

**UTILIZATION OF PETHIDINE INJECTION IN A QUASI-GOVERNMENT HOSPITAL IN GHANA**Afriyie Kwame Daniel^{1*}, Aryeetey Justus¹, Annoh Joseph¹, Darkwah Thomas¹, Dogbe Justice²¹Ghana Police Hospital, Pharmacy Department, PMB CT 104, Accra-Ghana²Korle-Bu Teaching Hospital, Plastic Surgery and Burns Centre, Pharmacy Department, Accra.***Corresponding author e-mail:** dspdan77@yahoo.com**ABSTRACT**

Pethidine is often used in management of moderate to severe pain which improves quality of life. Though used in several countries, its rational use is of concern due to its potential adverse effects. This cross-sectional descriptive study assessed pethidine utilization from 2012-2014, and prescribing trend from December 2014 to March, 2015 at the Ghana Police Hospital. Data collecting tools were used to obtain information on prescribing and utilization patterns at the dispensary within study periods. Of the 292 patient cards with pethidine analyzed, inpatients were 92.5 %, and 81% were on national insurance. Patients from the Obstetrics and gynaecology (80.5 %) had the highest proportion of pethidine prescription. Majority of indications and doses for which pethidine was prescribed were in line with National Guidelines. Proportion of annual pethidine usage to annual hospital utilization declined from 6.3 to 5.4%, in 2012 to 2014. Study revealed decline in pethidine use at the hospital, and its prescribing was with caution.

Keywords: Analgesics, opioid, pethidine, usage pattern, rational.**INTRODUCTION**

Use of analgesics are crucial role in ameliorating mild, moderate or severe pains of patients during headaches, accidents, labour delivery, cancers, surgery and other musculoskeletal pain- associated conditions. Hospital pharmacists ensure the availability of appropriate opioid and non-opioid analgesics for pain management. They also recommend to prescribers, the use of opioid therapy often for moderate-severe pain, and the use of non-opioids and other adjuvant medications when required for mild to moderate pain. Common injectable opioid analgesics available at hospitals in Ghana are pethidine, morphine, fentanyl and tramadol. Pethidine is one of the most commonly used and investigated opioid analgesic used in the management of moderate to severe, pre and postoperative pain.^[1,2,3] Due to its poor oral bioavailability, and it being metabolized extensively in the liver, it is only available in the injectable formulation.^[4]

In spite of the wide use of pethidine injection in pain management being well documented in literature,

there are conflicting views and concerns of its efficacy in labour pain management, side-effects when compared with other opioids such as morphine and tramadol, and non-opioid analgesics such as paracetamol injection. However, most studies done on pethidine use, especially in labour are often scanty and cannot be used to draw strong conclusions.^[5,6] Pethidine like all opioids cross the placenta and can cause neonatal respiratory depression, and other known side effects such as nausea, vomiting and dysphoria in pregnant women in labour have been well documented.^[7,8] Findings from other studies revealed that, it has no benefit in patients with difficult labour, and that labour pains are not sensitive to morphine and pethidine but only induces heavy sedation.^[9,10] Another study revealed that, pethidine could be used with other analgesics to achieve desired pain relief without inducing adverse side effects in patients with renal failure.^[11]

The use of pethidine has always been substantial, and its usage in especially postoperative pain management has been questioned.^[12,13] A report revealed that, as prescribing of opioids for pain management has increased, so has deaths due to

prescription of opioids.^[14] Other studies also found that, opioids are frequently misused, sometimes abused and prescription opioid misuse and overdose remains a major public health concern; and its impact on patients, their families, and society is enormous.^[15,16] The Center for Disease Control and Prevention (CDCP) estimates over 15,000 people die from prescription opioid overdose, which is more than the number of people who die of overdoses due to cocaine and heroin combined.^[17]

Irrational drug use still remains a global problem, and is of greater concern with usage of drugs with serious potential side effects, narrow therapeutic indices and potential of increased resistance, among other factors. According to Latta *et al.*,^[6] due to lack of good evidence to support preferential use of pethidine in spite of its limitations, has resulted in it being widely prescribed in hospitals. Hence, assessment of drug use patterns is necessary to provide baseline evidence, which would promote rational drug prescribing and use in especially developing countries.^[18,19] The Ghana Police Hospital provides health care to police personnel, their dependents, general public, crime suspects, national health insurance holders, and in general police operations nationwide. Over the past years, there have been reports of increasing use and misuse of pethidine in the hospital. However, there has not been any study to provide empirical evidence to substantiate these complaints. Hence, this study sought to describe the utilization and prescribing pattern of pethidine injection at the Ghana Police Hospital. Findings from this study would no doubt provide the much needed evidence for stakeholders to establish the rationality of pethidine use in the hospital, and possibly provide insights to improve its prescribing in the hospital.

METHODS

In this cross-sectional descriptive study, pethidine utilization by patients in the various units of the Ghana Police Hospital was obtained with the aid of a designed data collecting tools, after documentation in the dangerous drugs book.

Ghana Police Hospital is a 100-bed facility located in Cantonments, Accra. It is the headquarters of the Ghana Police Health Service, with over 10 peripheral (regional) health clinics under its administration. It also serves as a referral center during national disasters. The main pharmacy provides pharmaceutical services to both in-patients and outpatients throughout the week.

In this study, pethidine utilization pattern within the study period was obtained from both in-patients and outpatients folders and cards. Data collecting tool

was used to obtain information on pethidine prescriptions and cards from the Main pharmacy; dose, duration, diagnosis, gender, units (outpatient/inpatient/specialist) where patient received the prescription, category of patient, and the total quantity of pethidine issued from the main dispensary from December 2014-March 2015. The hospital's pethidine consumption pattern from 2012-2014 was obtained from the dangerous drug book records with a quantitative tool. The method and data collection tool was in line with the pharmacy department's drug consumption and prescribing monitoring format, and approved by the hospital administration. Some of the limitations in this study were; detailed demographic data on patients and prescribers were not captured, as well as specialty of the prescribers.

Data analysis: Data generated were entered into Excel Spreadsheet (2007), after manual verification and cleaning. Descriptive statistics (percentages) was used to present most of the results. Statistical analysis of annual means of pethidine use was done with the aid of Graphpad 6 prism (San Diego, CA, USA). P value less than 0.05 was considered statistically significant.

RESULTS

Patient characteristics: Of the total 292 pethidine prescriptions analyzed within the study period, it constituted 29.4% of total pethidine (992) issued at the main pharmacy to patients from various units in the hospital. A higher proportion of prescribed pethidine was observed in female patients 88.0%, whilst only 12 % for male patients. Data also revealed that, paediatric patients who received prescribed pethidine constituted only 6.9 % as against a much higher proportion of adult patients 93.1%. Further analysis of results showed that, 81% of the total patients were on national health insurance scheme (NHIS), whilst only 19% were not on NHIS; police personnel, their dependents and crime suspect. The proportion of outpatients who were prescribed pethidine constituted only 7.5% whilst the proportion of in-patients with prescribed pethidine was as high as 92.5%. Analysis of proportion of prescribed pethidine by specialties revealed that, 80.5% was generated from the gynaecological unit. The details of analysis of patients characteristics is presented in table 1.

Pethidine dosage pattern for patients: Analysis of pethidine doses from patient records showed that, 89.4% of the patient cards had 100mg of pethidine prescribed as start dose, whilst 9.9% of patients had pethidine prescribed in divided doses of 50mg or 25

mg; 6 hourly or 4 hourly. Only 0.7% of the cases analyzed were prescribed as 100 mg when necessary.

Pattern of pethidine prescribed based on diagnosis:

Of the total cases of in-patients and out-patients analyzed within study period with pethidine prescriptions, 80.5% were prescribed for expectant female patients at the labour ward or gynaecological ward. Sickling crisis cases at paediatric ward and surgical cases also accounted for 6.9% and 3.8% respectively of cases for which pethidine injection was prescribed. Surgical cases included; hernia, appendicitis, amputations, cholecystectomy, prostatectomy among others. Other diagnosis observed in this study which pethidine was prescribed were; burns and joint pains, vehicular accident injuries, gunshot injuries and infection related pain. The detailed proportions for the pattern of pethidine prescribing based on diagnosis are presented in table 2.

Trend of pethidine usage (annual and mean) at the hospital from 2012 to 2014: Between 2012 to 2014, the total number of pethidine injection issued from the Main pharmacy was 15,800. Of this total, the proportion of pethidine issued to patients represented 33%, 35% and 32% for 2012, 2013 and 2014 respectively. Analysis of the trend of pethidine use from the main pharmacy records revealed that, the annual mean of pethidine usage were 435.0 ± 52.1 , 452.5 ± 28.7 and 420.8 ± 29.8 for 2012, 2013 and 2014 respectively. One way Anova analysis of the annual means showed no statistical significant ($p=0.8438$) difference between the usage of pethidine from 2012 to 2014 in the hospital.

Wide variation in monthly utilization of pethidine was observed in 2012 as seen in its standard error of mean. Further analysis of data revealed a decreasing trend in the proportion of annual pethidine usage to annual hospital utilization from 6.3%, 5.7% to 5.4% for 2012, 2013 and 2014 respectively. The detailed monthly utilization of pethidine and comparison of pethidine usage with total hospital utilization from 2012 to 2014 is presented in table 3 and table 4 respectively.

DISCUSSION

Prescribing pethidine is associated with the specialty of physicians, hospital location, patient race, insurance coverage and physician's gender.^[20] Pan *et al.*,^[21] in their survey of trend and characteristics of pethidine use in Taiwan found, higher prevalence of pethidine use in males than females. On the contrary, higher prevalence of pethidine use in females than

males was observed in a study in Thailand.^[22] Findings from this study were similar to that of the latter study and Panda *et al.*,^[19] as pethidine prescription were higher in female patients than males. This could be attributed to the observation that, pethidine appears to be the commonly prescribed analgesic for labour delivery, as 80.5% of the total of pethidine prescriptions for females (88%) were from the obstetrics and gynaecology department (O&G) of this hospital.

Prescribing opioids appear to increase with age, and use appears to be minimal in paediatrics. Vallano *et al.*, found that,^[23] majority of patients treated with opioids were within 41 to 65 years. In a study of usage pattern of opioids injections for in-patients in Thailand, 70% of patients (18-59 years) and 21% of patients (≥ 60 years) were prescribed pethidine, with paediatric population (<18 years) accounting for only 9%.^[22] Findings from this aspect of our study was similar to the previous studies, suggesting that pethidine was less likely to be prescribed to paediatric patients (6.9%) compared to adults in the management of moderate to severe pain in the hospital. This may also be attributed to the fact that, elderly patients have higher risk of suffering from both acute and chronic pain.^[24]

Most hospitals in developing countries have their accidents and emergency units as part of, or being integral part of the outpatient department. However, in emergency departments, patients are often with multiple clinical conditions coupled with limited medical and or medication history, so other opioid analgesics than pethidine are considered safer.^[25] The very high percentage of in-patients (92.5%) who received pethidine prescriptions for management of pain compared to outpatients (OPD) in this study implies that, prescribers were less likely to prescribe pethidine for the management of moderate to severe pain for outpatients and or patients in the accident and emergency department. This observation is commendable, as most hospitals are making efforts to reduce the use of pethidine in emergency departments whilst promoting use of safer alternatives for pain management.^[26]

According to Dorn *et al.*,^[27] opioids were least likely to be prescribed to uninsured and African Americans outpatients in United States with chronic abdominal pain. Our study revealed that, a high proportion of patients (81%) who received pethidine injection at the hospital were insured on the national health insurance scheme compared to the proportion of police, their dependents and crime suspects who were not on NHIS. The comparable proportion of insured

patients who were prescribed pethidine to the percentage of patients from the O&G suggests a strong association between these groups of patients; as most of the patients who went for delivery at the hospital were on national health insurance scheme. Furthermore, our perception that, most of the patients from the O&G were insured was confirmed by the ward in-charge. What could account for this association is that, pregnant women are entitled to free medical care during delivery under the national health insurance scheme in Ghana, hence the comparable proportions between patients from the O&G and national health insurance scheme patients who received pethidine prescriptions. Besides this, pethidine is half the price of morphine (\$1 USD) on the national health insurance list, making it more affordable to both the institution to stock, and patients to purchase in health institutions. The low cost of pethidine could be a contributing factor for being on the national health insure list and also the hospital, as observed in other studies that, low cost of pethidine also influenced its choice in health institutions.^[20]

Pethidine injection is one of the common opioids used in obstetrics, especially for labour analgesia.^[6,22] Analysis of pethidine prescription by specialty units confirmed the strong association between pethidine use and specialty,^[20] which in this case was the obstetrics and gynaecology unit (80.5%). Our findings were similar to that of Turkey *et al.*^[28] in United Kingdom where majority of consultant and midwife-led units (84.4 %) used pethidine over diamorphine or morphine, due to tradition and familiarity rather than drug efficacy. Though prescribing of pethidine by specialty in this study showed that, OPD and paediatric units were the next highest units after O&G their proportions of use were about 10 times less compared to the O&G. The surgical unit used about half the proportion of prescribed pethidine in the paediatric unit (6.9%) and OPD (7.5%). Almost all the pethidine prescribed from the paediatric unit were for the management of sickle cell disease (SCD), in which studies have shown that, management of pain associated SCD improves quality of life and reduces mortality of these patients.^[29] Furthermore, pethidine is the analgesic of choice for SCD management in the national treatment guidelines.^[30] The rest of the specialist units in the hospital prescribed approximately 2% of requested pethidine within the study period. Proportion of prescribing of pethidine observed at the OPD of this hospital which also serves as the accident and emergency unit was far lower than the 38% reported in the survey of 18 New South Wales hospitals.^[25]

Studies have showed that, pethidine is still frequently prescribed for patients who receive shorter courses of narcotics^[20,31] and has been found to be associated with fewer side effects than morphine in short-term treatments.^[32] The current Standard Treatment Guidelines of the Republic of Ghana^[30] recommends that daily dose of pethidine given at 25-100 mg start, then/or 6 or 8 hourly as required with caution for several indications such as; sickle cell crisis, labour analgesia, eclampsia, septic abortion, pre-term delivery, priapism, urinary tract calculi, burn and diverse acute or chronic pain. The presence of pethidine injection on the essential list and STG^[30], attest to the fact that Ghana as a nation recommends its use though with caution. Hence its use at the Ghana Police Hospital is in line with the national treatment guidelines. Todd also reported that,^[33] multiple dose administration of pethidine over a period of time increases the occurrence of its possible adverse side effects. Analysis of the various doses of pethidine administered revealed, majority of patients (89.4%) were prescribed 100 mg start especially for delivery, though the ward in-charge said “they often request 100 mg but often administer 50 mg start, which could be repeated depending on the condition of the patient”. The doses administered at 50 mg or 25 mg in divided doses 4-6 hourly constituted a small percentage of pethidine prescriptions, and these were mainly from the children’s ward. It was only in two cases which pethidine was prescribed; 100 mg when necessary. Our findings revealed that in almost all the cases, doses of pethidine prescribed at the hospital were for shorter duration, hence, minimizing the risk of its possible side effects which is attributed to mainly its metabolite normeperidine. Since none of the doses prescribed was sufficiently high nor duration of use prolonged, patients with normal renal function are less likely to suffer from possible adverse effects of normeperidine, the toxic metabolite of pethidine^[21,33,34]. All the doses at which pethidine injection was administered were in line with recommendations of the STG, and were all far below the stipulated maximum daily dose of 400 mg. Analysis of prescribed pethidine doses in this study suggests adherence to caution in its prescribing as stated in the STG and other updated pain management protocols.^[6]

The STG recommends several indications for pethidine use as stated earlier, and also in other acute or chronic pain conditions such as; burns, sickle cell crisis, joint inflammation, colic, spinal cord injury post-operative or traumatic musculo-skeletal injury among others. Other indications for pethidine use in emergency departments from a similar study were;

abdominal pain, chest pain, back pain, migraine or headaches, renal colic, pancreatitis, trauma or fracture and in cases of morphine allergy.^[25] Our study revealed that, all the cases for which pethidine was prescribed were in line with recommended indications in the STG and similar to that of the latter study.^[25] Furthermore, a high proportion of pethidine issued from the main pharmacy in this study was prescribed for delivery or labour pain, with sickle crisis, surgery, joint and burn pains, gunshot injuries, pain from vehicular accidents and infection related pain accounting for only 18.5%. Therefore, majority of pethidine prescribed for these medical conditions were in line with recommendations of STG.

Many arguments, research findings and clinical guidelines are against the use of pethidine in management of moderate to severe pains in several countries, primarily because of fear of its possible toxicity.^[9,10,26,35] On the contrary, several other countries such as Spain, Thailand, Israel, South Wales and Taiwan among others still use pethidine^[21,22,25,36,37]. The rationale for its continual use in many nations is due to the fact that, pethidine use in short-term treatments has been found to be relatively safer than morphine.^[21,32,33,34] Analysis of trend of annual pethidine usage from 2012 to 2014 indicated that, there was no significant difference in the total number of vials used per year within this past three year period. Neither was there any significant difference in the relative proportions of the annual

pethidine usage relative to the total quantity of pethidine used within that period which ranged from 32-35%. Further, analysis of data revealed a slight decreasing trend in the proportion of annual pethidine usage to annual hospital utilization from 2012 to 2014. This observation provides evidence which counters concerns of increasing use of pethidine in the hospital.

CONCLUSION

In conclusion, evidence from the study does not support the current perception of increasing use and misuse of pethidine in the Ghana Police hospital. Prescribing of pethidine was found to be the analgesic of choice for management of labour delivery. When its prescribing was compared with national treatment guidelines, it showed prudent prescribing as almost all the conditions for which it was prescribed are recommended in the STG. Also, prescribed doses were far below maximum daily dose though within therapeutic range, and often used as start doses. A further study to assess the incidence of possible side effects with its use for shorter duration is recommended.

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Table 1. Characteristics of the patients that received pethidine prescription from the Main Pharmacy.

| Patient characteristics (n=292) | Number of patients (%) |
|-------------------------------------|------------------------|
| Sex | |
| Female | 257 (88.0%) |
| Male | 35 (12.0%) |
| Category of Patients | |
| Police, dependents & crime suspects | 55 (19.0%) |
| NHIS patients | 237 (81.0%) |
| Age | |
| Paediatric (<18 years) | 20 (6.9%) |
| Adults (≥18 years) | 272 (93.1%) |
| Out-In Patients | |
| Out-patients (OPD) | 22 (7.5%) |
| In-patients | 270 (92.5%) |
| Specialty Units/Ward | |
| Gynaecology | 235 (80.5%) |
| OPD | 22 (7.5%) |
| Paediatric | 20 (6.9%) |
| Surgical | 9 (3.1%) |
| Other units/ward | 6 (2.0%) |

Table 2: Pattern of pethidine prescribing based on diagnosis at the hospital

| Diagnosis | Number Of Cases (n=292) | Percentage % |
|-------------------------------|--------------------------------|---------------------|
| Labor pains (Delivery) | 235 | 80.5 |
| Sickling crisis | 20 | 6.9 |
| Surgery | 11 | 3.8 |
| Burns and Joint pains | 8 | 2.7 |
| Gunshot injuries | 8 | 2.7 |
| Accidents injuries(Vehicular) | 7 | 2.4 |
| Infection related pain | 3 | 1.0 |
| Total | 292 | 100 |

Table 3: Monthly utilization pattern of pethidine injection at the Ghana Police Hospital from 2012-2014.

| Month | YEAR | | |
|--------------|-------------|-------------|-------------|
| | 2012 | 2013 | 2014 |
| January | 800 | 400 | 400 |
| February | 600 | 400 | 450 |
| March | 220 | 400 | 400 |
| April | 300 | 600 | 600 |
| May | 700 | 600 | 300 |
| June | 500 | 500 | 500 |
| July | 300 | 500 | 400 |
| August | 400 | 250 | 400 |
| September | 300 | 400 | 500 |
| October | 400 | 530 | 500 |
| November | 400 | 450 | 400 |
| December | 300 | 400 | 200 |
| Total | 5220 | 5530 | 5050 |

Table 4: Trend of pethidine usage in comparison with total hospital client utilization

| YEAR | Annual Hospital Utilization(X) | Total Pethidine usage (P) | Percentage of P/X % |
|-------------|---------------------------------------|----------------------------------|----------------------------|
| 2012 | 82,630 | 5220 | 6.3 |
| 2013 | 97,791 | 5530 | 5.7 |
| 2014 | 94,258 | 5050 | 5.4 |

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