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Awareness and pattern of pentazocine use in patients with sickle cell disease in two sickle cell clinics in Lagos state, Nigeria

Foluke A. Ayeni[1*], Patricia U. Ogbo[1], Ebele E. Onwuchuluba[1], Morenike R. Haruna[1]

[1]Department of Clinical Pharmacy and Biopharmacy, University of Lagos, Akoka, Lagos Nigeria.

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* *Corresponding Author:*
faayeni@unilag.edu.ng_
https://orcid.org/0000-0002-0494-9665
+234 812 527 3785

ABSTRACT

Background: Sickle cell disease (SCD) is a genetic disorder which leads to acute or chronic pain and thus requires the use of opioids and non-opioid medications. Pentazocine is a commonly used opioid among sickle cell patients for the management of moderate to severe pain. Patients understanding of the purpose and pattern of pentazocine use will encourage rational use and discourage misuse, especially outside the hospital setting. This study was set to assess the awareness and pattern of use of pentazocine among SCD patients.

Methods: The study was a cross-sectional, descriptive, questionnaire-based study conducted in two sickle cell clinics in Lagos State. A pretested questionnaire based on extant literature was employed to obtain patients sociodemographic data. Data was also obtained regarding prescribed medications, as well as patients' awareness and use of pentazocine. These data were analyzed using descriptive and inferential statistics in SPSS, version 21.0.

Results: Of the eighty respondents interviewed, most, 68 (85.0%) were single, 42 (52.5%) were females, and 50 (62.5%) had tertiary education. Mean age was 26.49 8.16 years. Commonly prescribed painkillers were Ibuprofen (31.4%), Paracetamol (28.9%), Diclofenac (26.9%) and Pentazocine (20.0%). Less than half, 32 (40%) were aware of pentazocine use in managing moderate to severe pain. Of these, 16 (50%) used it outside the clinic. 56.3% of those who used pentazocine outside the clinics used it because they had "unbearable pain". There was a significant association between age and Pentazocine awareness (p = 0.02) but not use (p = 0.54). Respondents aged 21-30 years had better awareness of Pentazocine use compared to other age groups.

Conclusion: The awareness of pentazocine use among SCD patients in the two centers studied in Lagos, Nigeria was found to be inadequate despite its wide spread use outside the clinic without clinicians' supervision. Proper education on disease condition and its management should be encouraged among SCD patients to encourage appropriate use of pentazocine, as well as other analgesics used in the management of SCD and discourage misuse.

1. Introduction

Sickle cell anemia (SCD) is a genetic hematological disorder occurring in about 300,000 births annually across the globe, with about 200,000 cases of sickle cell in Africa.[1,2]

While SCD affects approximately 100,000 Americans, SCD occurs in 1 out of 365 black or black American births, and 1 out of 16,300 Hispanic- American births.[3] SCD is a major health problem, increasing in health significance and identified as an under-recognized and under-funded cause of under-five mortality, particularly in Africa.[4-6] The disease is a condition where the red blood cells (RBC) are sickled in shape thereby restricting freedom of blood flow and causing occlusion of the vessels.

Genetic mutations of the RBCs (RBCs) that contain haemoglobin S (HbS) or HbS in combination with other abnormal beta-alleles, when exposed to deoxygenated environment undergo polymerisation and become rigid resulting in defective haemoglobin and leading to the production of adhesive sickle shaped RBCs and vaso-occlusion.[7]

Occlusion causes pain, which is the cardinal feature of SCD, and this pain could be acute recurrent, chronic or neuropathic pain, and last for any length of time .[7,8] To this end, painkillers are a major part of the management of SCD. The approach to SCD pain management is dependent on whether the pain is acute, chronic or a mixture of both, and on whether the patient is opioid naïve or opioid tolerant.[9] While acute pain has a stepwise approach, chronic pain is multidisciplinary, such as the use of analgesics, nerve block, physiotherapy, orthopedic intervention or surgery.[9] Pain in SCD patients could be excruciating, hence opioids and non-opioid medications are used for its management. While non-opioids could successfully manage mild to moderate pain and be effective in relieving the inflammatory components of infarctive bone pain, opioids are used when pain is severe and excruciating. Commonly used non-opioids include ibuprofen, paracetamol, diclofenac, and aspirin; and commonly used opioids include morphine, codeine, pethidine, tramadol and pentazocine.[10]

Pentazocine is a narcotic, synthetic opioid painkiller once thought to be non-addictive. Pentazocine was introduced to replace the more addictive narcotics, however, it is currently being listed as a drug of concern despite its beneficial properties for patients in chronic pain. It is used to treat moderate to severe pain in adults and children who are at least 12 years old and is available in 25mg tablets, 50mg capsules as well as in injectable forms. It works by changing the way the brain and nervous system respond to pain. Pentazocine has been shown to be very effective in combating pain in SCD patients who are constantly predisposed to pain. As such there is need for SCD patients to have adequate knowledge on the use this medication.

Adequate knowledge of medication by patients has been found to help with adherence to therapy thereby avoiding drug therapy problems and issues of drug abuse and misuse. One study showed that lack of adequate knowledge of disease might be a result of inadequate education by the health provider.[11] On the other hand, adequate knowledge and experience of euphoric effects may also lead to deliberate use of medication just for euphoria thereby leading to dependence and addiction. Studies have shown that previous experience of the associated euphoria, poverty and out-of-pocket healthcare expenditure are major drivers of pentazocine use outside the hospital with or without prescriptions.[12] Utilization of drugs like Pentazocine requires monitoring by the health provider. While the use of Pentazocine might effectively relieve pain, it is important that the trend and pattern of use by patients be given attention since it is the commonest opioid analgesic used in Nigeria for pain management in SCD.[13] The knowledge of pentazocine use and associated addiction tendencies among patients if ascertained can inform interventions to curtail misuse.

A study done in a tertiary hospital in Ilorin, Nigeria showed that after patient's bone pain and osteomyelitis were successfully relieved by Pentazocine given through hospital prescription, the patients continued with the drug outside the hospital and became addicted to it. These patients consequently feigned pain in order to get Pentazocine prescription in the hospital and carried out antisocial behavoiurs in the community just to have access to the drug.[14] Another study done in a Tertiary hospital in Lagos, another part of Nigeria showed that only 2% of the 350-study-population were at risk of dependence because of their pattern of use of pentazocine even though 27.9% of health providers estimated that majority of SCD patients on pentazocine were addicted.[15] To this end, it is important to study the pattern of use of Pentazocine and other analgesics among SCD patients. The objectives of the study therefore were to assess the awareness and pattern of use of pentazocine among SCD patients attending two sickle cell clinics in Lagos Nigeria.

2. METHODS

2.1 Study Setting

This study was conducted in Lagos State which is situated in the south-western part of Nigeria. It is the commercial nerve center of the country and home to about 21 million people.[16] The study was carried out at the sickle cell center (SCC), a specialised sickle cell clinic, and the hematology clinic of the Lagos University Teaching Hospital (LUTH), a tertiary health care centre. Both are in Idi-Araba, within coordinates of 6.5191º N and 3.486ºE of the state. Hematology clinic, LUTH run weekly clinics while SCC on the other hand run daily clinics, with a combined estimated number of three hundred patients seen per month.

2.2 Study Design

This study was a cross-sectional, descriptive, questionnaire-based survey among patients with sickle cell disease (SCD) who attended the two clinics.

2.3 Sample size/Study Population

Eighty (80) SCD patients attending the two sickle cell clinics, SCC Idi-araba, and hematology clinic, LUTH during the period of study were conveniently and consecutively recruited into the study. Eligible patients included all consenting patients aged 18 years and above in both clinics. Those excluded from the study on the other

hand were patients younger than 18 years, and those who declined to give informed consent.

2.4 Study Instrument

A structured, interviewer administered questionnaire comprising of two sections was developed based on extant literature to collect required data. Section A obtained information on patient's sociodemographic data (age, gender, occupation, education, and marital status). Section B obtained information on prescribed medications, patient's awareness and use of pentazocine, severity of pain, use of pentazocine outside of the clinic, and reasons for use. Information about the dosage form used, the dose used, who recommended pentazocine to them, and whether they also recommended it to others were obtained. Severity of pain was rated using the numerical rating pain scale, classified as none: 0, mild: 1-3, moderate:4-6, and severe: 7-10.[17,18] Awareness of pentazocine was rated by the number and percentages of patients who knew what it was used for. The developed questionnaires were pretested by administering them to five SCD patients before the commencement of the main study. The patients sampled for the pretest were subsequently excluded from the main study after appropriate amendments for clarity in the questionnaire. Thereafter the pretested questionnaires were administered to the respondents to elicit the desired responses.

2.5 Ethical Approval

Ethical approval for the study was obtained from the Health Research and Ethics Committee of Lagos University Teaching Hospital, LUTH (Health Research Committee Assigned No: ADM/DCST/HREC/APP/985). Informed consent was obtained from all recruited patients. Confidentiality and anonymity were assured.

2.6 Data analysis

The data collected were coded and analyzed using IBM Statistical Package for the Social Sciences (**SPSS**), version 21.0. Data were analyzed using descriptive statistics such as frequencies and percentages. Bivariate analysis using chi square was used to determine differences in proportions between the two clinics, and also the association between pentazocine awareness and/or use, and patient variables. Level of significance was placed at $p < 0.05$.

3. Results

3.1 Sociodemographic Characteristics: Of the eighty (80) sickle cell disease (SCD) respondents recruited for the study, 42 (52.5%) were recruited from the haematology clinic of the Lagos University Teaching Hospital (LUTH), while the remaining 38 (47.5%) were recruited from the Sickle Cell Centre, (SSC) Idi-araba. A total of 42 (52.5%) respondents were females and 38 (47.5%) were males. Almost all, 68 (85%) respondents were single, and about half, (45.0%) were within 21-30-year age group. Mean age was 26.49 8.16. A higher proportion of the respondents 50, (62.5%) had tertiary education and 33, (41.3%) were still students (Table 1). There was a statistically significant difference in gender distribution in respondents attending sickle cell clinics in both hospitals ($p = 0.01$).

3.2 Analgesics prescribed for SCD patients: Figure 1 shows the distribution of analgesics prescribed in both clinics for the management of sickle cell induced pain. Ibuprofen, Paracetamol, Pentazocine and Diclofenac were commonly prescribed. More patients in SSC were prescribed Ibuprofen (31.4%) and Diclofenac (22.9%), while more patients in haematology clinic LUTH were prescribed Paracetamol (28.9%) and Diclofenac (28.9%). The frequency of Pentazocine prescription in SSC was higher than for LUTH (20.0% vs 10.5%). Aspirin, Dihydrocodeine and other analgesics were less commonly prescribed in both clinics.

Table 1: Sociodemographic characteristics of sickle cell patients

Characteristics		LUTH N=42 (%)	SSC N=38 (%)	All Patients N=80 (%)	P value
Mean Age	26.49 ± 8.16				
	= 20	7 (8.8)	16 (20.0)	23 (28.8)	
	21 – 30	22 (27.5)	14 (17.5)	36 (45.0)	
	31 – 40	9 (11.3)	5 (6.3)	14 (17.5)	
	41 - 50	4 (5.0)	3 (3.8)	7 (8.8)	
	Male	14 (17.5)	24 (30)	38 (47.5)	
	Female	28 (35.0)	14 (17.5)	42 (52.5)	
	Single	33 (41.3)	35 (43.8)	68 (85.0)	
	Married	8 (10.0)	3 (3.8)	11 (13.8)	
	Divorced	1 (1.3)	0 (0.0)	1 (1.3)	
	Primary	1 (1.3)	3 (3.8)	4 (5.0)	
	Secondary	6 (7.5)	15 (18.8)	21 (26.3)	
	Tertiary	31 (38.8)	19 (23.8)	50 (62.5)	
	Post Graduate	4 (5.0)	1 (1.3)	5 (6.3)	
	Student	13 (16.3)	20 (25.0)	33 (41.3)	
	Self-employed	16 (20.0)	9 (11.3)	25 (31.3)	
	Employed	11 (13.8)	7 (8.8)	18 (22.5)	
	Unemployed	2 (2.5)	2 (2.5)	4 (5.0)	

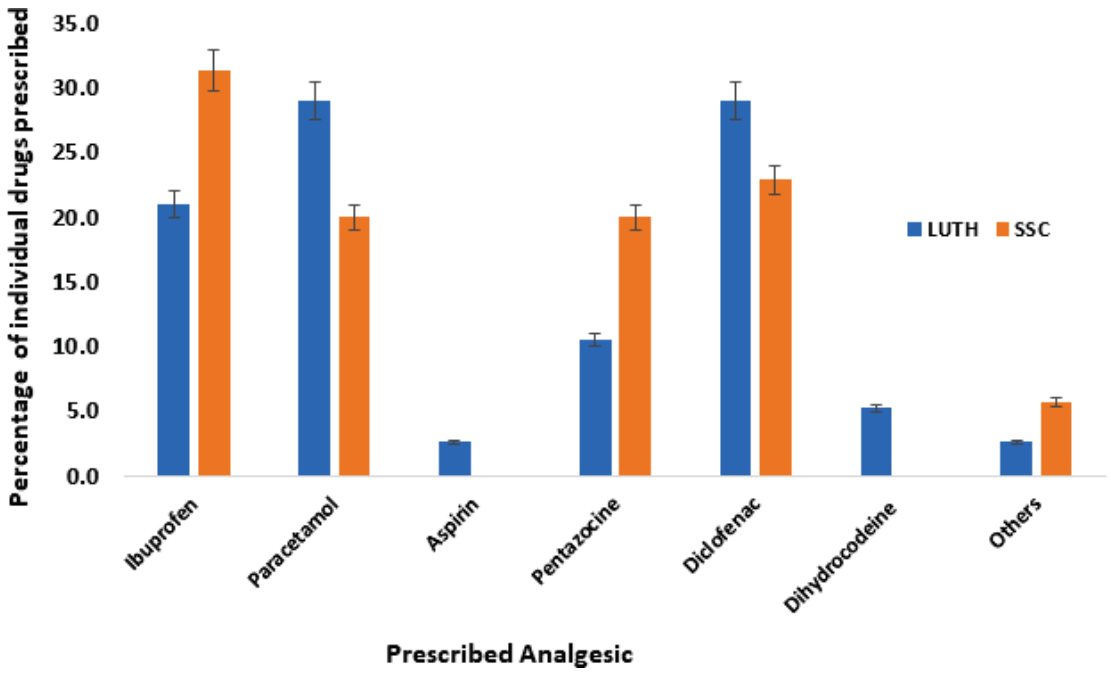

Figure 1: Prescribed analgesics in LUTH and SSC clinics for the management of sickle cell pain.

3.3 Awareness and pattern of Pentazocine use: Respondents' awareness and use of Pentazocine for the management of sickle cell induced pain is presented in Table 2. Almost all the respondents, 74, (92.5%) experienced pain. Of these, 55, (68.8%) respondents experienced significant pain (p = 0.003) which led to hospitalization. A total of 32 (40.0%) of respondents were aware and know that Pentazocine is used for the management of moderate to severe pain. Again, of these, half, 16 (5.00%) used Pentazocine outside of the hospital clinic to manage their pain. A further 43.8 and 56.3% out of those who used pentazocine outside of the clinics used it because it was prescribed for them, and because they had severe pain respectively. This led to almost all of the respondents who used pentazocine outside of the clinic, (93.8%) experiencing pain relief. Most, 68.8% of the respondents used the injectable form of pentazocine, while about 31.3% used the oral tablets. Majority, 62.5% also took the medication once daily. Similar proportions of respondents, about half of those who used pentazocine outside of the clinic, (43.8%) recommended Pentazocine to other SCD patients and experienced one form of side effect or the other.

3.4 Association of Pentazocine awareness and use with sociodemographic variables: Respondent's age was significantly associated with pentazocine awareness but not with pentazocine use. Respondents within 21-30-year age group had significant higher awareness of pentazocine being used in the management of SCD pain (21.3%; p = 0.02). There was no association between other sociodemographic variables and pentazocine awareness and use (Table 3).

Table 2: Awareness and use of Pentazocine among sickle cell patients

Variable (N=80)	LUTH n (%)	SSC n (%)	Total n (%)	p-value
Pain as a result of SCD	39 (48.7)	35 (43.7)	74 (92.5)	0.07
Hospitalised due to pain	36 (48.6)	19 (25.7)	55 (68.8)	0.003
Awareness of Pentazocine use	19 (23.8)	13 (16.3)	32 (40.0)	0.32
Used Pentazocine outside the hospital (N=32)	10 (31.3)	6 (18.8)	16 (50.0)	0.72
Reason for Pentazocine use (N=16)				
On prescription	6 (37.5)	1 (6.3)	7 (43.8)	0.18
Presence of severe pain	4 (25.0)	5 (31.3)	9 (56.3)	
Pentazocine strength used				
50mg Tab	4 (25.0)	1 (6.3)	5 (31.3)	0.33
30mg Injection	6 (37.5)	5 (31.3)	11 (68.8)	
Frequency of use				
Once daily	6 (37.5)	4 (25.0)	10 (62.5)	
Twice daily	2 (12.5)	2 (12.5)	4 (25.0)	0.68
Three times daily	1 (6.3)	0 (0.0)	1 (6.3)	
Greater than three times daily	1 (6.3)	0 (0.0)	1 (6.3)	
Achieves pain relief with Pentazocine	9 (56.25)	6 (37.5)	15 (93.8)	0.42
Pentazocine was recommended	4 (25.0)	3 (18.8)	7 (43.8)	0.70
By a friend	1 (6.3)	0 (0.0)	1 (6.3)	0.14
By a relative	0 (0.0)	2 (12.5)	2 (12.5)	
By a Healthcare professional	3 (18.8)	1 (6.3)	4 (25.0)	
Ever recommended Pentazocine to others?	4 (25.0)	3 (18.8)	7 (43.8)	0.05
Perceived side effect of Pentazocine	4 (25.0)	3 (18.8)	7 (43.8)	0.70

Table 3: Association of Pentazocine awareness and use with sociodemographic variables

Variable		Pentazocine awareness N = 80 n = (%)	Pentazocine use N = 32 n (%)	p-value 1*	p-value 2**
	< 20	4 (5.0)	2 (6.3)		
	21 – 30	17 (21.3)	8 (25.0)		
	31 – 40	9 (11.3)	4 (12.5)		
	41 - 50	2 (2.5)	2 (6.3)		
	Female	15 (18.8)	8 (25.0)		
	Male	17 (21.3)	8 (25.0)		
	Primary	1 (1.3)	0 (0.0)		
	Secondary	5 (6.3)	4 (12.5)		
	Tertiary	22 (27.5)	9 (28.1)		
	Postgraduate	4 (5.0)	3 (9.4)		
	Christianity	25 (31.3)	14 (43.8)		
	Islam	7 (8.8)	2 (6.3)		
	Student	11 (13.8)	7 (21.9)		
	Self employed	10 (12.5)	6 (18.8)		
	Government employed	10 (12.5)	3 (9.4)		
	Unemployed	1 (1.3)	0 (0.0)		
	Single	27 (33.8)	13 (40.6)		
	Married	5 (6.3)	3 (9.4)		

Key: *p-value – Pentazocine awareness versus sociodemographic parameters;
**p-value – Pentazocine use versus sociodemographic parameters

4. Discussion

The management of sickle cell disease has improved over the years resulting in patients enjoying a longer lifespan, while still witnessing varied types of pain. This study assessed patients' awareness and use of pentazocine in patients with Sickle Cell Disease (SCD) attending two sickle cell clinics in Lagos.

The study found that SCD patients who attended the two clinics studied were mainly female students less than 30 years old. This suggest that students are exposed to the use of analgesics in attempts to control the associated vaso-occlusive crisis (VOC) and pain common in SCD. The chronic debilitating pain signals the use of stronger analgesics and in trying to control their pain, they use opioids. Unfortunately, opioids have dependency potentials and social implications. Corroborating the findings of this study is a study carried out in the Southeast of Nigeria that found a high prevalence of SCD among students aged 20 to 30 years.[19] Also, Adewoyin et al.[13] in a study to determine the clinical and socio-demographic determinants of pentazocine misuse among patients with SCD in Benin City found that the median participants' age was 32 years. In Lagos, Okonkwo et al.[20] documented a high use of psychoactive substance among students. Students aged 18 years and above are at increased risk of misuse of opioids especially pentazocine used in pain management.

Healthcare professionals are often faced with challenge of balancing the provision of pain relief and reducing dependency.[21] They should provide adequate counselling to patients regarding the use and side effects of opioids.

The findings of this study show that most SCD patients experienced moderate pain during the illness, with about two thirds of them not aware of what pentazocine is used for. The poor awareness on pentazocine use could propagate the misuse in the community. In this study, most patients who were prescribed pentazocine used it outside the hospital facility after their first prescription. That means that respondents resorted to self-medicating with pentazocine after initial contact with healthcare professionals. The proximity to hospital is a major driver of access to medications. Access to analgesics could be facilitated either by further demands for more prescriptions, generation of unwanted prescriptions, and connivance with other healthcare professionals. Corroborating these assertions is a recent study carried out in Nigeria which found a high prevalence of self-medication with analgesia (28.8%), and pentazocine dependence.[19] This behaviour has a lot of consequences and contributing factors could be multifactorial. Reduction in pain, and the feeling of euphoria could contribute to the urge to keep taking the medications. Our study found that most participants who used pentazocine outside the hospital experienced reduced pain. A study done in a tertiary hospital in Ilorin, Nigeria showed that the patients continued with the use of pentazocine outside the hospital after a successful reduction in pain and became addicted to it.[14] Another study found a significant association between working in hospitals (doctors, pharmacists, and nurses), and abuse of pentazocine.[13] The abuse of pentazocine could result in musculoskeletal and psychological side effects as opined by Adewoyin and colleagues.

In this study, it is worrisome to observe that SCD patients not only purchase pentazocine on their own after the initial prescription from a clinician, but also recommend the medication to their friends and family members with SCD experiencing pain. These findings suggest an inherent obscure distribution channel for the opioids. This hidden misuse of pentazocine among SCD patients must be borne in mind when counselling SCD patients already on pentazocine or intending to start its use. Unfortunately, in Nigeria, pentazocine is among the analgesics that are readily available as over the counter medications without prescription in pharmacies despite its addiction characteristics.[13] The availability of pentazocine in the open markets and street hawking of drugs further increases access. Hence drug abuse has quickly become a national issue and analgesics are among the class of medication that are implicated.[20] To curtail the menace caused by misuse of the opioids, government and hospital administrators should ban or place restrictions on the purchase, distribution, and use of opioids without prescriptions. Healthcare professionals should prescribe doses of the medication that is needed to control pain. Public enlightenment campaigns to educate on the dangers of opioid misuse should also be organized regularly.[21]

In managing pain associated with SCD, different analgesics have been used in varying degrees. In this study, the most prescribed analgesic was Ibuprofen (31%) in SCC, followed by diclofenac (29%) in LUTH. Pentazocine was prescribed in about 20% and 10% in sickle cell clinic and LUTH respectively. This use of pentazocine in both clinics is low, despite the pain experiences or the category of pain these participants were confronted with. This could be due to inadequate pain assessment, and inertia in prescribing opioids for fear of dependence. However, most respondents have been hospitalized due to excruciating pain at one time or the other. Contradicting our finding, is a study of pain management in children with SCD done in Lagos, which found paracetamol (75%) and pentazocine (66.7%) as the most frequently used analgesics. The study not only failed to conform to the WHO guidelines on dosing of analgesics in children, but also reported inadequate pain assessment by healthcare providers.[22] In our study, injectable pentazocine was in high use compared to oral forms. Supporting this finding is a study that recorded high use of injectables and noted that the buttocks, upper arm, and the thigh were the commonest site of injection, which resulted in ulcers, and deep wounds.[13]

This study revealed the important role patient education plays in the rational use of drugs and management of SCD. The survey was however only available to SCD patients who attended sickle cell clinics within the study period, hence the small sample size. This might not totally rule out biases, and the generalizability of the results to the general population. Therefore, the results should be interpreted with caution. A multicenter study with a larger sample size might be required to substantiate our findings.

5. Conclusion

This study found that more than half of SCD patients in our study population were not aware of the role of pentazocine in the management of SCD. This did not however discourage its use without prescription outside of the clinic. Proper education on disease condition and its management should be encouraged among SCD patients to encourage appropriate use of pentazocine, as well as other analgesics used in the management of SCD and discourage misuse.

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Disclosure

The authors declare no conflict of interest.

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