution of patients based on age group

Out of the population of 100, 23 patients (23%) were between the age range of 41-50 years, followed by 22 patients (22%) between 51-60 and 61-70 yrs, 13 patients (13%) were between 31-40 yrs and above 70yrs whereas rest 7 patients (7%) were between 21-30yrs. Majority of the cases were between 41-50 yrs - 23 (23%).

Table 2 Distribution of patients based on age group (N = 100)

Age (years)	Numbers of patients	Percentage (%)
18-20	0	0
21-30	7	7
31-40	13	13
41-50	23	23
51-60	22	22
61-70	22	22
>70	13	13

The severity of pain during admission and discharge

On admission, there were 2 cases (2%) of minor pain, 52 cases (52%) with moderate pain and 46 cases (46%) with severe pain. On discharge, 88 cases (88%) with minor pain, 8 complained of moderate pain (8%) and 4 cases (4%) had complete relief from pain. This shows that the pain severity dropped in every patient during their discharge i.e., the benefit is attained by the use of the anti-inflammatory drugs.

Table 3 Severity of pain during admission and discharge (N = 100)

Severity of pain (based on scoring)	At admission		At discharge	
	No. of cases	% of cases	No. of cases	% of cases
No pain (score-0)	0	0	4	4
Minor pain (score 1-3)	2	2	88	88
Moderate pain (score 4-6)	52	52	8	8
Severe pain (score 7-10)	46	46	0	0

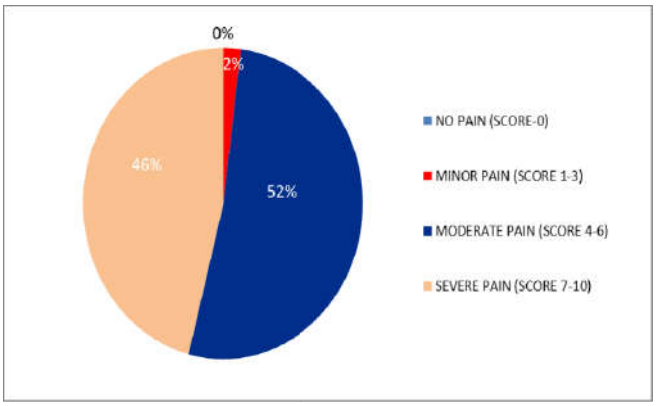


Figure 3.1 Severity of pain during admission

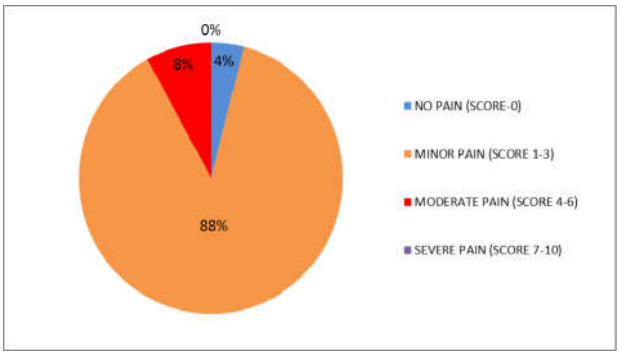


Figure 3.2 Severity of pain during discharge

Pain-related quality of life during admission and discharge

At admission, there were 58 patients with pain-related QOL between 71-80% followed by 34 patients with 61-70%, 5 patients with 51-60%, 2 patients with 81-90% and 1 patient with less than 50% pain-related quality of life.

At discharge 51 patients had 81-90% QOL followed by 38 patients within the range of 91-100%, 9 patients with 71-80% and rest 2 patient had QOL ranged 61-70%. There were no patients with less than 60% of pain-related QOL.

Table 4 Pain-related quality of life during admission and discharge (N = 100)

Percentage of pain related QOL (%)	At admission		At discharge	
	No. of cases	% of cases	No. of cases	% of cases
<50	1	1	0	0
51-60	5	5	0	0
61-70	34	34	2	2
71-80	58	58	9	9
81-90	2	2	51	51
91-100	0	0	38	38

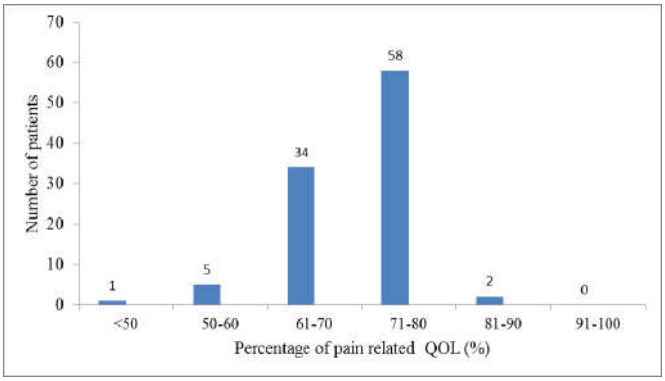


Figure 4.1 Pain-related quality of life during admission

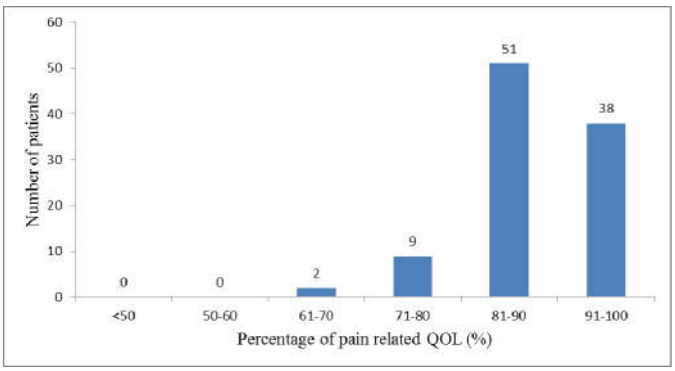


Figure 4.2 Pain-related quality of life at discharge

An average of 18.17% improvement/betterment due to anti-inflammatory use was established in the patient's pain-related quality of life.

Table 4.1 Average pain-related quality of life during admission and discharge (N = 100)

Average % of pain related QOL at admission	Average % of pain related QOL at discharge	Average % of betterment
70.8	88.55	18.17

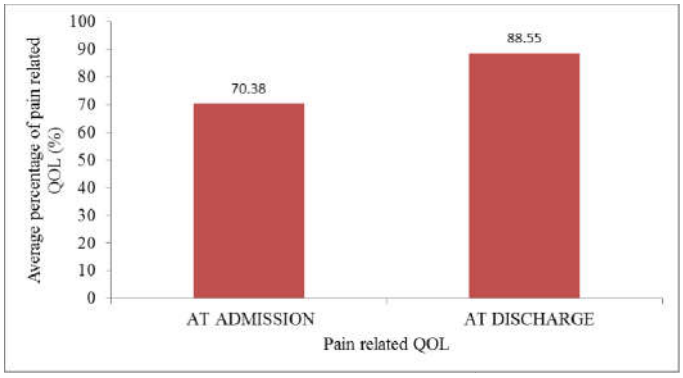


Figure 4.3 Average pain-related quality of life during admission and discharge

Suspected adverse drug reactions observed in the study sample

The drugs resulted in suspected ADR were methylprednisolone 8 cases (24.24%), hydrocortisone 7 cases (21.21%), prednisolone 5 cases (15.15%), fluticasone and budesonide 3 cases (9.09%), etoricoxib 2 cases (6.06%), dexamethasone, methotrexate, meloxicam, colchicine and denosumab 1 case (3.03%).

Table 5 Suspected adverse drug reactions observed in the study sample

Suspected adr	Drug	No.of cases	% of adr
Oral candidiasis	Dexamethasone	1	3.03
Hyperglycemia (fluctuating)	Methylprednisolone hydrocortisone prednisolone	2 5 1	24.24
Bp variations (hypertension)	Methylprednisolone budesonide etoricoxib	2 3 1	18.18
Hyperthyroidism	Methylprednisolone prednisolone hydrocortisone	1 1 1	9.09
Pneumonia	Fluticasone	2	6.06
Impaired wound healing	Methylprednisolone	2	6.06
Kidney injury	Etoricoxib meloxicam	1 1	6.06
Osteoporosis	Prednisolone hydrocortisone	1 1	6.06
Super infection	Prednisolone	1	3.03
Sleep apnea	Methylprednisolone	1	3.03
Dyspnea	Denosumab	1	3.03
Muscle weakness	Prednisolone	1	3.03
Anaemia	Methotrexate	1	3.03
Bronchospasm	Fluticasone	1	3.03
Diarrhoea	Colchicine	1	3.03

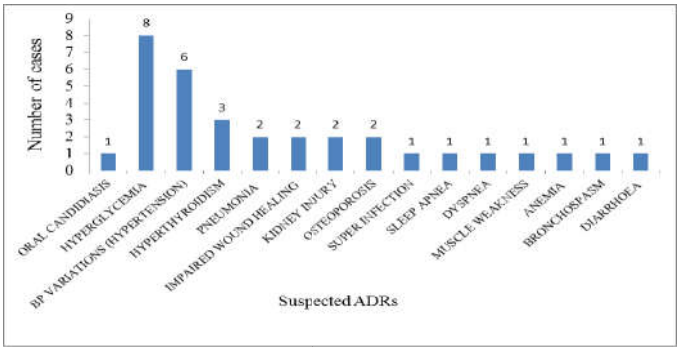


Figure 5 suspected adverse drug reactions observed in the study sample

Types of drug-drug interactions (based on severity) identified in the treatment charts

A total of 104 drug interactions were found in which 19 were major, 71 were moderate and 14 were minor interactions**.**

Table 6 Types of drug-drug interactions (based on severity) identified in the treatment charts

Types of drug interaction	Number of drug interactions	Percentage of drug interactions(%)
Major	19	18.26
Moderate	71	68.26
Minor	14	13.46

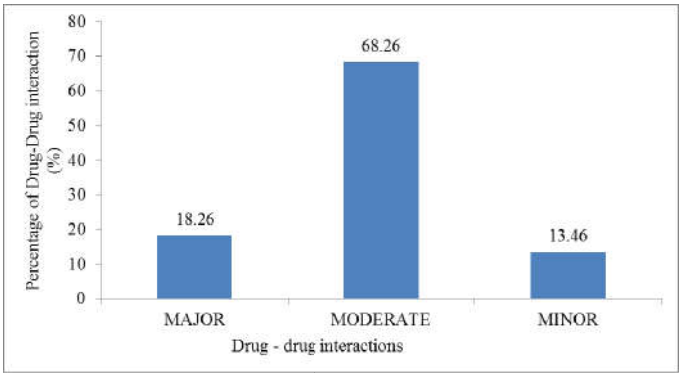


Figure 6 Types of drug-drug interactions based on severity identified in the treatment charts

Drugs causing interactions in the treatment chart

Out of the total interactions, Hydrocortisone resulted in 30 (27.52%) interactions, methylprednisolone 13 (11.92%), budesonide 12 (11%), methotrexate 10 (9.17%), betamethasone 7 (6.42%), prednisolone, dexamethasone and deflazacort 5 (4.58%), hydroxychloroquine, meloxicam and indomethacin 4 (3.66%), sulfasalazine, etoricoxib, denosumab and artesunate 2 (1.83%), cyclosporin and colchicine 1 (0.91%).

Table 7 Drugs causing interactions in the treatment chart

drugs	number of interactions	percentage of interactions (%)
hydrocortisone	30	27.52
methylprednisolone	13	11.92
budesonide	12	11
methotrexate	10	9.17
betamethasone	7	6.42
prednisolone	5	4.58
dexamethasone	5	4.58
deflazacort	5	4.58
hydroxychloroquine	4	3.66
meloxicam	4	3.66
indomethacin	4	3.66
sulfasalizine	2	1.83
etoricoxib	2	1.83
denosumab	2	1.83
artesunate	2	1.83
cyclosporine	1	0.91
colchicine	1	0.91

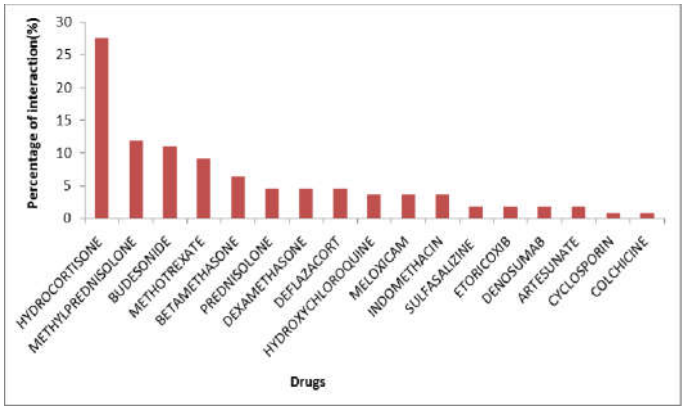


Figure 7 Drugs causing interactions in the treatment chart

Types of drug choice problem faced in the study

Several drug choice problems were faced like inappropriate drug selection (15.15%), duplication of therapeutic drug group (69.69%), contraindications (12.12%) and treatment without indication (3.03%).

Table 8 Types of drug choice problems faced in the study

Types of drug choice problem	Frequency	Percentage (%)
Inappropriate drug	5	15.15
Duplication of therapeutic group	23	69.69
Contraindication	4	12.12
Treatment without indication	1	3.03
Untreated condition	0	0

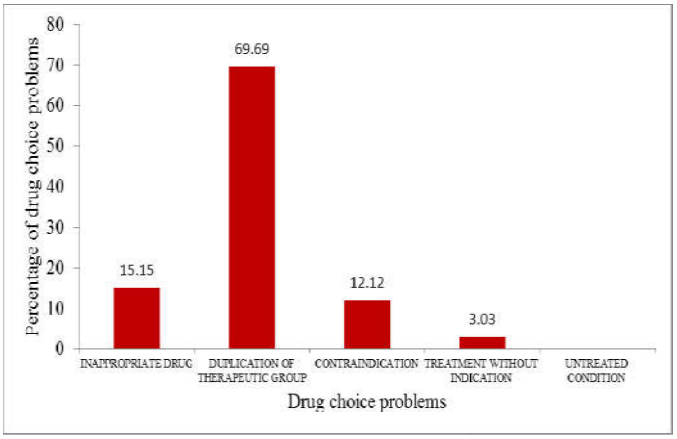


Figure 8 Types of drug choice problem faced in the study

The drugs that need tapering

The drugs which required tapering were budesonide (26.36%), hydrocortisone and methylprednisolone (23.63%), dexamethasone (12.72%), prednisolone (7.27%), deflazacort (2.72%), beclomethasone (1.81%) and fluticasone and colchicine (0.9%).

Table 9 The drugs that need tapering

Drug	No. Of drugs required tapering	% of drugs required tapering
Budesonide	29	26.36
Hydrocortisone	26	23.63
Methylprednisolone	26	23.63
Dexamethasone	14	12.72
Prednisolone	8	7.27
Deflazacort	3	2.72
Beclomethasone	2	1.81
Fluticasone	1	0 .9
Colchicine	1	0.9

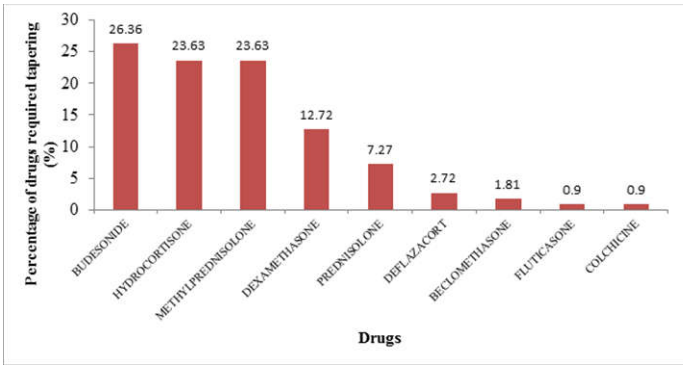


Figure 9 The drugs that need tapering

Developed co-morbidities in the study sample

The co-morbidities with the anti-inflammatory use were identified – pneumonia 2 cases (0.02%) and one case of oral candidiasis and anaemia (0.01% each).

Table 10 Developed co-morbidities in the study sample

Drug	Co-morbidity	No.of cases	% of cases
Fluticasone	Pneumonia	2	0.02
Dexamethasone	Oral candidiasis	1	0.01
Methotrexate	Anaemia	1	0.01

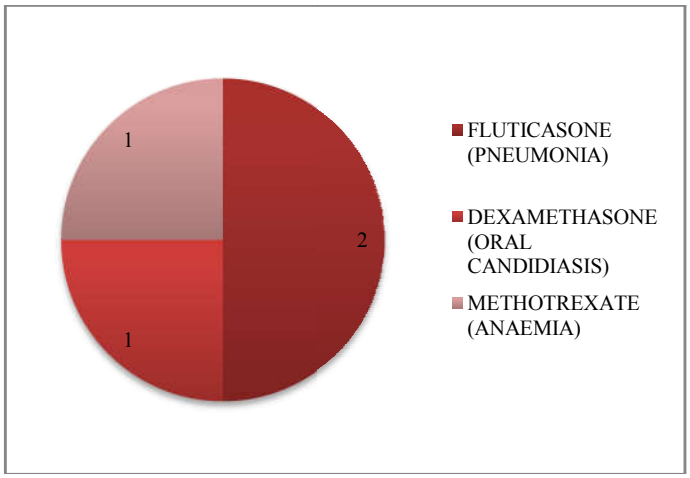


Figure 10 Developed co-morbidities in the study sample

Total challenges identified in the study

The factors like suspected ADR (11.61%), drug-drug interactions (36.61%), drug choice problem (11.61%), no tapering of dose (38.73%) and co-morbidities (1.4%) were the major challenges for incomplete recovery.

Table 11 Total challenges identified in the study

types of challenges	number of challenges	percentage (%)
suspected adverse drug reaction	33	11.61
drug interaction	104	36.61
drug choice problem	33	11.61
dose tapering error	110	38.73
comorbidities	4	1.4

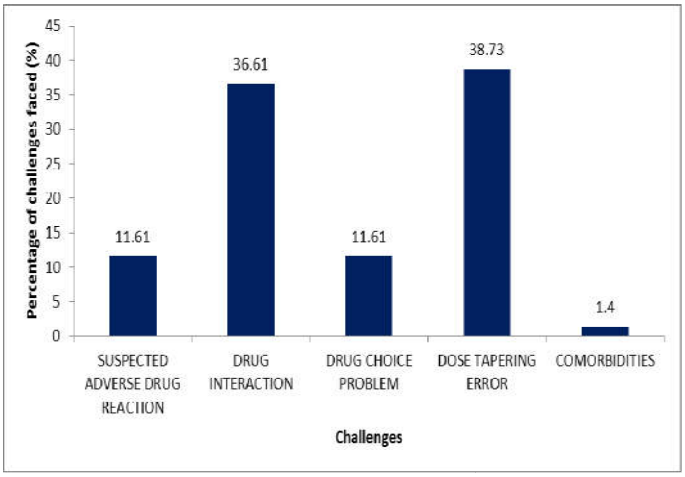


Figure 11 Total challenges identified in the study

Measures identified to overcome the challenges

The following are the simple measures identified to overcome the challenges faced.

Table 12 Measures identified to overcome the challenges

Challenges	Measures identified to overcome challenges
Drug Interactions	Major: Drug replacement by non-interacting drug Moderate: Altering interval of administration according to the half-life of the drug. Minor: Monitoring patient
Drug Choice Problem	Improper choice: Drug replacement by right drug indicated for the treatment Duplication: Avoid the use of the same class of drug Contraindication: Withdrawal ofcontraindicated drug.
Co-morbidities	Appropriate treatment should be initiated.
Tapering	Follow standard guidelines for tapering.

DISCUSSION

Anti-inflammatories are widely prescribed among today's scenario in arresting inflammation and improving the quality of life which is impaired by acute or chronic inflammation. These drugs inhibit the activation of various inflammatory biomarkers. Thus, prevents worsening of one's chronic condition and also prevents the birth of new complications due to unwanted excess inflammation. Like any other drugs, these anti-inflammatories can also cause harm to human life if not properly utilised. The anti-inflammatory drugs are short term friends and long term foe.

The overall data of 100 patients who were admitted in the medicine and orthopaedic departments of a tertiary care teaching hospital were collected. In our study, female preponderance was seen 59% and males were 41%. Patients of age 18 and above were taken into the study and majority of them enrolled were of the age group of 41-50 yrs (23%), followed by 22 patients (22%) between 51-60 and 61-70 yrs, 13 patients (13%) were between 31-40 yrs and above 70yrs whereas rest 7 patients (7%) were between 21-30yrs.

In our study, commonly used anti-inflammatories were budesonide (20.25%), hydrocortisone and methylprednisolone (17.08%), dexamethasone and prednisolone (11.39%), hydroxychloroquine (3.79%), etoricoxib (3.16%), methotrexate (2.53%), deflazacort, beclomethasone, denosumab (1.89%), artesunate, meloxicam, azathioprine and sulfasalazine (1.26%) and cyclosporine, colchicine, indomethacin and mesalamine (0.63%).

From our study, we found that at admission there were 2 cases (2%) of minor pain, 52 cases (52%) with moderate pain and 46 cases (46%) with severe pain. On discharge, 88 cases (88%) with minor pain, 8 complained of moderate pain (8%) and 4 cases (4%) had complete relief from pain. This shows that the pain severity dropped in every patient during their discharge i.e., the benefit is attained by the use of the anti-inflammatory drugs. A similar outcome was observed in studies like Acute anti-inflammatory effects of inhaled budesonide in asthma conducted by PG Gibson *et al*, 2001. Safety and efficacy of meloxicam in the treatment of osteoarthritis conducted by D Yocum *et al*, 2000. Inhaled corticosteroids in patients with stable chronic obstructive pulmonary disease conducted by MB Drummond *et al*, 2008.

From our study, it was clear that during admission, pain-related QOL was around 71-80% in 58 patients, 61-70% in 34 patients, 51-60% in 5 patients and less than 50% in 1 patient. The similar poor health-related QOL was studied by Thommasen and Zhang in DM and Hypertension[38], Strine *et al* in Asthma, arthritis, DM and heart diseases[39], Katz and Mc Horney in Hypertension and DM[40], Carellar *et al* in IBD and Vinck *et al* in multiple sclerosis[41].

We found that the factors like suspected ADR (11.61%), drug-drug interactions (36.61%), drug choice problem (11.61%), no tapering of dose (38.73%) and co-morbidities (1.4%) were the major challenges for incomplete recovery.

The drugs resulted in suspected ADR is methylprednisolone (24.24%), hydrocortisone (21.21%), prednisolone (15.15%), fluticasone and budesonide (9.09%), etoricoxib 2 cases (6.06%), dexamethasone, methotrexate, meloxicam, colchicine and denosumab (3.03%). Similar results were seen in studies like Incidence of serious complications of corticosteroid therapy in Rheumatoid arthritis conducted by HC Smyllie *et al*, Complications of long term steroid therapy for asthma conducted by Philip Liebermann *et al*.

We also found the occurrence of oral candidiasis as an adverse drug reaction (3.03%) and new co-morbidity (25%) due to dexamethasone use which was similar to the study conducted by Chizu Fukushima *et al* titled Salivary IgA and oral

candidiasis in asthmatic patients treated with inhaled corticosteroid.[28]

We have a suspected ADR of fluctuating blood glucose levels in 8 cases which accounted for a total of 24.24% suspected ADR. Similar results were seen in study Inhaled corticosteroid and the risks of diabetes onset and progression conducted by Samy Suissa *et al*.[24]

The 5 cases of inappropriate drug use were seen for example hydrocortisone in hypoxic brain injury with myoclonus and COPD. 4 contradictory drugs were used, for example, one with methylprednisolone in DVT and another budesonide use in respiratory failure etc.

The co-morbidities with the anti-inflammatory use was identified as pneumonia 2 cases (0.02%) and one case of oral candidiasis and anaemia (0.01% each).

The occurrence of pneumonia in our study was supported by number of studies like Inhaled corticosteroids in COPD and the risk of serious pneumonia conducted by Samy Suissa *et al*[25], Inhaled corticosteroid use in chronic obstructive pulmonary disease and the risk of hospitalization for pneumonia conducted by P Ernst *et al*[32], Systemic adverse effects of inhaled corticosteroid therapy: a systematic review and meta-analysis conducted by BJ Lipworth *et al*[42], Pneumonia risk in COPD patients receiving inhaled corticosteroids alone or in combination: TORCH study results conducted by C Crim *et al*[43], Reported pneumonia in patients with COPD conducted by Peter M A Calverley *et al*[20], Inhaled corticosteroids in patients with stable COPD conducted by Drummond MB *et al*[22], Potential adverse effects of inhaled corticosteroids conducted by H William Kelly *et al*[44].

In our study, the anti-inflammatories causing drug-drug interactions were hydrocortisone 30 (27.52%) interactions, methylprednisolone 13 (11.92%), budesonide12 (11%), methotrexate 10 (9.17%), betamethasone 7 (6.42%), prednisolone, dexamethasone, deflazacort 5 (4.58%), hydroxychloroquine, meloxicam and indomethacin 4 (3.66%), sulfasalazine, etoricoxib, denosumab and artesunate 2 (1.83%), cyclosporin and colchicine 1 (0.91%).

The common classes of drugs that were potentially interacting were fluoroquinolone antibiotics, alpha and beta-blockers, calcium channel blockers, angiotensin-converting enzyme and angiotensin II receptor blockers, loop diuretics, methylxanthines, beta 2 agonists, insulin, hydantoin derivatives, COX 1 inhibitors, coumarin analogues and to smaller extent gastric acid inhibitors.

We came across drugs which required tapering: budesonide (26.36%), hydrocortisone and methylprednisolone (23.63%), dexamethasone (12.72%), prednisolone (7.27%), deflazacort (2.72%), beclomethasone (1.81%) and fluticasone and colchicine(0.9%).

Measures identified to overcome challenges are as follows

Drug Interaction

- Major: Drug replacement by the non-interacting drug.
- Moderate: Altering interval of administration according to the half-life of the drug.
- Minor: Monitoring patient

Drug Choice

- Improper choice: Drug replacement by right drug indicated for the treatment
- Duplication: Avoid the use of the same class of drug
- Contraindication: Withdrawal of contraindicated drug.

Co-morbidities

- Appropriate treatment to be initiated.

Tapering errors

Follow standard guidelines for tapering.

CONCLUSION

Anti inflammatory use has become an important practice for the treatment of several chronic diseases like respiratory disease (asthma, COPD etc), autoimmune diseases like (rheumatoid arthritis, systemic lupus erythematosus etc) and many more for the suppression of innate inflammatory pathway to prevent the persistent and recurrent inflammation.

However, when the anti-inflammatories are used irrationally, it may cause new complications that can be worse thus, the inappropriate use of these drugs not only cause substantial economic burden but also decreases the immunity of the patients.

Treatment chart shows the way towards the improper use of drugs, irrationalism that is no or improper drug dose tapering may lead to ineffective, unsafe treatment which results in prolongation of illness distress and harm to the patients.

Although there has been success with anti-inflammatory therapy in chronic diseases triggered by primary inflammation dysregulation or autoimmunity, there are considerable limitations. In particular, the inflammatory response is critical for survival. As a result, redundancy, compensatory pathways, and necessity narrow the risk: benefit ratio of anti-inflammatory drugs.

The active participation of clinical pharmacist in the clinical ward rounds and medication chart review can ensure the proper use of drugs by identifying the challenges and overcoming them by tempering the drug need with realisation that they can cause potential adverse drug reactions and also with careful attention to the dose and duration of the therapy, concominant risk factors and combined use of more specific drugs to reduce the disease activity and to prevent the birth of new co-morbidites which finally reduces the cost of therapy and ultimately benefits the patients.

Thus we conclude, this study provides insights for the challenges associated while treating inflammation in chronic diseases and creating awareness about the needful and proper use of anti-inflammatories in healthcare setups.

CONFLICT OF INTEREST: None

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