Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20162893

Research Article

Drug utilization 90%: an innovative method in assessing quality of drug prescription with specific reference to non-steroidal anti-inflammatory drugs prescription

Dhananjay Kulkarni[1]*, Kokila B. N.[2], Santosh Kumar Sahu[3], Ravindra Kumar G.[1]

[1]Department of Pharmacology, Konaseema Institute of Medical Sciences and Research Foundation (KIMS & RF), Amalapuram, Andhra Pradesh, India,
[2]Department of Pharmacology, KVG Medical College, Sullia (DK), Karnataka, India,
[3]Department of Orthopaedics Konaseema Institute of Medical Sciences and Research Foundation (KIMS and RF), Amalapuram, Andhra Pradesh, India

Received: 12 August 2016
Accepted: 16 August 2016

***Correspondence to:**
Dr. Kulkarni Dhananjay,
Email: ksdhanu@rediffmail.com

ABSTRACT

Background: DU90% is useful tool for assessing drug prescribing pattern. In this, drugs constituting 90% of the prescription volume are identified. Size of the DU90% segment helps us to assess rational prescribing. Large number of drugs in the DU90% segment indicates less rational prescribing, whereas small number suggests more rational prescribing.
Methods: Study was carried out in orthopaedic out-patient department (OPD) for a period of three months. Only OPD based NSAID containing prescriptions were included. Data was analyzed based on demographic parameters, prescription indices, fixed dose combinations (FDC) and co-prescription of gastro-protective agents (GPA). DU90% was calculated based on defined daily dose (DDD) with their respective value in Anatomical Therapeutic Chemical (ATC) classification code. Defined daily dose is calculated as DDD/1000/day.
Results: Diclofenac (38%) was the commonest NSAID prescribed. Diclofenac +chymotrypsin (25%) was the commonest FDC prescribed. Piroxicam (19%) was the commonest NSAID prescribed in monotherapy form. Co-prescription of GPA was high (96%). 5 of the 7 prescribed NSAIDs constitute to DU90% segment.
Conclusions: Preferential cyclooxygenase-2 (COX-2) inhibitor NSAIDs were more preferred. Number of prescribed NSAIDs constituting to DU90% is more, thus prescription pattern needs further rationalization. Further large scale study is required to bring out more details about NSAID prescription pattern and its rational use.

Keywords: DU90%, FDC, DDD, NSAID, Prescription pattern, GPA

INTRODUCTION

DU90% is an innovative approach to assess drug prescribing. Using this approach, the drugs that represent 90% of the drug prescription/sales volume are identified.[1] The rationale behind the development of DU90% rests on an assumption that a low number of products prescribed is associated with more rational prescribing practices. Furthermore, the approach can be used to assess what proportion of the drugs that represent 90% of the volume is made up by drugs listed in essential drug list.[2]

DU90% does not directly reflect the quality of prescribing but it seems to be a useful tool in the quality assessment process through indicating areas that need to be analysed in more depth. The approach can be used for exploring drug prescribing data in a rapid, effective and inexpensive way.[3] DU90% identifies the number of drugs making up to 90% of the total volume, measured in Defined Daily Dose (DDD) or number of prescriptions (NP), during a certain period of time. According to DU90% concept a physician using few, well known and proved drug alternatives in the daily practice, would provide a more rational prescribing and hence a higher quality of care. It is a purely descriptive prescription indicator.[4] Size of the DU90% segment helps us to assess rational prescribing. A very large number of drugs in the DU90% segment indicate less rational prescribing. On the other hand, a small number of drugs in DU90% could suggest a more rational prescribing. The assumption that less is better is used as prescribing indicator in DU90%.[2]

The defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults. It will only be assigned for drugs that already have an anatomical therapeutic chemical (ATC) classification code. DDD is a unit of measurement and does not necessarily reflect the recommended or prescribed daily dose.[5] Drug consumption data presented in DDDs only give a rough estimate of consumption and not exact picture of actual use. DDDs are not established for topical preparations, sera, vaccines, anti-neoplastic agents, allergen extracts, general and local anaesthetics and contrast media.[4] DDD is most commonly calculated as DDD/1000/day.

The treatment of pain and inflammation is an important area of therapeutics. Over the past two decades, non-steroidal anti-inflammatory drugs (NSAIDs) have played a central role in these indications. NSAIDs constitute the largest single group of drugs used worldwide, constituting more than 20% of all drug prescriptions.[6] In India over 400 formulations of NSAIDs are marketed, resulting in wide spread exposure of patients to this class of drugs and its adverse effects.[7] Hence studies that evaluate the pattern, extent and frequency of NSAID prescriptions are valuable, thus in this regard this present study attempts to assess NSAID prescription pattern using DU90% methodology.

METHODS

A prospective, non-interventional, cross sectional (observational) study was carried out in the out-patient department of orthopaedics, Konaseema Institute of Medical Sciences (KIMS), Amalapuram, Andhra Pradesh. Necessary Institutional ethics committee clearance for the conduct of the study was taken. The study was conducted over a period of three months (March to May 2016). During the study period NSAIDs containing prescriptions were included in the study. Prescriptions of in-patients, surgical intervention patients, serious life threatening injury patients or patients who refuse to give consent for the screening of their prescriptions were not included.

Since it was a non-invasive and descriptive study, patient's willingness to screen their prescription will be considered as their consent. Due co-operation from the staff of orthopaedic department was sought. Personal details of the patients were kept confidential. All the relevant prescription data was noted down in a specialized proforma for Microsoft excel entry.

Descriptive statistical analysis of the data using tabular forms, percentage and bar diagrams was done. Data on demographic parameters, prescription indices, fixed dose combinations and gastro-protective drugs was high lightened. DU90% was calculated based on number of prescriptions as well as by defined daily dose (DDD) with their respective value in anatomical therapeutic chemical (ATC) classification code. Here Defined daily dose is calculated as DDD/1000/day and the formula used was:

$$\frac{\frac{\text{DDD}}{1000}}{\text{day}} = \frac{\text{Total no of dosage units prescribed X strength of each dosage}}{\text{DDD X duration of study X total sample size}}$$

RESULTS

Overall 200 NSAIDs containing prescriptions were included in this study. Female cases (56%) were more than male counterparts. Maximum cases (48%) belong to 26 years to 59 years of age group. Table 1 highlights demographic profile and prescription indices of the present study. Number of NSAIDs prescribed in 200 prescriptions was 248; hence average NSAID prescribed per prescription was 1.24. Antibiotics were prescribed in 40 prescriptions. Calcium supplementations were prescribed to 120 cases; mainly to above 40 year female patients.

In this study NSAIDs were prescribed both as monotherapy and as FDCs. Monotherapy was prescribed in 88 cases and FDCs to 160 cases. Table 2A shows details of NSAID containing FDCs. Diclofenac+chymotrypsin (25%) was the commonest FDC prescribed, followed by etodolac+paracetamol (20%) combination. Thiocolchicoside was the commonest non-NSAID component found in FDC. Paracetamol was only prescribed (72) in FDC form, either with other NSAIDs (48) or with tramadol (24). In this study co-prescription of Gastro-protective agents (GPA) was high. Table 2B shows details of GPA co-prescription. Almost all NSAID prescriptions (96%) were associated with GPA co-prescription. Ranitidine was the commonest GPA (83.33%) prescribed.

Figure 1 shows details of NSAIDs prescribed in monotherapy and in FDC form. Piroxicam, indomethacin and lornoxicam were only prescribed in monotherapy

form, whereas etodolac, paracetamol and aceclofenac were only prescribed in FDC form.

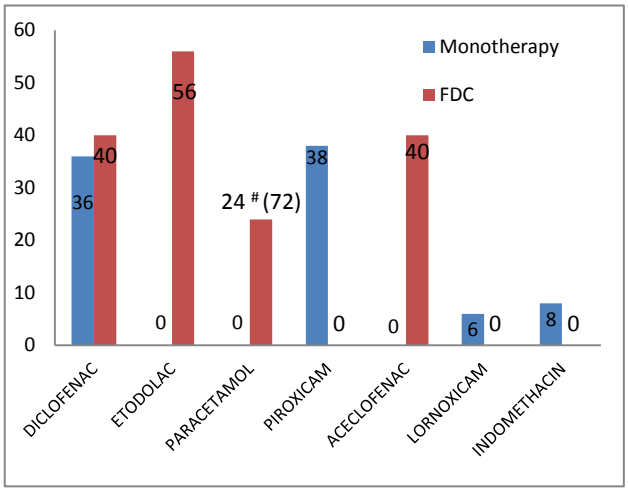
Table 1: Demographic profile and prescription indices.

Demographic profile	
Total sample size	200(n)
Male	88
Female	112
Age	
25 years and below	56
26-59 years	96
60years and above	48
Prescription indices	
Total number of drugs prescribed	728
Average Number of drugs per prescription	3.64
Number of prescription containing calcium supplementation.	120
Average number of NSAIDs per prescription	1.24
Number of FDCs containing NSAIDs prescribed	160
Number of NSAIDs prescribed in monotherapy form	88
Number of analgesic gel prescribed	08
Number of antibiotics prescribed	40

Table 2: Details of NSAID containing FDCs and co-prescription of GPA.

A. Fixed Dose combinations of NSAIDs		
FDC of NSAIDs	**Number of prescriptions**	**Percentage (n = 160)**
Diclofenac + chymotrypsin	40	25
Etodolac + Paracetamol	32	20
Etodolac + Thiocolchicoside	24	15
Tramadol + Paracetamol	24	15
Aceclofenac + thiocolchicoside	24	15
Aceclofenac + Paracetamol	16	10
B. Co-prescription of gastro-protective agents (GPA)		
GPA drug	**Number of Prescriptions**	**Percentage (n = 192)**
Ranitidine	160	83.33
Pantoprazole	32	16.67

Diclofenac was the only NSAID which was prescribed in both forms. Piroxicam was the commonest NSAID prescribed in monotherapy form. Etodolac was the commonest NSAID prescribed in FDC form. With the combination of both forms, overall Diclofenac (76) was the commonest NSAID prescribed followed by etodolac (56), aceclofenac (40), piroxicam (38), paracetamol (24), Indomethacin (8) and lornoxicam (6) respectively. Number of paracetamol FDCs prescribed were 72, of these 24 was with tramadol combination. Only these 24 FDCs were shown in Figure 1, as the rest 48 FDCs were with other NSAIDs like etodolac and aceclofenac and are already included in their respective sections.



#Overall paracetamol FDCs were 72, of this 24 is with tramadol and is shown in figure, rest 48 is with other NSAIDs like etodolac and aceclofenac and thus already included in their respective sections.

Figure 1: Details of NSAIDs prescribed in FDC and in monotherapy form.

Table 3 shows various indications for NSAID prescription in this study. Low backache (28%) was the commonest indication, followed by joint sprain (21.5%), trauma (18%) and others (32.5%) respectively.

Table 3: Indications for NSAID prescription.

Clinical conditions	No. of prescriptions	Percentage (n=200)
Low backache	56	28
Joint sprains	43	21.5
Trauma	36	18
Tendinits and bursitis	30	15
Arthritides	29	14.5
Others	06	03

Table 4 shows details of drug constituting DU90% (based on number of prescription and DDD). For each drug defined daily dose (DDD) and ATC code was provided. DDD/1000/days was calculated as per its formula for each drug. Out of seven different NSAID prescribed, five of them constitute to DU90% and these are diclofenac, etodolac, aceclofenac, paracetamol and piroxicam respectively. Only indomethacin and lornoxicam were out of purview of DU90%.

Table 4: Details of NSAIDs constituting to DU90%.

Drugs	ATC CODE	DDD	No. of prescription (n=248*)	DDD/1000/days
Diclofenac	M01AB05	100 mg	76	29.56
Etodolac	M01AB08	400 mg	56	43.55
Aceclofenac	M01AB16	200 mg	40	15.56
Paracetamol FDC With other NSAIDs(48**) and With Tramadol (24)	N02BE71 N02AJ13	325 mg	24	18.67
Piroxicam	M01AC01	20 mg	38	14.77
Indomethacin	M0IAB01	100 mg	08	3.11
Lornoxicam	M01AC05	12 mg	06	3.11

*Here n is 248 as some prescriptions has more than one NSAID, although total number of prescriptions for the study were 200. Hence average NSAIDs prescribed per prescription was 1.24.
**48 is not part of the calculation, as NSAID in these FDCs of paracetamol is taken as principal component and is already included in their respective column.

DISCUSSION

The study was conducted in out-patient orthopaedic department for a period of three months. Overall 200 NSAID containing prescriptions were included and analyzed in this study. Overall diclofenac was the commonest NSAID prescribed in this study, same trend was observed in Dhaka prescription study.[8] Similarly diclofenac was also the commonest NSAID prescribed in a study conducted by VS Manohar et al.[9] In this present study none of the selective cyclooxygenase-2 (COX-2) inhibitors were prescribed, instead preferential COX-2 inhibitors (diclofenac, etodolac and aceclofenac) and traditional NSAIDs (like piroxicam) were more preferred.[10]

High frequency of preferential COX-2 inhibitor and non-selective NSAID prescription points towards the changing trends observed in the prescriber‘s preference for NSAID prescription after the withdrawal of rofecoxib.[11] This changing trend might be due to increased awareness and recent reports of cardiovascular (CVS) complications associated with various selective COX-2 inhibitors.[9] Similarly a study conducted in New York, shows that COX-2 inhibitors constituted 37% of NSAID prescription before the withdrawal of rofecoxib. After withdrawal, their frequency decreased to 16% within one year and progressively decreased further in follow up studies.[12]

Low backache was the commonest indication for NSAID prescription. Similar indication is seen in other studies, like in Dhaka study, where low backache and trauma were the commonest indications for NSAIDs; another study in Dhaka also shows similar findings.[8,13] Present study shows high prevalence of co-prescription of GPAs (96%). High frequency of GPA prescription can be attributed to prescriber‘s preference for non-selective NSAIDs, which are more prone to cause gastritis and peptic ulceration. Similar high trend was also observed in two different Spanish studies where frequency of GPAs co-prescription was 64% and 85% respectively.[14,15] This high co-prescription of GPA can also be attributed to defensive trend observed by prescribers in order to decrease NSAID induced complication, especially after the withdrawal of rofecoxib.[16] In our study ranitidine was the commonest GPA prescribed and was more preferred than pantoprazole, unlike the study done by VS Manohar et al where proton pump inhibitors were more preferred.[9]

In this study NSAID containing FDCs are prescribed in large numbers (n=160). Diclofenac+Chymotrypsin combination is the commonest FDC prescribed followed by Etodolac+Paracetamol, aceclofenac+paracetamol, tramadol + paracetamol and others. This high prevalence of FDC prescription is similar to a study conducted in Uttaranchal, where FDC prescription frequency was more than 49%.[17] A similar combination of NSAID FDCs were also prescribed in Ahmedabad study.[18] However many combination of NSAID as FDCs is not recommended as these combinations have no drug synergism and moreover the combination can increase the chances of adverse events and overall cost of prescribing.[19] Nevertheless some useful analgesic combinations do exist, such as combination of tramadol with paracetamol. They synergise with each other as site of actions are different for both the drugs.[20]

The anatomical therapeutic chemical (ATC) classification divides drugs into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties.[21] The DDD is the assumed average maintenance dose for a drug used for its main indication in adults. The DDD provides a fixed unit of measurement that is independent of price and formulation, and makes it easier to compare drug

utilisation across studies. The major benefit of studying drug utilization using DDD is that the dosage and the duration of use are both factored in to the calculation. The dosage, frequency and duration of use are variable in different patients, and these differences can be overcome by using the DDD as a measure of drug consumption.[22] DU90% which can also be expressed in terms of DDD, basically assess what number of drugs constitutes to 90% of prescription, less the number of drugs constituting DU90%, more rational is the prescribing.[2]

Five of the seven NSAIDs prescribed in this study constitute to DU90%. As more drugs constitute to DU90%; prescription pattern needs further rationalization. In this study only preferential COX-2 inhibitors and traditional NSAIDs are part of DU90%. This finding is similar to study done by J Ćalasan et al where only preferential COX-2 inhibitors were part of DU90%.[23] Contrary to our result COX-2 inhibitors were the major constituents of DU90% in Korean study.[24] Similarly in PGI Chandigarh, before the withdrawal of rofecoxib, COX-2 inhibitors were the major component of DU90%.[25]

After the withdrawal of rofecoxib (2004) and subsequent news of increased CVS adverse effect seen with selective COX-2 inhibitors, prescribers increasingly replaced COX-2 inhibitors with non-selective NSAIDs and preferential COX2 inhibitors, considering it as a class effect and not as individual drug effect.[26] This observation can very well be noted in our study as DU90% segment is mainly constituted by preferential COX-2 inhibitors and non-selective NSAIDs.

CONCLUSION

DU90% is one of the innovative tool for assessing drug prescribing pattern. It also helps in understanding drug utilization over a period of time. In this study, of the seven NSAIDs, five were part of DU90%. As more drug constitute to DU90%; prescription pattern needs further rationalization. Preferential COX-2 inhibitors were more preferred than selective COX-2 inhibitors. Large scale study of DU90% with involvement of more departments will help further to highlight prescription pattern of NSAIDs and its rational use.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kulkarni D, Kokila BN, Sahu SK, Kumar RG. Drug utilization 90%: an innovative method in assessing quality of drug prescription with specific reference to non-steroidal anti-inflammatory drugs prescription. Int J Basic Clin Pharmacol 2016;5:1746-51.