



Rational and irrational use of analgesics: A review

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ABSTRACT

Analgesic misuse is a worldwide problem in developed as well as developing countries. Heavy use of analgesics, particularly over-the-counter (OTC) products, has long been associated with chronic renal failure. Several studies have reported associations between chronic renal failure and use of other forms of analgesics, including acetaminophen, aspirin, and other non-steroidal anti-inflammatory drugs (NSAIDs). This review highlights the appropriate use, problems, impact of inappropriate use of analgesics and enumerates strategies to improve rational use of analgesic drugs.

Keywords: Analgesics, Rational, Irrational, Misuse, Prescribers, Consumers

INTRODUCTION

The introduction of analgesic drugs was a landmark event and soon these drugs become the most widely used medication not only for the relief of pain and fever but also for their anti-inflammatory effect. Apart from that these pain killers are most widely used; they are the abused class of drugs worldwide. [1]

The choice of analgesic is governed by the severity of pain, the individual needs and the circumstances of the patient [2]. Analgesics are available as over the counter (OTC) products and are widely misused and abused, probably because, their uses are not always without severe adverse effects. Sporadic consumption of analgesics may relieve the symptoms of pain for a time; the actual pathology may sometimes be aggravated, complicated and even turn to fatality in some cases. [3]

Irrational drug prescription patterns consist of poly pharmacy, use of drugs that are not related to diagnosis, or unnecessarily expensive, inappropriate use and irrational self-medication, with many insufficient quantities consumption of drugs. [4] Breaking patients' beliefs about the abuse and misuse of analgesics is a key factor in controlling the unnecessary use of analgesics. Also understanding patients' attitude to analgesic usage may facilitate more effective communication between the clinician and patient, as well as aid in the development of strategies to educate patients

and the public [5], therefore this review addresses the misuse, causes, impacts of analgesics as well as suggest strategies to promote rational use of these drugs .

PAIN MANAGEMENT

Pain is the commonest symptom that takes patients to doctors in Nigeria, but the complaint does not mean that an analgesic is needed. Although drug therapy is the mainstay of pain treatment, it is not all pains that are needed to be relieved by drugs. Simple measures such as good food, exercise, position changes, massage, hydrotherapy, relaxation and resting can be used to control some types of pain [6].

The first step in managing pain is to identify the disease, lesion, or injury origin of pain, which until recently comprised the entire diagnostic process [7]. There are several approaches to management of pain and combining approaches can result in additive or greatly enhanced effect [8]. Optimal management of pain requires that the clinicians should have a conceptual framework for what is happening to the patient in mind and body [9].

The non-pharmacological therapy of pain management is considered to help the standard pharmacological treatment in pain management. This management aims to treat the affective, cognitive, behavioral and socio-cultural dimensions of the pain. This is dependent on the abilities and

preferences of the patient, it should be underlined for the patients that these are used together with medical and pharmacological treatments, the use of non-pharmacological methods should be included to the care plan when patient is appropriate and willing [10].

The management of pain requires the management of the whole patient, rather than the irrational prescription of analgesic resulting to abuse of this important class of drugs without providing adequate relief of pain [11].

IMPORTANCE OF ANALGESICS

Analgesics currently represent the mainstay of pain management, with an array of drugs available, aspirin, acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), these are classified as non-narcotic (non-opioid) analgesics while the mixed agonist and antagonists are narcotic (Opioid) analgesics [12].

NON-NARCOTIC /NON-OPIOID ANALGESICS

These are non-opiates that relieve pain without depressing the CNS. Several analgesics, unrelated to the opiates have in addition to analgesic effects anti-inflammatory and antipyretic properties [12]. They include;

Aspirin: Aspirin is used more widely for pain relief than are any other classes of drugs. Aspirin alleviates pain by virtue of a peripheral action; direct effects on the CNS also may be involved. Aspirin has analgesic, anti-inflammatory and antipyretic properties which many drugs under this group do not have. The dose of aspirin depends on the condition being treated. The types of pain usually relieved by aspirin are those of low intensity that arise from integument structures rather than from viscera, especially headache, myalgia, rheumatoid arthritis and rheumatic fever, neuralgia, dysmenorrhea and arthralgia [12, 13].

Acetaminophen: Analgesia is achieved through central but not peripheral inhibition of prostaglandin. Although effective in mild pain, acetaminophen is not anti-inflammatory. Acetaminophen is a suitable substitute for aspirin for analgesic, it is particularly valuable contraindicated (e.g. those with peptic ulcer) or when the prolongation of bleeding time caused by aspirin would be disadvantage. Therapeutically, it is used for pain relief in the symptomatic treatment of various musculoskeletal and joint disorders [13].

Non-steroidal anti-inflammatory drugs (NSAIDs): NSAIDs reduce pain by inhibiting the conversion of arachidonic acid to prostaglandins

catalyzed by COX isozymes. Nonselective NSAIDs inhibit COX-1 and COX-2, the nonselective action inhibits the formation of both gastroprotective-mediating prostaglandins and pain-promoting prostaglandins, increasing the risk of serious toxicities such as gastrointestinal (GI) ulceration and bleeding. To mitigate risk of GI adverse events, proton pump inhibitors are recommended for use in some patients using NSAIDs. They include ibuprofen, piroxicam, diclofenac, naproxen have been used successfully to relieve biliary pain, acute pain of renal colic, postoperative pain, mild pain of sickle cell crisis, and ectopic bone formation pain and dysmenorrhea [9].

NARCOTIC / OPIOID ANALGESICS

Opioid analgesics bind to opioid receptors (primarily the mu opioid receptor), mimicking the action of endogenous ligands. In general, opioid drugs produce analgesia through opioid receptor binding on cell membranes, producing simultaneous activity at multiple presynaptic, postsynaptic, and nervous system sites. Pain consists of both sensory and affective (emotional) components. Opioid analgesics are unique in that they can reduce both aspects of the pain experience, especially the affective aspect [9].

They can be subdivided into

Strong opioid analgesics: They are mainly used in the treatment of severe acute opioid sensitive pain and chronic opioid sensitive cancer pain. Their use in chronic non-cancer pain is somewhat controversial because of fears of dependence and respiratory depression [9]. However, in practice such problem rarely occurs and those fears should not prevent patients being given effective analgesic therapy. Strong opioids include full agonists such as morphine, diamorphine, hydromorphone, methadone, pethidine, oxycodone, levorphanol, fentanyl and alfentanil. Partial agonists such as etazocine, butorphanol, halobuprione and dezocine [12,13]. However, the use of some of these agents can be compromised by their propensity to precipitate withdrawal symptoms in opioid dependent individual. Although opioids in general are less effective in reducing neuropathic pain than nociceptive pain, buprenorphine is very effective in neuropathic pain due to its potent local anesthetic action and voltage-gated sodium channel blockade via the local anesthetic binding site. Buprenorphine efficacy in blocking sodium channels is superior to meperidine, lidocaine, tramadol, morphine, and bupivacaine. Methadone exerts modest NMDA antagonism and inhibition of 5-HT and norepinephrine reuptake. Thus, methadone may be useful in neuropathic pain due

to its cooperative actions as an NMDA receptor antagonist and mu-opioid receptor agonist [14].

Weak opioid analgesics: Codeine is traditionally the weak opioid analgesic of choice, alternatives include dextropropoxyphene and dihydrocodeine. They are often given with non-opioid analgesics for the treatment of moderate to severe opioid sensitive pain [9]. Tramadol is a centrally acting, weak mu opioid receptor agonist and inhibits norepinephrine and serotonin reuptake to promote serotonin release [15]. Tramadol has shown some efficacy in fibromyalgia and neuropathic pain. Because peripheral activity is absent, there are no effects on blood pressure, ulcer, or heart failure. As such, tramadol may be especially useful as an alternative analgesic in high-risk patients [14].

Analgesics like acetaminophen, NSAIDs like ibuprofen, diclofenac, ketorolac and ketoprofen, and opioids like fentanyl are safe and effective analgesics for use in paediatrics in various surgical procedures that produce mild, moderate and severe painful stimuli. However, the side effects of these need to be taken into consideration with constant monitoring carried out [16].

Morphine is the drug of choice in treatment of acute myocardial infarction (AMI) pain but pentazocine is the most commonly used analgesic in clinical practice, because of the beneficial pharmacological actions of buprenorphine and detrimental adverse reactions of pentazocine in the management of pain in AMI, the rational use of safer and cardio protective opioid analgesics like buprenorphine is promoted [17].

ANALGESIC USE IN TERMINAL DISEASE

Pain relief in terminal disease involves the treatment of the cause of pain as well as treatment of the pain itself, together with explanation, reassurance and supportive care to improve any mental and social complicating factors. Patients should be assessed individually and wherever possible treatment should be given by mouth. It should be administered regularly and the treatment should follow the accepted three step analgesic ladder published by WHO in 1986. The stages are as follows:

- i. Non-opioid analgesic such as aspirin or NSAIDs or acetaminophen may be given.
- ii. A weak opioid analgesic such as codeine or dextropropoxyphene plus a non-opioid analgesic, an adjuvant may also be given.
- iii. A strong opioid analgesic preferably oral morphine, a non-opioid analgesic may also be given as an adjuvant [18].

MISUSE OF ANALGESICS

Research conducted by Builders et al, in 2011 indicated misuse, overuse of analgesic drugs by the community practitioners [19]. Also in this community most of the patients were on self-medication preferred injectable to oral analgesics and had already taken analgesics before coming to the hospital [20].

Acetaminophen, a common household analgesic was inappropriately used for headache [20, 21], the abuse of acetaminophen for headache is further confirmed by a research carried out by Edmeads [22], in which several recent data suggest the daily use (or more accurately abuse) of analgesics actually worsen or perpetuates headache [23]. The common reasons for the use of this medicine as such is due to the OTC availability of the drug and the common knowledge of its indications [20, 24]. Caution is taken when acetaminophen is administered to patients with renal impairment, plasma concentration of acetaminophen and its glucuronide and sulphate conjugates are increased in patients with moderate renal failure and in patients on dialysis. It has been suggested that acetaminophen itself may be generated from these metabolites [23].

Research had also shown that acetaminophen and other NSAIDs were the drugs most commonly used for self-medication [21, 24]. Self-medication can be defined as obtaining and consuming drugs without the advice of a physician either for diagnosis, prescription or surveillance of treatment [25].

The use of dipyrone, indomethacine and phenyl butazone, irrational use of these drugs of uncertain safety status had been reported [20,26], chronic analgesic nephropathy, particularly chronic interstitial nephritis and renal papillary necrosis, results from daily use for many years of mixtures containing at least two analgesics and caffeine or dependence-inducing drugs [26].

Negligence of pain management in dentistry and is evidenced by the observed poor quality of Sub optimal analgesic prescription patterns had been described [27].

Indiscriminate use of parenteral analgesics varies considerably among prescribers and patients [19, 20], the reasons is the route is faster and more effective than the oral administration. Analgesic treatment guideline states that injectable analgesics are rarely necessary; they should be reserved for patients with acute pain. Pharmacokinetics and clinical trials indicated that oral forms of drugs are

effective as injections, with oral medications more cost effective [28, 29]. Inappropriate of prescription of analgesics in trade name had been demonstrated [19, 30, 31]. Research had shown that to promote rational use of drugs, drugs should be prescribed in their international non-proprietary names [32, 33].

ANALGESIC NEPHROPATHY CAUSES OF IRRATIONAL USE OF ANALGESICS

Prescribers-lack of education and training is one of the factors influencing irrational use of analgesics, Russel in 1994 carried out a study which showed that physicians with patterns of higher appropriateness rating were found to be younger than recently trained with fewer years of professional experience. They also had more post graduate training [34].

Patient-drug misinformation, this can lead to confusion and hesitancy about taking OTC analgesics. For example, university students are constantly under pressure to work hard to achieve their goals, leaving little room for minor illness, which together with a typical student's social life could lead to the consumption of analgesics as a 'quick fix'. Misconceptions plus the student lifestyle could therefore lead to misuse of analgesics [35]. Continuous analgesic use and the factors influencing this behavior had been investigated, result showed that women generally have a higher intake of analgesics than men, and also that increasing age was associated with continuous analgesic use [35, 36].

Advertising may play an important role in the consumer's choice of analgesic product, misleading advertisement, pressure and promotions from pharmaceutical companies [35,37], this tends not only to influence choice of analgesics but to encourage people to use drugs in situations where they may not be needed and unnecessarily use of expensive analgesics [20].

Lack of adherence to analgesic treatment guidelines in a research conducted by Builders et al, resulted in a significant degree of analgesic misuse by the physicians [19], also another study was carried out which showed that pain prevalence was high in those with analgesic treatment that did not adhere to guidelines than those considered as having appropriate adherence to guidelines. Adherence to analgesic guideline was higher in the large hospitals than in the medium and small hospital, adherence to analgesic guideline improves the quality of prescribing, reduce cost and educate prescribers [38, 39]. Lack of adequate regulatory systems, For example, 36% of countries with a

national policy on drug have no implementation plan [40].The concept of essential drug list (EDL) must be adopted and implemented, good infrastructure and monitoring system are responsible for successful implementation. Countries with a strict and logical drug registration and regulation system have a more cost- effective drug prescription [37].

CONSEQUENCES OF ANALGESIC MISUSE

The impact of this irrational use of analgesics is summarized below

1. Reduction in the quality of analgesic therapy can lead to increased morbidity and mortality. This may result from unavailability of analgesics due to shortage of analgesics supplied. Study had indicated that availability of all analgesics prescribed in the hospital prevented irrational use of these drugs; therefore reduce morbidity and mortality (39).
2. Increased risk of unwanted effects such as adverse drug reactions. Daily use of painkillers led to drug dependence in 1978 and up to date [37]. Abuse of analgesics has long been associated with the development of chronic renal failure which can lead to end-stage renal disease (ESRD) [41].
3. Risk of infections, due to improper use of injections, this can manifest in injection related disorders such as abscesses, polio, hepatitis and AIDS [37].
4. Psychosocial impacts, People believe there is a pill for every illness, at the onset of all kinds of minor disorders; they immediately take acetaminophen, which does not require a prescription. This had caused an apparent increased demand for acetaminophen [20].
5. Poly pharmacy. This involves the use of inessential combination of analgesics. Study had shown the daily consumption over several years of mixtures containing at least two antipyretic analgesics, usually combined with caffeine and/or codeine, both creating a psychological dependence [41]. Combining two or three parenteral analgesics, combining three oral analgesics or combining oral analgesics with two parenterals at the same time had also been demonstrated [39].
6. Research conducted by Kondro in 1997, showed that inappropriate prescribing of drugs led to unnecessary hospital admissions and visits to physicians [42]. This is also associated with high cost of hospital, the incidence of ESRD and expenditures related to its treatment has been increasing consistently and in 2002 the direct cost amounted to \$8,211 billion [43].

FACTORS UNDERLYING IRRATIONAL USE OF ANALGESICS

Misuse of analgesics is affected by many different factors, the uses of drug system is complex and varies from country to country. Analgesics may be imported or manufactured locally. They may be prescribed in the hospitals, health centers and can also be purchased in a pharmacy or drug shop since

they are over the counter drugs. Patients include a very wide range of people with differing knowledge, belief and attitudes about medicines, also, different cultures see drugs in different perspective, and this can affect the way analgesics are used [20]. Sources of analgesics are indicated in Fig.1.

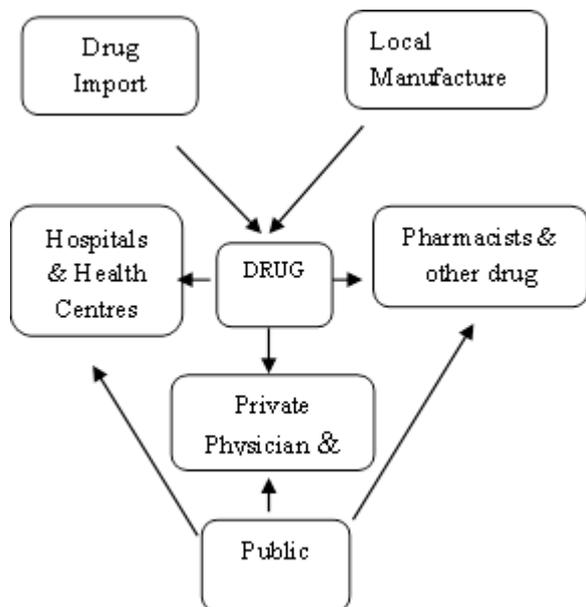


Fig.1: Components of the drug use system

MINIMISING ANALGESIC MISUSE

Improvement of rational use of analgesics can be achieved using measures that address the various components of drug use system. These include Regular organization of trainings and workshops for the prescribers placing emphasis on the side effects and analgesic drug interactions [19, 37, 39]. All health providers should be involved in this program in order to identify possible problems with a view of finding lasting solutions which will enhance rational drug use. There is also need for continue analgesic education programme for the consumers, highlighting the hazard associated with analgesics abuse [20]. Compliance with analgesic treatment guidelines, particularly in institutional setting must be ensured. Hospital pharmacists may be given the responsibility of ensuring that prescriptions comply with treatment guideline. This can be applied to cancer treatment [37]. Some of the factors that positively influence the use of clinical guidelines are clarity of guidelines, strong evidence, adequate funding of guidelines and

support by opinion leaders especially professional bodies [44]. Regulatory strategies such as controlling content in drug advertising, restricting prescribing to generic should be adopted. The National Drug Policy advocates the use of generic instead of branded drugs. Generic prescription has got special importance for rational use of drug as regards to cost, safety and efficacy by permitting the identification of the products by its scientific names [30].

CONCLUSION

Many studies have been carried out to document drug use patterns and they showed that over prescribing, multi-drug prescribing, misuse of drugs, unnecessary expensive drugs and overuse of analgesics and injections are the most common problems of irrational use by health care providers and consumers. Drug use is the end of the therapeutic consultation. Ensuring that the correct drug is given to the correct patient is a high priority

for all health professionals. By ensuring a correct diagnosis, prescribing as few drugs possible and explaining to the patient, which drugs are for which

condition, patient understanding is enhanced and compliance is improved.

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