REVIEW OF LITERATURE
Chapter 3

REVIEW OF LITERATURE

3.6 Global Misuse

Prescription drug misuse is a global public health problem. Many medications with sedative, anxiolytic, analgesic or stimulant properties have the potential to be inappropriately used without medical supervision. However, because these substances have useful physiological effects, many issues related to understanding prescription drug misuse can differ from those associated with other misused substances like drugs of abuse.

There is currently a lack of consensus about what constitutes prescription misuse and a wide range of opinions have been proposed. Inappropriate medication use is frequently defined on the basis of characteristics of users (i.e., any non-prescribed use), the reason for use (i.e., use for recreational purposes), the presence of clinically significant symptoms (i.e., meeting diagnostic criteria for abuse and dependence) or on the presence of any of these factors. In cases where multiple criteria are used to define misuse there is often a lack of differentiation among them and various studies use more specific criteria to exclude or include certain types of misuse from consideration altogether. Due to considerable variability in the classification of medication misuse both within and between studies, it is currently difficult to interpret the clinical significance of existing findings or to determine the true magnitude of problems associated with any particular form of misuse (Barrett, Meisner et al. 2008). In spite of
these differences in description and interpretation of drug misuse, there is no doubt that unnecessary use of medicines without medical supervision has become a global problem. A number of studies from different countries have investigated this problem in different contexts and in different age groups. However little information is available from India describing the magnitude of analgesic misuse. Therefore, prescription analgesic misuse among young adults is not only an important public health issue, but also has a possible relationship with poor pain management and has the likelihood of progressing to prescription opioid abuse and dependence in later life.

In the United States of America (USA) national surveys have shown a significant increase in non-medical use of prescription drugs with a particular increase in use of analgesics. In the year 2007, Joseph A. Califano, Jr., Chairman and President of the National Center on Addiction and Substance Abuse at Columbia University called for a major shift in American attitudes about substance abuse and addiction and a major overhaul in the nation’s healthcare, criminal justice, social service, and education systems to curtail the rise in illegal drug use and other substance abuse (Manchikanti, 2007). Califano in 2005, also noted that while America has been congratulating itself on curbing increases in alcohol and illicit drug use and in the decline in teen smoking, abuse and addiction of controlled prescription drugs like opioids, central nervous system depressants and stimulants, have been silently, but sharply rising. All the statistics continue to show that prescription drug abuse is escalating with increasing emergency department visits and unintentional deaths due to consumption of prescription controlled substances. While the problem of drug prescriptions for controlled substances continues to increase, so are the cases of under-treatment of pain. Present information show that there were 6.4 million or 2.6% Americans using prescription-type psychotherapeutic drugs without medical supervision in the past
month. Of these, 4.7 million used analgesics. Current non-medical use of prescription-type drugs among young adults aged 18 - 25 increased from 5.4% in 2002 to 6.3% in 2005. In 2006 non-medical use of psychotherapeutic drugs has increased to 6.2% in the population of 12 years or older with 15.17 million persons, second only to marijuana use and three times the use of cocaine. Parallel to opioid supply and non-medical prescription drug use, the epidemic of medical drug use is also escalating with Americans using 80% of world's supply of all opioids and 99% of hydrocodone. Opioids are used extensively despite a lack of evidence of their effectiveness in improving pain or functional status with potential side effects of hyperalgesia, negative hormonal and immune effects, addiction and abuse. The multiple reasons for continued escalation of prescription drug abuse and overuse are lack of education among all segments including physicians, pharmacists, and the public, ineffective prescription monitoring programs with lack of national funding and a reactive approach on behalf of numerous agencies (Manchikanti, 2007).

3.2 Global Misuse - Australia

Apart from the USA, misuse of analgesics is an important health issue in different other countries and contexts. In a study from Australia, analgesic nephropathy or analgesic abuse-associated analgesic nephropathy (AA-AAN) has been recognized as a disease of the twentieth century. It was recorded that the emergence of AA-AAN was due to aggressive marketing of analgesics and the susceptibility of individuals with addictive personalities to analgesic abuse. Analgesic abuse resulted in major morbidity and mortality from renal disease and renal failure, premature atherogenesis with cardiovascular diseases, and other aspects of the analgesic syndrome, which had heavy demands upon health budgets. Legislative restriction of analgesic sales in Australia has resulted in a decline in analgesic abuse and end-stage renal failure from AA-AAN. There have also been changes in the analgesic syndrome. However, the long-term risks
of transitional cell carcinoma of the uroepithelium remain a problem as a legacy of analgesic abuse and AA-AAN. NSAID-associated analgesic nephropathy (NSAID-AAN) has emerged as a distinct clinical syndrome and may become a significant health problem in view of the widespread use and misuse of NSAIDs (Nanra, 1993). Another study has also observed that overuse and abuse of phenacetin-containing mixed analgesics has contributed to end-stage renal disease. Combination analgesics, especially those co-formulated with caffeine, have been implicated as imparting a greater risk of analgesic-associated nephropathy (AAN) than single or co-formulated analgesics without caffeine. This has led to a recommendation that the sale of "two plus caffeine" analgesic mixtures be reclassified from over-the-counter to prescription only availability. There is a rational basis for co-formulating acetylsalicylic acid (ASA) and acetaminophen (paracetamol) as this reduces the dose of each, without altering efficacy. The co-formulation of caffeine with these analgesics has a significant adjuvant effect and increases analgesic efficacy 1.4 to 1.6-fold. Currently available animal and human data do not support the notion that the nephrotoxic risk from co-formulated ASA and acetaminophen is higher than the risk from either ASA or acetaminophen alone, in equivalent analgesic doses. There are no epidemiological data that implicate caffeine in AAN, and only limited evidence that links excessive acetaminophen usage to renal disease. There is no evidence that caffeine increases analgesics papillotoxicity directly. The presence of caffeine in mixtures of analgesics is no more addictive than other sources of caffeine. There is no evidence to suggest that adding caffeine to analgesic mixtures enhances the potential for promoting analgesic misuse in the general population. Thus distinct therapeutic benefits of ASA, acetaminophen and caffeine appear to outweigh any known risk. It is doubtful if preventing the availability of these products will significantly affect the role of analgesic abuse / overuse in end-stage renal disease. Better risk management would
come from a focused educational program, developed in close collaboration between industry, healthcare professionals and consumer organizations, such a program must warn against the potential dangers of analgesic and NSAID misuse (Bach and Berndt, et al., 1998).

A study was done to investigate the current knowledge and behaviour of New Zealand musculoskeletal physiotherapists regarding recommendation of non-prescription medications for the treatment of musculoskeletal sprains and strains. 2438 New Zealand physiotherapists were surveyed, of whom approximately 948 work in musculoskeletal physiotherapy. Of 278 respondents (29.3% response rate), 213 (81.0%) sometimes or often recommend oral NSAIDs to patients, and 216 (82.1%) recommend oral paracetamol.

In another context the extent of drug abuse in mass sport is only poorly documented. Studies about drug abuse investigated only the prohibited substances according to the Olympic movement anti-doping code, e.g., about the use of anabolic androgenic steroids (AAS) by school children or young students. However, only few investigations investigated drug abuse in mass sport regarding the easily accessible OTC drugs of the class of NSAID. These drugs permit an athlete to compete at his normal level of performance despite injuries or pain. However, the masking of pain may exacerbate the injury. Precautions should be taken to prevent the unwarranted or unmonitored use of anti-inflammatory agents during treatment of sport injuries. The abuse may be extensive since most people consider OTC drugs, such as aspirin and ibuprofen, harmless. Studies in Switzerland among endurance athletes in mass sport examining the use of medications before an event showed a prevalence between 5 and 10% of NSAID. Although this seems a small number, further investigations should focus on the use of medications among different age groups and preventive
information to abstain from the use of certain medication for competitors in mass sport should be worked out (Braund and Abbott 2011).

3.3 Global Misuse - Asia

In a study from China drug / psychoactive substance use among adolescent students was surveyed in a south-west province. A cluster sample was drawn from this province of nine districts or cities. Each district / city provided two schools from 11 grade senior high school and a total of 18 schools were selected randomly. A total of 2649 students completed this self-report questionnaire and participants had a mean age 17.1 +/- 0.9 years. The response rate was 92.7 to 95.6% for each of the specific substances or drugs. The life time prevalence of regular substance use (at least 15 times during in any one month) was, in rank order of prevalence - tobacco 6.3%, non-steroidal anti-inflammatory drugs (NSAIDs) 2.9%, alcohol 2.9%, solvent 0.3%, sedative / hypnotic 0.2% and cannabis 0.04%. The life-time prevalence of at least some use were alcohol 66.1%, NSAID 59.3%, tobacco 27.4%, sedative / hypnotic 5.2%, heroin 3.1%, solvents 2.8%, amphetamine-type stimulants (ATS) 0.7% and cannabis 0.3%. The prevalence of current regular use (at least 15 times in the past month) were tobacco 4.2%, alcohol 1.6%, NSAID 0.8%, sedative / hypnotic 0.1%, solvents 0.1% and cannabis 0.1%. The prevalence of current use at any level were alcohol 15.2%, NSAID 9.6%, tobacco 7.1%, sedative / hypnotic 0.5%, solvents 0.4%, cannabis 0.1%, heroin 0.1%, and ATS 0.04%. The median age at onset substance use was between 10.7 and 13.4 years. Therefore, drug misuse has appeared among teenage students in an area from China. The most widely used substances were alcohol and cigarettes. The rates of solvent, tobacco and alcohol use among males were substantially higher than in females (Liu, Zhou et al. 2001).

Although systematic data on prescription drug misuse is not available in India, one study has demonstrated a high consumption of prescription medications among
children with significant consumption of analgesics. One hundred and seventy two children were prescribed, in 212 episodes of illness, antimicrobial agents (28.4%), followed by anti-diarrheals (10.9%), nutritional products (9.4%), analgesics (7.5%) and steroids (6.8%). Ampicillin (22.7%) and cotrimoxazole (12.7%) were the most commonly prescribed antimicrobials. Tetracyclines, which are not indicated in children below 8 years, were used in 7.1% of total exposures of chemotherapeutic agents. Penicillin, a comparatively safe and useful drug, was used only in 4.5% exposures. Analgin and hydroxyquinolines, both having significant adverse drug reactions, were used frequently. Corticosteroids were used for simple ailments like diarrhea, fever and jaundice. ORS was used in only 13.9% episodes of diarrhoea. Adverse drug reactions were noted in 30 (17.4%) cases and death in 6 (3.5%) cases. The average cost per prescription for neonates was Rs 32.43 and for a child was Rs 30.65. Weight of the children was not taken prior to prescribing drugs. There is need for prescription audit as there is high consumption rate of drugs, with overuse of antimicrobial and nutritional products, and misuse of steroids (Prakash, Mathur et al. 1989). Another study conducted by Sharma B et al., in Jammu city, North India among the urban population showed that the improper use of OTC drugs due to lack of knowledge of their side effects and interactions could have serious implications. There is always a risk of interaction between active ingredients of hidden preparations of OTC drugs and prescription medicines, as well as increased risk of worsening of existing disease pathology. This study also indicated low knowledge about dose/duration, side effects and interactions of commonly used analgesics (NSAIDs). The study participant’s knowledge about the above parameters was extracted by asking direct questions or indirectly by enquiring about the drug use in sub-therapeutic dose for inadequate period or over use of drugs, use of drugs with a potential to aggravate the existing pathology for which it is used (NSAIDS for epigastric pain) and concomitant use of drugs with
potential interactions (NSAIDS and antihypertensive drugs or iron/calcium preparations and antimicrobials or irrational drug combinations) (Sharma B et al. 2005).

Non-medical use of prescription analgesics in urban Bangalore, South India was studied. With a sample size of n=700 participants with a mean age of 28 years (SD 5), it was observed that over a period of past 12 months the non-medical use of prescription analgesics (NSAIDs) was 26%. The majority reported "use without prescription," while "use in ways other than as prescribed" was also reported. In all cases, chemist shops were the main source of obtaining the drugs non-medically. In multivariate logistic regression analyses, non-medical use was found to be significantly associated with participants' baseline characteristics like gender, education, current employment status, and marital status. Sixty-five percent stated that although "doctor's prescription is not required for common complaints, we can decide ourselves," while 60% stated, "it's okay to deviate from a prescription as needed." One hundred percent said that "using prescription medicines is more socially acceptable, and safer, compared to alcohol or illicit drugs." (Nattala P et al. 2015).

3.4 Global Misuse - Southwest Asia / Middle East

A similar study in children was reported from Israel. Fever in children is a common and usually benign symptom. It is known that antipyretic treatment is effective in the prevention of simple febrile seizures. Caregivers' administration of antipyretic medications to children has been reported, but data concerning the formulations used, actual doses administered, and effects of ethnicity and socioeconomic status on administration practices are incomplete. The aim of another study was to identify the factors affecting antipyretic administration (higher-than-recommended doses in particular) by caregivers to their febrile children in two different cultural-ethnic backgrounds. This cross-sectional survey study, conducted from January to March 2002, was part of a larger, ongoing survey study of the differences in caregivers'
knowledge, beliefs, and attitudes concerning children's fever in the two major cultural-ethnic groups in the Negev District in Israel, i.e., Jews and Bedouin Moslems. It was conducted at the Pediatric Emergency Department (PED), Soroka Medical Center, Beer-Sheva, Israel. A structured questionnaire was administered to Jewish and Bedouin Moslem parents or usual caregivers of young (0 - 60 months) children attending the PED due to fever. Each child's weight was obtained from the PED medical record. After completion of the interview, the reported antipyretic dose per kilogram of body weight was calculated. Less-than-recommended dose was defined as <9 mg / kg for acetaminophen and <4.5 mg / kg for ibuprofen. Higher-than-recommended dose was defined as >16.5 mg / kg for acetaminophen and >11 mg / kg for ibuprofen. On survey, the proportion of people who were parents was 98% and grandmothers 2%. Differences existed between the two cultural-ethnic groups in the source of knowledge regarding antipyretic use in children (a significantly larger proportion of Jewish caregivers received their knowledge concerning antipyretic use from package inserts compared to Bedouin caregivers (25.7% vs. 6.0%; P < 0.001), and a significantly lower proportion of Jewish caregivers used "other" sources (15.8% vs. 39.0%; P < 0.001). Most (65.2%) caregivers indicated that they administered antipyretics for no or minimal elevations in body temperature, 52.7% administered individual acetaminophen doses within 10% of the recommended dose, 34.8% administered a higher-than-recommended dose, and 21.4% repeated the dose at intervals of ≤ 3 hours. More Bedouin than Jewish caregivers exposed their children to higher-than-recommended antipyretic doses (48.0% vs. 21.8%; P < 0.001). After adjusting for maternal education and work-for-income status, child's age, child's order in the family, and number of children in the family, a significant and independent inverse relationship was found between child's weight and higher-than-recommended acetaminophen doses, in which for each additional kilogram of body weight, a 30%
decrease in the proportion of children administered higher-than-recommended doses was found (Odds Ratio OR, 0.7 for each additional kg; 95% CI, 0.59 - 0.89; P = 0.002). In addition, a significant and independent relationship was found between the formulation of acetaminophen and the administration of higher-than-recommended doses (OR, 4.9; 95% CI, 2.32 - 10.23; P < 0.001), with rectal suppositories related to the administration of higher-than-recommended dose by 4.9-fold. The results of this survey concerning antipyretic treatment of children by their Jewish and Bedouin Moslem caregivers suggest that lighter body weight and the use of acetaminophen rectal suppositories were associated with the administration of higher-than-recommended doses of acetaminophen (Bilenko, Tessler et al. 2006). (Liu, Z., W. Zhou, et al., 2001).

Therefore, it is obvious that analgesic misuse is seen in various parts of the world in different contexts and age groups. Further, medically un-supervised use of non-steroidal analgesics can cause a number of adverse events including gastrointestinal and renal consequences. Prescription analgesic misuse is common among young adults (18 - 25 years) and can also have a relationship with poor pain management. Further, misuse of non-steroidal analgesics for poorly controlled pain can progress to misuse of prescription opioid analgesics leading to opioid dependence.

In fact, in a study of predictors of buprenorphine-naloxone dosing for maintenance treatment in opioid dependent youth (15 - 21 years) 75.4% participants had a history of current pain (Chakrabarti, Woody et al. 2009). This investigation examined baseline patient characteristics to predict dosing of buprenorphine-naloxone, a promising treatment for opioid addiction in youths. This study of 69 opioid-dependent youths was a secondary analysis of data collected during a National Institute on Drug Abuse (NIDA) Clinical Trials Network study. Outpatients aged 15 - 21 were randomized to a 12-week buprenorphine-naloxone dosing condition (including 4 weeks of taper).
Predictors of dosing included socio-demographic characteristics (gender, race, age and education), substance use (alcohol, cannabis, cocaine and nicotine use) and clinical characteristics (pain and withdrawal severity). Most of the participants (75.4%) reported having either "some" (n=40, 58.0%) or "extreme" (n=12, 17.4%) pain on enrollment. Maximum daily dose of buprenorphine-naloxone (19.7mg) received by patients reporting "extreme" pain at baseline was significantly higher than the dose received by patients reporting "some" pain (15.0mg) and those without pain (12.8mg). In the adjusted analysis, only severity of pain and withdrawal significantly predicted dose. During the dosing period, there were no significant differences in opioid use, as measured by urinalysis, by level of pain. These data suggest that the presence of pain predicts buprenorphine-naloxone dose levels in opioid-dependent youth and those patients with pain have comparable opioid use outcomes to those without pain, but require higher buprenorphine-naloxone doses.

3.5 Global Misuse - United States of America

Two surveys totaling 9062 respondents were performed of the American public. The Roper survey, conducted in 1997 and the National Consumers League (NCL) survey, conducted in December 2002. These surveys were intended primarily to assess the public's use of and attitudes toward NSAIDs and OTC analgesics. Ibuprofen based drugs were the most frequently used OTC in both surveys (57% Roper, 33% NCL) (Wilcox et al., 2005). In the Roper survey, 17% of respondents used NSAID, with 38% using both prescription and OTC. 46% of exclusive OTC users believed OTCs were safer, 56% of exclusive users of prescription NSAID believed they were safer. 60% and 29% of exclusive OTC and prescription NSAID users were neither aware of nor believed that they were at risk for side effects from NSAIDs respectively. 26% of respondents used more than the recommended dose on the label, 22% believed warning symptoms would always precede any NSAID induced complications. In the
NCL survey, 83% had used an OTC agent in the last year, with 15% reporting daily use and 49% were not concerned about potential side effects. 30% believed there were less risk with OTC analgesics and 44% consumed more than the recommended dosage on the label. OTC analgesics including NSAIDs are widely used, are frequently taken inappropriately and potentially dangerously. Users are generally unaware of the potential for adverse side effects. Gastrointestinal (GI) toxicities from NSAIDs, both over-the-counter (OTC) and prescription, continue to be reported, increasingly in conjunction with cardiovascular, hepatic and renal complications.

In 1985 in the United States, 4 billion work days were lost because of pain, amounting to about 23 days per person for full-time, part-time and at-home workers. For those employed full time, 550 million days were lost. Based on an average income of $23,000 per year, losses as a direct result of pain are estimated at $55 billion (Abbott et al., 1998).

Another study reported NSAID use among persons with CKD in the United States. A total of 12,065 adult (aged 20 years or older) participants in the cross-sectional National Health and Nutrition Examination Survey (1999-2004) responded to a questionnaire regarding their use of over-the-counter and prescription NSAIDs. NSAIDs (excluding aspirin and acetaminophen) were defined by self-report. Current use (nearly every day for 30 days or longer) of any NSAID was reported by 2.5%, 5.5%, and 7.5% of the US population with no, mild, and moderate to severe CKD respectively. Nearly all of the NSAIDs used were available over-the-counter. Among those with moderate to severe CKD who were currently using NSAIDs, 10.2% had a current NSAID prescription and 66.1% had used NSAIDs for 1 year or longer. Among those with CKD, disease awareness was not associated with reduced current NSAID use (3.8% vs 3.9%, aware vs unaware; P=.979) (Plantinga et al., 2011).
3.6 Global Misuse - South America

In a study from Brazil, 70 pharmacies located in Sao Paulo were randomly selected and visited to investigate over-the-counter availability of analgesics. 7 researchers posed as ordinary clients presenting with a standardized complaint of symptoms according to a scenario previously defined. The client asked for medicines to relieve his / her pain or discomfort. After the seller's suggestion the client asked for two drugs randomly selected from a drug list containing 30 trademarked drugs commonly prescribed to arthritis patients. These drugs should be available only on prescription. In only 12.8% of the pharmacies did the seller initially suggest the client to consult a physician. The sellers “prescribed” non-steroidal anti-inflammatory drugs (NSAIDs), vitamins, analgesics and corticosteroids in respectively 42.8, 20.0, 14.3 and 5.7% of the visits. From the drug list, the client could secure 67.7% of the NSAID, 65.0% of the corticosteroids and 20.0% of the sedatives without presenting a prescription ((Ferraz, Pereira, et al., 1996 and Liu, Zhou et al., 2001).

3.7 Global Misuse - Africa

Chronic consumption of analgesics has been shown to increase the risk of end-stage renal disease. In Nigeria, these drugs are readily available as there is no legislation regulating their consumption. Using a pre-tested questionnaire, subjects in Zawan B ward in Jos were interviewed regarding analgesic use. Cumulative lifetime dose of drugs consumed was calculated by obtaining the product of the average number of pills consumed in a week by duration of use in years. Common analgesics regularly consumed were paracetamol (58.1%), analgesic mixtures (28.9%) and; NSAIDS (13%). Common indications for use of these drugs were musculoskeletal pains, headache, fever and stress (Aqaba et.al., 2004).

Another study was done to assess the pattern of sale and use of Non-Steroidal Anti-Inflammatory Drugs in Rural and Urban centres in Nigeria. 56 drug outfit managers in
patent medicine store, pharmacy, hospital drug unit and market centre visited in their outlets, were evaluated with respect to years of experience, educational level and registration status. 86% of the drug outfit managers had less than tertiary education with 59% of the sampled outfits being unregistered and unlicensed. 74% of the sample population procured their NSAIDs from sources where adequate pharmaceutical care is unlikely. 79% have clinical conditions likely to be worsened by NSAID misuse. 11.1% of the respondents who are categorized as geriatrics ingest NSAIDs daily while over 23% of this class require more than two (>2) different NSAIDs at a time (Awofisayo et. al., 2008).

From the FIFA studies, it is often reported that the athletes take the pain killers as a preventive. They take them to prevent a pain which may occur, to be totally insensitive. In 2010, published recently in the British Journal of Sports Medicine, South Africa showed higher levels of NSAID misuse. 39% of all players took a painkilling agent before every game of football. There were huge differences between countries with some teams doling out over three medications per player per game. Painkilling medication can be particularly dangerous in professional sport. In high-intensity exercises like football, a player's kidneys are continuously working hard, making them more vulnerable to damage from strong drugs (Alaranta et al., 2008).

3.8 Global Misuse - Europe

Studies in Switzerland among endurance athletes in mass sport examining the use of medications before an event showed a prevalence between 5 and 10% of NSAID. This seems a small number, further investigations should focus on the use of medications among different age groups and preventive information to abstain from the use of certain medications for competitors in mass sport should be worked out (Mahler 2001).
According to the National Drug Strategy Household Survey, in 2010, 30% of the Australian population aged 14 years and older had used analgesics for non-medical purposes in the previous 12 months. Ibuprofen-codeine preparations first entered the Australian over-the-counter (OTC) market in October 2002 (National Drug Strategy Household Survey, 2013). Prospective case series of 27 patients, collected from Victorian hospital-based addiction medicine specialists between May 2005 and December 2008 was done to investigate morbidity related to misuse of over-the-counter (OTC) codeine-ibuprofen analgesics. The patients were taking mean daily doses of 435-602 mg of codeine phosphate and 6800-9400 mg ibuprofen. Over half of the patients (World Health Organization, 1994) reported only using analgesics. 3 patients had a history of alcohol use disorder (Frei and Nielsen et al., 2010).

In Canada, headaches lead to time away from work and impairment of functioning in more than 34% of the population. Some of those with pain consult a physician. Pain, in fact, is the most common reason for medical consultation. Many more simply buy an over the-counter (OTC) medication and treat themselves, while the rest do both. One study found that 37% of patients who received a prescription for analgesics were taking an OTC medication for pain concomitantly. Eighty-five percent of all analgesics are sold over the counter and pain-relievers as a group post the highest sales among OTC drugs. In pharmacies in Montreal there are over 60 OTC analgesic formulations, revolving around 3 drugs - acetaminophen, acetylsalicylic acid (ASA) and ibuprofen. It has been estimated that 20-30 billion tablets of ASA are taken each year in the United States. Over the past 15 to 20 years, approximately 187 billion tablets of acetaminophen have been consumed by 170 million US adults, for an average of 9-13 billion annually or 50-70 tablets per person per year. Current use is higher than these figures indicate. Acetaminophen has grown as a proportion of OTC analgesics used
during this period and the use of ASA has fallen concomitantly (Chakrabarti and Woody, et al., 2009).

Therefore, prescription analgesic misuse among young adults is not only an important public health issue, but also has a possible relationship with poor pain management and has the likelihood of progressing to prescription opioid misuse and dependence in later life.

### 3.9 Information from Sikkim

Sikkim, a small mountainous state in the eastern Himalayas, observed great changes in its political structure, social structure, economic life and cultural values during the past hundred years. The state borders Nepal to the west, China's Tibet Autonomous Region to the north and east, and Bhutan to the southeast. The Indian state of West Bengal lies to the south. Sikkim with a population of 6.11 lakh (Datta et al., 2015) is a multi-ethnic state, inhabited by ethnic population of Lepchas, Bhutias and Nepalis. Lepchas are traditional inhabitants of Sikkim, whereas Bhutias and Nepalis (approximately 70% of Sikkim’s population) have migrated from Tibet and Nepal, respectively. Sikkim was annexed to India as its 22nd state in 1975. As a result, a lot of migration took place from other parts of India, with introduction of new substances of misuse including prescription analgesics. National Family Health Survey-3 (NFHS-3, 2005-06) by Govt. of India has shown a significant increase in alcohol abuse in Sikkim among both males (45.4%) and females (19.1%) of 15-49 years age group from its previous report of NFHS-2. This also shows a growing trend towards alcohol and analgesic misuse, abuse and addiction.