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Research Article

**UTILIZATION PATTERN OF NSAIDs; A PROSPECTIVE
ANALYSIS OF PATIENTS IN A TRAUMA CARE CENTRE**Niby ^{1*}, Elna Paul ¹, Jeethu k shaji ¹, Lalitha S ², Sivakumar T ³¹ Pharm D Interns, Nandha College of Pharmacy, Erode, Tamil Nadu, India.² Associate professor, Department of Pharmacology, Nandha College of Pharmacy, Erode, Tamil Nadu, India.³ Principal, Nandha College of Pharmacy, Erode, Tamil Nadu, India.**Abstract:**

Background and purpose: NSAIDs are commonly used for managing mild to moderate pain while in most trauma patients injuries are too severe to be relieved by NSAIDs alone. NSAIDs are the most used and abused drugs in the world today. Therefore, the aim of this study was to analyze the drug utilization pattern of NSAIDs in a trauma care centre. **Objectives:** To evaluate the number of patients exposed to specified NSAIDs within a given time period, estimate (e.g. on the basis data on a disease) to what extent NSAIDs are properly used, overused or underused. Determine the pattern or profile of NSAID use and the extent to which alternative NSAIDs are being used to treat particular conditions. **Methodology:** A prospective observational study on drug utilization and prescribing pattern of NSAIDs in a trauma care Centre was carried out for a period of 6 months and 1200 prescriptions of different condition were randomly selected. Data were analyzed using descriptive statistics and the results were presented by using frequency distribution table with Microsoft excel. **Results:** The most common indication for NSAIDs in our study was Fractures (41.58%), Arthritis (16.91%), Spine disorders (13.41%), Crush injuries (7.16%), ACL tears (2.55%) and others (18.41%). The present study shows that acetaminophen (97.75%) was the most frequently used non-opioid analgesic followed by Non-selective COX-inhibitors (71.41%) and preferential COX-2 inhibitors (55.75%). The duration of administration ranged from 5-15 days (mean 5.95 days) which conformed to the standard practice. About 4.08% patients took Acetaminophen more than 4g/ day according to this survey and that shows overdose of acetaminophen. **Conclusion:** Our study has shown that NSAIDs continue to be the drug of choice as analgesics & anti-inflammatory agents for fractures & degenerative joint diseases in this trauma care center. Non-selective COX inhibitors are preferred over the preferential COX 2 Inhibitors. Exclusion of selective cox-2 inhibitors can be seen. Acetaminophen is a viable alternative to the NSAIDs, High prevalence of GPAs co-prescription was noted here as non-selective NSAIDs prescribed according to the standard guidelines.

Keywords: NSAIDs, drug utilization, COX-inhibitors, Acetaminophen.***Corresponding author:**

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INTRODUCTION:

Non-steroidal anti-inflammatory drugs (NSAIDs) are the most used and abused drugs in the world today (annually about 20,000 tons of Aspirin is consumed in United States alone). Pain and fever being the most common complaints, these drugs naturally are in great demand and doctors have no hesitation to cater to this. [1]The most recent practice guidelines released by the American Society of Anaesthesiologists (ASA) Task Force in 2012 stated that under treatment of postoperative pain results in multiple undesirable physiologic and psychological outcomes including pulmonary complications, extended hospital or intensive care unit stay, unplanned readmission, and the development of chronic pain. The prevalence of acute postoperative pain is about 80 %, of which 86 % report moderate to severe pain. [1].

Two forms of cyclooxygenase, COX-1 and COX-2. The first COX-1 is present in the most of the cells and tissues and it is for regulation of physiological processes of the organs but COX-2 is inducible peripherally as expression of an injury because the principal role of COX products are swelling and pain, effects of the NSAIDs are due to the inhibition of cyclooxygenases and in particular to COX-2 inhibition while many side effects associated with NSAIDs are due to inhibition of COX-1. Under this aspect classic NSAIDs block both COX1 and COX2 without selectivity while selective COX-2 inhibitors seem to present similar analgesic efficacy inducing a lower gastrointestinal toxicity. [2] Current available NSAID therapies are reversible competitive inhibitors (except aspirin), variably blocking both COX-1 and COX-2 isoforms (ibuprofen, diclofenac, ketorolac, ketoprofen, mefenamic acid, piroxicam, meloxicam, lornoxicam, and indomethacin) or selective inhibitors of COX-2 (celecoxib, rofecoxib). [1]

Currently the guidelines of American Society of Anesthesiologists, Task Force on acute Pain Management and Italian Group of Analgesia, advocate that NSAIDs have a significant role in post-operative pain control. [4] The use of NSAIDs is particularly interesting in a trauma care setup, if the pathophysiology of postoperative nociceptive inflammatory pain is known: nociceptors, the nerve endings of primary sensory neurons such as A δ and C fibers which are stimulated directly or sensitized by the substances released by traumatized inflamed tissues. The set of inflammatory mediators in the tissues after injury such as prostaglandins, bradykinin, and leukotriene's, serotonin, substance P, thromboxane, platelet activating factor, etc., activates

nociceptors and induces primary and secondary hyperalgesia. The inflammation increases the excitability of neurons with reduction of the threshold, potential duration and intensity of activation of these nerve endings which leads to the expansion of the receptive field to the tissue closest not damaged the peripheral hyperalgesia. [3] Also the prostaglandins play a fundamental role in bone fracture repair stimulating both bone formation and bone reabsorption binding different receptors and that NSAIDs are routinely used as analgesic regimen for pain control in postoperative periods of patients undergoing to surgical repair. More recently, beneficial effects of ketorolac in rib fractures have been reported. [3]The drug reduces pain, decreases incidence of pneumonia and number of hours of postoperative ventilation. NSAIDs are well known to be associated with gastrointestinal, renal, and cardiovascular side effects. [1]

One of the most pressing problems facing public health providers and administrators in many countries is ensuring the rational use of drugs. The Conference of Experts on the **Rational Use of Drugs**, convened by the World Health Organization (WHO) in Nairobi in 1985, defined rational use as follows: The rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community. [5] Periodic evaluation of drug prescribing patterns needs to be done to enable suitable modifications in prescription of drugs to increase the therapeutic benefit and decrease the adverse effects. Rational drug prescribing can be defined as appropriate drugs prescribed in the right dose, at correct time intervals and for a sufficient duration. [7]

Prescription pattern monitoring studies (PPMS) are drug utilization studies with the main focus on prescribing, dispensing and administering of drugs. They promote appropriate use of monitored drugs and reduction of abuse or misuse of monitored drugs. NSAID use in the hospital must be monitored. [7] This is usually performed by the pharmacy department. Specific elements to be monitored include the amount of different NSAIDs used during a given period and trends in NSAID use over time. In addition to monitoring, audits should be undertaken to explore the appropriateness of NSAID use. So, This drug utilization of NSAIDs in a trauma care centre was designed because, a large number of NSAIDs are being using for the post-operative pain management. [7]

MATERIALS AND METHODS:

Study design: A prospective observational study on drug utilization and prescribing pattern of NSAIDs in trauma care Centre.

Study site: Ganga Medical Care and Hospital Pvt. (Ltd) Coimbatore, Tamil Nadu.

Duration: The study is carried out for a period of 6 months from February 2017 – July 2017.

Study Population: It covers most of the inpatients in hospital.

Sample size: 1200 prescriptions of different condition are randomly selected.

Study criteria: Musculoskeletal pain included. Low backache, rheumatoid arthritis, osteoarthritis, cervical spondylosis, avascular necrosis, sciatica, myalgia and joint pain. Adult patients aged above 18 years and willing to give consent were included. Patients who had Gastro-esophageal reflux disease (GERD), peptic ulcer, patients with cardiovascular diseases and pregnant women were excluded.

Data collection: We collected cases from different ward of hospital, ICU, NICU, HDU etc. During data collection patients were informed about the study using patient information format. A regular ward round into the different ward was carried out. The medical charts of the patients were screened for

appropriateness in all possible ways. Patient demographics like age, weight, date of admission, the length of stay, medical histories including drug allergies were entered into the specially designed data entry form. Patient medical history has also been categorized. ADR's of NSAIDs were analyzed by NARANJO scale and reported.

Data analysis: The major parameters analyzed in our study are: Prescribing pattern of NSAIDs (generic form and capitalization), NSAIDs usage pattern (overused or underused), Appropriateness of NSAID usage, Duration of therapy. Relevant drug interactions, ADR's and other medication related events.

Statistical method: Data were analyzed using descriptive statistics and the results were presented by using frequency distribution table with Microsoft excel .

RESULTS AND DISCUSSIONS:**Based on age and gender-**

When we categorized the patients according to the age group and gender. We found that out of 1200 patients, 762 patients were males and 438 patients were females. On the basis of age distribution, patients belong to the age less than 18 is 124, 18-45 is 503, 46-60 is 273 and greater than 60 is 300.

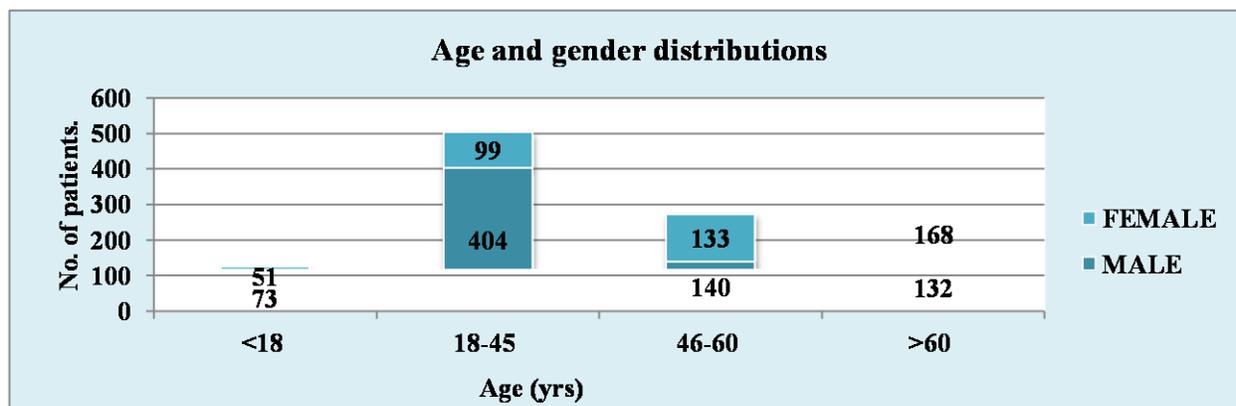


Figure no: 1 Age and gender distributions

Based on indication-

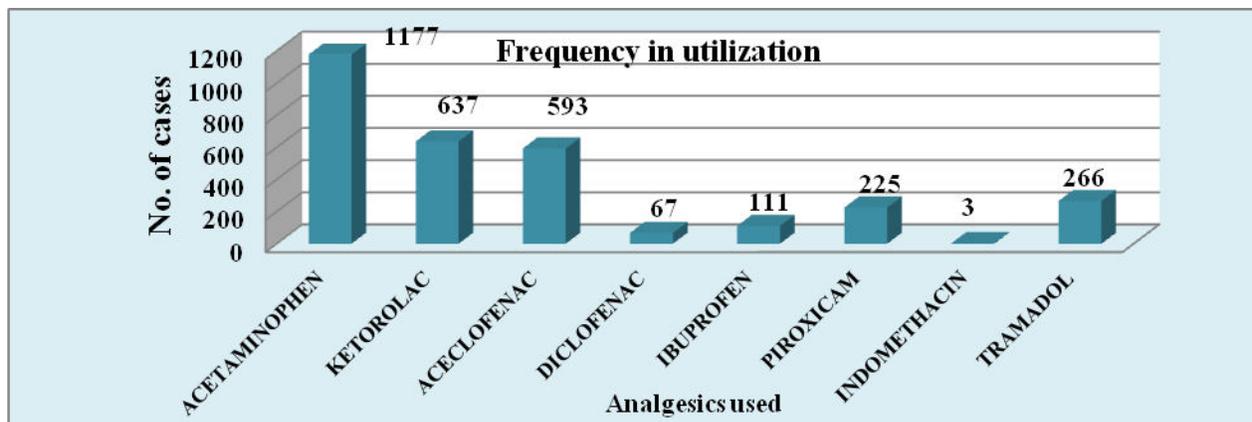
The most common indication for NSAIDs in our study was Fractures (41.58%), Arthritis (16.91), Spine disorders (13.41%), Crush injuries (7.16%), ACL tears (2.55%) and others (18.41%). Fracture was the condition for which NSAIDs were most commonly prescribed followed by other injuries, arthritis, spine disorders, crush injuries and ACL tear. NSAIDs are prescribed for the pre and post operative pain management in these conditions.

Table No: 1 Indication of NSAIDs

INDICATION	MALE	FEMALE	TOTAL (n=1200)	PERCENTAGE (%)
Osteoarthritis	37	111	148	12.33%
Rheumatoid arthritis	5	23	28	2.33%
Chronic arthritis	16	11	27	2.25%
Scoliosis	7	13	20	1.66%
Other spinal disorders	79	62	141	11.75%
Wrist/hand fractures	97	32	129	10.75%
Foot/ankle fractures	162	42	204	17.00%
Femur fracture	111	55	166	13.83%
Acl tear	24	6	30	2.50%
Crush injuries	69	17	86	7.16%
Others	160	61	221	18.41%
Total	767	433	1200	

Based on frequency in utilization of NSAID-

The present study shows the use of conventional NSAID with high frequency of acetaminophen (98.01%) followed by ketorolac (53.08%), aceclofenac (49.41%) and piroxicam (18.75%). Even though gastrointestinal toxicity is the major limitation of non-selective NSAID, there was no clinically significant toxicity recorded in this study. This suggest that non selective NSAIDs are relatively safe for short term use (<10days), though it does not exclude the long term toxicity. This result shows similarity when comparing with a study done by **M. Hyllested *et al.***, (2002).The study concluded that paracetamol is a viable alternative to the NSAIDs, especially because of the low incidence of adverse effects, and should be the preferred choice in high risk patients. [8]

**Figure no: 2 Frequency in utilization of NSAIDs****Based on pharmacological classification of NSAIDs**

The present study shows that acetaminophen (97.75%) was the most frequently used non-opioid analgesic followed by Non-selective COX-inhibitors (71.41%) and preferential COX-2 inhibitors (55.75%). **Praveen Kumar Ingle *et al.***, (2015) did a study of rational prescribing and dispensing of prescriptions with NSAIDs in orthopaedic outpatient department. The study shows more use of traditional NSAIDs and underutilization of COX2 inhibitors. The study suggests that there is the immense scope of improvement for prescribing in the hospitals. [9]

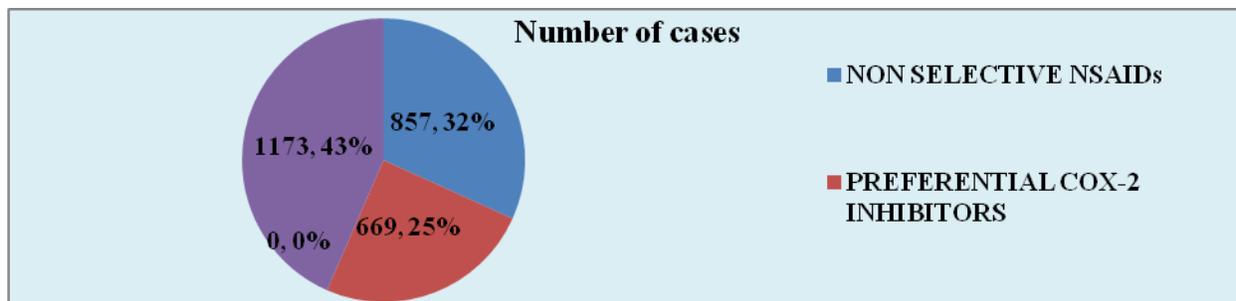


Figure no: 3 Pharmacological subclass of NSAIDs.

Based on the pattern of analgesics and route of administration

The route of administration depends upon the dosage form of a particular drug. Also depends upon the severity of the pain and the patient's condition. For example, in post-operative patients, Acetaminophen is administered through parenterally for the two days after surgery, but it changes into orally after two days. **Ravindran. D et al.**, (2009) did a study on Perioperative use of non-steroidal anti-inflammatory drugs and the route by which they were administered. The study reveals that NSAIDs were still widely used as analgesics for many surgical procedures. Intravenous (IV) NSAID administration is the preferred route because of its reliability and speed of onset. [10]

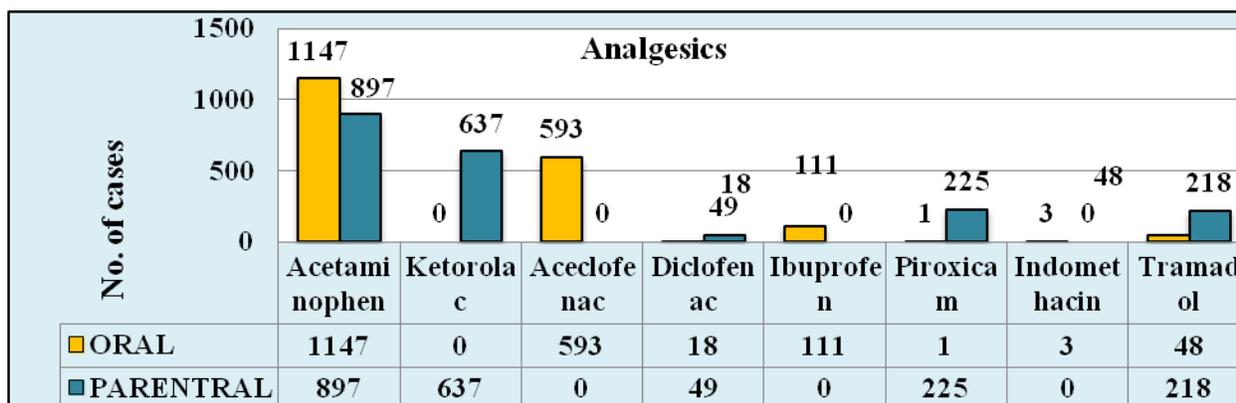


Figure no: 4 Pattern of analgesics & route of administration

Based on No. of NSAIDs used

About 46.91% (563/1200) prescriptions containing multiple NSAIDs were analysed and mostly with a combination ratio with acetaminophen observed. Percentage of **single NSAIDs** (17.4%) was very low compared with **double NSAIDs** (35.91%) and prescription containing **multiple NSAIDs** (46.91%), another finding is regarding with combination of NSAIDs. Acetaminophen is the major combinative drug which can be seen in most of the case as single as well as with combination. The major combination used was acetaminophen with ketorolac followed by acetaminophen with aceclofenac and other combinations such as acetaminophen with piroxicam.

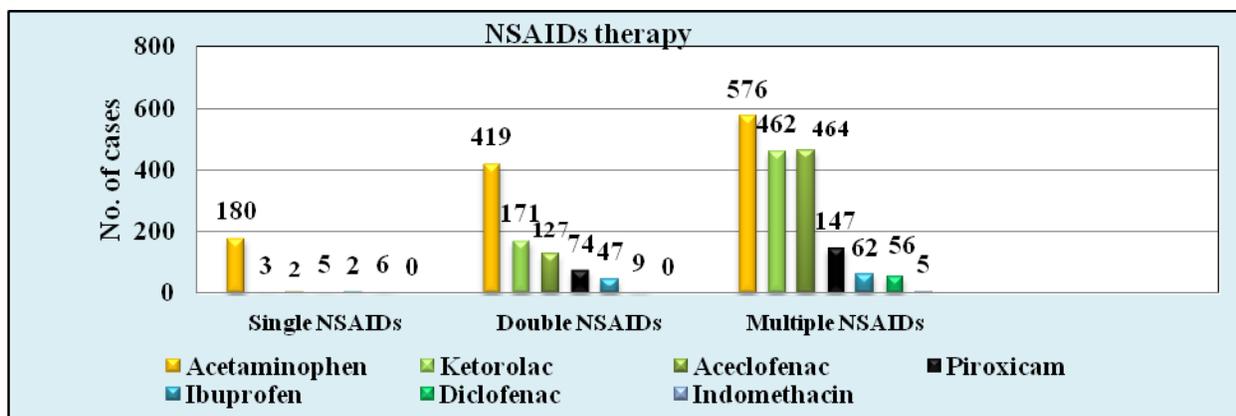


Figure no: 5 Number of NSAIDs used

Based on gastro protective agents used

Proton pump inhibitor, Pantoprazole was most commonly co-prescribed (95.91%) compared with H2 Blockers (4.08%). Amongst the H2 Blockers, Ranitidine was most commonly co-prescribed. **Birendra Shrivastava *et al.*, (2016)** performed a study on NSAIDs related gastrointestinal side effects and their management, which conclude that PPIs significantly reduce gastric and duodenal ulcer and their complications in patients taking NSAIDs or COX-2 inhibitors. Although superior to placebo, high-dose H2RAs can reduce the risk of NSAID-induced endoscopic peptic ulcers are significantly less effective than PPIs. [11]

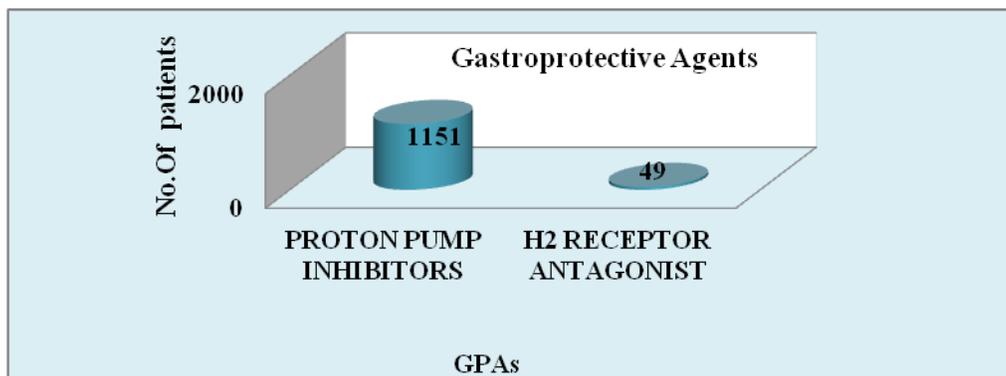


Figure No: 6 Various GPAs used

Acetaminophen was most prescribed drug according to this prescription reading every third prescription contained it and dosing error was so extremely high, it can cause serious liver problem even with less than maximum dose which is usually a 4 g/day. People were co-prescribed by multiple NSAIDs adjunct with acetaminophen reflects it is less far potent than other analgesics. About 4.08% patients took Acetaminophen more than 4g/ day according to this survey and that shows overdose of acetaminophen, which shows irrational prescribing habits of health practitioner and the poor knowledge of nurses. The duration of administration ranged from 5-15 days (mean 5.95 days) which conformed to the standard practice. This suggest that non selective NSAIDs are

relatively safe for short term use (<10 days), though it does not exclude the long term toxicity.

This study reports shows that only 1% prescriptions are prescribed by generic name, which shows irrational prescribing habits of physicians. The treatment of disease by the use of essential drugs prescribed by their generic names, has been emphasized by the WHO and National Health Policy of India.

CONCLUSION:

The correct use and choice of different analgesic depends on habit of hospital, beliefs of health and the routes of administration that is preferred. In acute setting, considering the contraindications and

reducing dosage in elderly, these drugs can be utilized with efficacy in all almost types of surgery. Their role is irreplaceable. This study shown that NSAIDs continue to be the drug of choice as analgesics & anti-inflammatory agents for fractures & degenerative joint diseases in this trauma care center. Non- selective COX inhibitors are preferred over the preferential COX 2 Inhibitors. Exclusion of selective cox-2 inhibitors can be seen. Acetaminophen is a viable alternative to the NSAIDs, especially because of the low incidence of adverse effects, and should be preferred choice in high-risk patients. High prevalence of acetaminophen over dose condition. High prevalence of GPAs co-prescription was noted here as non-selective NSAIDs prescribed according to the standard guidelines. An irrational prescribing habit of physicians, mainly brand names used in the prescription is a major finding of our study.

FUTURE RECOMMENDATIONS

Continuing medical education regarding appropriate use of NSAIDs, knowledge of its potential side effects and standard prescription pattern will play vital role in rational prescription of NSAIDs. For a developing country like India, a National Drug Policy is needed to rationalize the drug use. To achieve this, it is very important to determine drug use pattern and monitor drug use profile over the time. Further the practice of evidence based medicine will improve the patient compliance and post-operative pain management more efficiently while prescribing the drugs. These data must serve not only to increase awareness of the limitations and difficulties on the translation of these recommendations into clinical practice, but also stimulate the creation of strategies or tools to increase the appropriate therapy.

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