



Pentazocine abuse in Sickle Cell Disease Patients Seen at a Tertiary Hospital in Nigeria: A Chronic Menace

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Authors' contributions

*This work was carried out in collaboration between all authors. Author OEI did the study design,
literature search and statistical analysis. All the authors took part in data collection and analysis of
study. The final manuscript was read and approved by all authors.*

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ABSTRACT

Background: Pentazocine abuse in patients with Sickle cell disease (SCD) has not received adequate attention in Nigeria. Many of these SCD patients have had their conditions unduly worsened and quality of life severely breached by complications of pentazocine abuse. Despite the growing incidence observed in clinical practice and palpable tendency to degenerate further, given the current ease of access to the drug in our environment, it has remained underreported. This study evaluated the myriad physical complications and socioeconomic burden of pentazocine abuse on patients with SCD.

Method: This study was carried out on SCD patients (attending the adult hematology clinic) who abused parenteral pentazocine. Data were obtained mainly from detailed history and physical examination. The findings were analysed accordingly.

Results: Eleven SCD patients who abused pentazocine were recruited and comprised of 8 males (72.7%) and 3 females (27.3%). Their mean age was 34±6 years, 81.8% were not married, 81.8%

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had some kind of job and 22.2% of these suffered loss of job. The mean duration of pentazocine abuse was 7.4±3.7 years while mean dose of pentazocine injected by the study participants on daily basis was 279±228 mg; 63.6% needed no prescription papers to purchase the drug and 36.4% used forged prescription papers. The mean monthly expenditure on pentazocine was NGN 27,000±22,000 (Nigerian Naira). It was also noted that 18.2% (2) of the study participants abused other drugs alongside pentazocine. As high as 90.9% (10) had scars and/or ulcers; 63.6% (7) developed lymphedema while 90.9% (10) had some degree of fibrous myopathy. Majority (63.6%) of the participants had fixed contractures and/or deformities of their limbs (and digits) with varying degrees of loss of joint movement and/or gait abnormalities observed in 72.7% (8) of participants.

Conclusion: We advocate vigorous sensitization of both healthcare givers and SCD patients on the risk and complications (consequences) of pentazocine abuse. This is to underscore the need for more caution with pentazocine prescription and use. As much as possible oral formulations, when necessary, should be recommended since most of the observed physical complications were apparently due to the parenteral route of administration of the drug. Finally, any SCD patient presenting with the highlighted physical complications must be considered as a case of pentazocine abuse until proven otherwise.

Keywords: Sickle cell disease; pentazocine abuse; complications; socioeconomic.

1. INTRODUCTION

Pentazocine is an opioid analgesic with mixed receptor action, widely used for the management of moderate to severe pain. It was introduced in 1967 to address the need for very potent analgesic that had no risk of drug dependence (an aim that has been practically defeated). Pentazocine has a very reputable analgesic effect although it has been associated with several adverse effects including: skin fibrosis, ulceration, abnormal pigmentation, fibrous myopathy and contractures [1-3] as well as its potential for abuse [4,5]. Sickle cell disease (SCD) is fairly characterised by vaso-occlusive pain crises which may be excruciating and unremitting in addition to psychosocial and physical co-morbidities [6,7]. Consequently, pentazocine is so frequently used in the management of pain in sickle cell disease (SCD) patients in Nigeria that majority of the patients have been exposed to this drug.

Cases of pentazocine abuse have been reported across the globe. In Nigeria this phenomenon has equally been observed in sickle cell disease patients with the attendant adverse effects, [4,5] even lymphedema [5]. Many patients with SCD already have a suboptimal quality of life and life expectancy by virtue of their hemoglobinopathy. Thus inimical practice such as pentazocine abuse could compound the poor quality of life. Worthy of note is that a significant number of these SCD patients in our environment can access the drug without a doctor's prescription [5]. Efforts have been made in some countries to eradicate the abuse of pentazocine. The measures included classifying pentazocine as a

controlled drug (to prevent undue access to the drug) and the production of pentazocine brands containing naloxone (to counter the addictive potentials).

Despite the foregoing, the cases of pentazocine abuse in Nigeria, particularly in SCD patients, are increasing and no concrete intervention has been put in place to curb the menace. Moreover, there is a gross under reporting of pentazocine abuse (as well as its associated complications) in SCD patients in our locality; partly because of low index of suspicion and due to patients' reluctance to volunteer such information. This study is therefore aimed at highlighting some of the physical complications as well as socioeconomic burden associated with pentazocine abuse in SCD patients.

2. METHODOLOGY

Sickle cell disease patients (attending clinics at the University of Benin Teaching hospital), who abused pentazocine were consecutively recruited, interviewed and examined (after obtaining informed consent from them). Detailed history and physical examination were largely utilized in diagnosis of the complications of pentazocine abuse. The assessment of pentazocine-induced fibrous myopathy was made by observing a woody-hard muscle bulk and resultant loss of function with preceding history of repeated intramuscular pentazocine injections [3].

This work was carried out between 2011 and 2015. Ethical approval was obtained from the

ethics and research committee of the hospital. The data collated were analysed and discussed accordingly.

3. RESULTS

Eleven SCD patients with pentazocine abuse were recruited (within a four-year period) and comprised of 8 males (72.7%) and 3 females (27.3%). Their ages ranged from 22 to 43 years, with mean age of 34 ± 6 years as shown in Table 1. Majority (81.8%) were unmarried while on the other hand 81.8% had some kind of job (civil servants, artisans) that fetched them some income.

Table 1. Socio-demographic parameters

Parameters	Mean \pm 2SD
Age (years)	34 ± 6 (22 - 43)
Parameters	Frequency % (n)
Sex	
Male	72.7 (8)
Female	23.7 (3)
Employed	
Yes	81.8 (9)
No	18.2 (2)
Married	
Yes	18.2 (2)
No	81.8 (9)

In this group of patients the duration of pentazocine abuse varied between 3 to 15 years, with an average duration of 7.4 ± 3.7 years. The maximum dose of pentazocine injected by the study participants on daily basis also varied from 120 mg to 900 mg (mean dose of 279 ± 228 mg). Most of them (63.6%) needed no prescription papers to purchase the drug whereas 36.4% used forged prescription papers for their routine supplies. The estimated maximum expenditure on the purchase of pentazocine per month ranged from NGN 12,000.00 to as high as NGN 90,000.00; (Table 2). Out of the number that had jobs, 22.2% suffered loss of job as a result of a major physical complication of pentazocine abuse. It was also noted that 18.2% (2) of the study participants abused other drug (promethazine) alongside pentazocine.

Virtually all of them, 90.9% (10), had multiple scars and/or ulcers around the sites of injection of the drug as shown in Table 3. Those that have suffered some degree of lymphedema were 63.6% (7) while 90.9% (10) had some degree of fibrous myopathy. Majority (63.6%) of the participants had fixed contractures and/or

deformities of their limbs (and digits). Varying degrees of loss of joint movement and/or gait abnormalities were observed in as much as 8 (72.7%) participants.

Images of some of these physical complications are shown in the appendix (Figs. 1-4).

Table 2. Details of pentazocine abuse

Parameters	Mean \pm 2SD
DOA (years)	7.4 ± 3.7 (3-15)
MDD (x 30 mg)	9.3 ± 7.6 (4-30)
MASM(xNGN 10,000)	2.7 ± 2.2 (1.2-9.0)
Parameters	Frequency % (n)
MOS	
Forge prescription	36.4 (4)
No prescription	63.6 (7)
LOJ	
Yes	22.2 (2)
No	77.8 (7)
AOD	
Yes	18.2 (2)
No	81.8 (9)

Abbreviations: DOA – duration of pentazocine abuse; MDD – maximum daily dose; MASM – maximum amount spent monthly on pentazocine; MOS – means of drug supply; LOJ – loss of job; AOD – abuse of other drugs; NGN – Nigerian Naira.

4. DISCUSSION

Pentazocine abuse has been reported around the world and in different individuals including patients with SCD [1-5,8]. However it is not only underreported in patients with SCD but previous works have not highlighted the myriad physical complications and socioeconomic burden of parenteral pentazocine abuse on the patients with SCD. There is usually a genuine reason for initial exposure of SCD patients to pentazocine (for the treatment of excruciating pains of vaso-occlusive crisis). In this study, most of the physical complications resulted from abuse of parenteral pentazocine (injections). Our experience with oral formulations of pentazocine is very limited because of non availability. Nonetheless, it is possible to infer that these physical complications would be unlikely with oral formulations of the drug, considering the patho-mechanisms [1-3,5,9,10] of developing the complications. Based on the findings from this work, we posit a very strong probability of parenteral pentazocine abuse in any SCD patient presenting with multiple ulcers and scars (at sites other than the ankles), lymphedema, fibrous myopathy, contractures and fixed joint deformities.

Table 3. Occurrence of the physical complications of pentazocine abuse

Parameters	Present %(N)	Absent%(N)	Total %(N)
US	90.9 (10)	9.1 (1)	100 (11)
LYE	63.6 (7)	36.4 (4)	100 (11)
FM	90.9 (10)	9.1 (1)	100 (11)
CD	63.6 (7)	36.4 (4)	100 (11)
LOM	72.7 (8)	27.3 (3)	100 (11)

Abbreviations: US – ulcers and scars; LYE – lymphedema; FM – fibrous myopathy; CD – contractures and fixed deformities; LOM – loss of joint movement; N – number of participants

The study participants were recruited exclusively from an adult clinic and this would impact on the observed mean age of 34 ± 6 years. Similar to the finding in a report [8] from India, there were far more males (72.8%) than females. This may be related to the greater tendency of males towards substance abuse [11]. It was observed that most of the patients (81.8%) were not married; but could be largely due to their SCD status which they claimed interfered with their relationships. However the major physical complications of pentazocine abuse may make them unattractive to a potential spouse. On the other hand, their unmarried status may promote a vicious circle of pentazocine abuse. Interestingly though, 81.8% of this group of patients had a source of income (job) and perhaps funding for the drug supplies.

Astonishingly, these patients had high daily doses of pentazocine injections for such a long period; mean duration of 9.3 ± 7.6 years. The mean of the maximum dose of pentazocine that each participant injected daily stood at 279 ± 228 mg. This translated to spending fortunes to sustain the pentazocine abuse. Based on the maximum amount they could spend monthly on purchase of the drugs, the mean amount was noted to be NGN $27,000 \pm 22,000$. Some of these patients actually spent more than their monthly income on buying the drug each month, with tendency towards stealing and corruption. In addition to these wasted amounts, some (22.2%) lost their jobs purely as a result of major physical complications of pentazocine abuse (particularly the contractures and fixed deformities of the limbs). Worthy of note was the ease with which they accessed the drug from pharmacy and drug stores, as long as they could pay. Forged prescriptions were used by 36.4% of the patients while 63.6% needed no prescription papers at all. This occurred because there has been apparently no strict regulation on procurement of the drug and no effective system to authenticate drug prescriptions in our locality.

On physical examination, virtually all of them (90.9%) had multiple scars and/or ulcers arising

from pentazocine injections. These could result from poor injection techniques, precipitation of the drug [9] with local ischaemia and perhaps infections culminating in tissue damage. Due to repeated injections and background SCD, the ulcers usually run a chronic course with healing by fibrosis and scarring. They are common findings that have been reported in other works on pentazocine abuse [1,5,12-14]. The management of the ulcers included hospital admission, daily wound dressing, zinc therapy, skin grafting, hypertransfusion and even automated red cell exchange for some participants.

Lymphedema was noted in 63.6% of the patients. This may have arisen from multiple affection of the lymphatic drainage by inflammation, myopathy, ulceration, scarring and fibrosis associated with repeated injection of pentazocine [1-3,9]. For some it was recurrent while in others it was permanent and triggered misdirected investigations and treatment. This is one complication which though previously reported in our locality, [5] has been grossly underreported generally. Global data show filariasis to be the most common cause of secondary lymphedema whereas cancer therapy is the leading cause of the condition in industrialized countries [15]. Unfortunately, parenteral pentazocine abuse appears to be the most frequent cause of lymphedema in patients with SCD in our environment. There is no cure for lymphedema presently but treatments to manage and reduce the swelling include physiotherapy and compression bandages [16]. Volume reducing surgery and lymphatic microsurgery are not commonly performed [17].

Some form of fibrous myopathy was observed in 90.9% of the participants following clinical examination. We did not have the luxury of biochemical, radiological and histological investigations in order to conclusively establish this diagnosis, but history and examination findings were highly suggestive. This

complication has been severally documented in other related works [2,3,18]. The mechanism is unclear but easy precipitation of the drug in a neutral or slightly alkaline extravascular medium and subsequent initiation of inflammation and fibrosis may play a role [9]. The fibrous myopathy contributed to the contractures and deformities noted in 63.6% of the study participants. In this study, the patient that had no fibrous myopathy equally had no contractures and deformities. The contractures caused fixed flexion or extension at some joints with impaired movement, gait abnormalities and inability to walk (which is unrelated to avascular necrosis of femoral head) in some. Similar findings had been reported in an individual who was abusing parental pentazocine [10]. The management of these complications will include detoxification and withdrawal of pentazocine, use of corticosteroids or nonsteroidal anti-inflammatory drugs, collagenases and physiotherapy [2]. However there may not be any overall change in degree of disability [19].

These physical complications of pentazocine abuse pose huge socioeconomic challenge to the patients, their relatives and the society at large. Despite the massive financial losses in the management of the complications, many could not be completely resolved.

5. CONCLUSION

We advocate vigorous sensitization of both healthcare givers and SCD patients on the risk and complications (consequences) of pentazocine abuse. This is to underscore the need for more caution with pentazocine prescription and use. As much as possible oral formulations, when necessary, should be recommended since most of the observed physical complications were apparently due to the parenteral route of administration of the drug. Pentazocine should be classified as a controlled drug with strict measures in place to enforce regulation of its sales in our environment. The appropriate authorities should evolve effective ways of verifying the genuineness and traceability of doctors' prescriptions. Finally, any SCD patient presenting with these highlighted physical complications must be considered as a case of pentazocine abuse until proven otherwise.

6. LIMITATION

The diagnosis of pentazocine abuse was based on information volunteered by the patient and/or

relatives and this could be subjective since it is possible to conceal such information. Secondly, the participants were drawn solely from adult SCD patients who gave their consent. All these invariably affected the number of participants recruited in this study.

COMPETING INTERESTS

Authors declare that there is no conflict of interest regarding the publication of this paper. The authors are responsible for the writing and content of this work.

REFERENCES

1. Winfield J, Greek K. Cutaneous complications of parenterally administered pentazocine injection. *JAMA*. 1973;226:189-190.
2. Silva M, Sing P, Murthy P. Fibromyositis after intramuscular pentazocine abuse. *J Postgrad Med*. 2002;48:239.
3. Steiner J, Winkleman A, de Jesus P. Pentazocine-induced myopathy. *Arch Neurol*. 1973;28:408-409.
4. Makanjuola AB, Olatunji PO. Pentazocine abuse in sickle cell anaemia patients: A report of two case vignettes. *African J Drug & Alcohol Studies*. 2009;8(2):59-64.
5. Iheanacho OE, Halim NKD, Enosolease ME, et al. Case studies involving bilateral lower limb lymphoedema following pentazocine abuse in sickle cell disease patients. *Ann Trop Path*. 2013;4(1):47-52.
6. Edwards C, Whitfield K, Sudhakar S, et al. Parenteral substance abuse, reports of chronic pain and coping in adult patients with sickle cell disease. *J Nat Med Assoc*. 2006;98(3):420-428.
7. Yale SH, Nagib N, Guthrie T. Approach to the vaso-occlusive crisis in adults with sickle cell disease. *Am Fam Physician*. 2000;61:1349-1356.
8. Saxena S, Mohan D, Adityanji. Pentazocine abuse: Review and a report on eighteen cases. *Indian J Psychiatry*. 1985;27(2):145-152.
9. Schlicher JE, Zuchlke RL, Lynch PJ. Local changes at the site of pentazocine injection. *Arch Dermatol*. 1971;104(1):90-91.
10. Das CP, Thussu A, Prabhakar S, Banerjee AK. Pentazocine-induced fibromyositis and

- contracture. *Postgrad Med J.* 1999; 75(884):361-362.
11. Rahimian BI, Tabatabaee SM, Tosi J. Attitude to substance abuse: Do personality and socio-demographic factors matter? *Int J High Risk Behav Addict.* 2014;3(3):e16712.
 12. Mann RJ, Gostelow BE, Meacock DJ, et al. Pentazocine ulcers. *J R Soc Med.* 1982; 75(11):903-905.
 13. Fleming JP, Hopper A, Robson A, Singh M, Baker J. Pentazocine-induced cutaneous scarring. *Clin Exp Dermatol.* 2014;39(1):115-116.
 14. Kathuria S, Ramesh V, Singh A. Pentazocine induced ulceration of the buttocks. *Indian J Dermatol Venereol.* 2012;78(4):521.
 15. Saito Y, Nakagami H, Kaneda Y, et al. Lymphedema and Therapeutic Lymphangiogenesis. *Biomed Res Int.* 2013;2013:804675.
 16. International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema. *Lymphology.* 2009;42(2):51-60.
 17. Szuba A, Rockson SG. Lymphedema: Classification, diagnosis and therapy. *Vasc Med.* 1998;3(2):145-156.
 18. Goyal V, Chawla JM, Balhara YP, Shukla G, Sing S, Behari M. Calcific myofibrosis due to pentazocine abuse: A case report. *J Med Case Rep.* 2008;2:160.
 19. Burnham R, McNeil S, Hegedus C, Gray DS. Fibrous myopathy as a complication of repeated intramuscular injections for chronic headache. *Pain Res Manag.* 2006; 11(4):249-252.

APPENDIX

Images of Some Physical Complications of Pentazocine Abuse In The Participants



Fig. 1. Multiple ulcers and scars



Fig. 2. Multiple scars and lymphedema



Fig. 3. Lymphedema and fixed flexion of the knees



Fig. 4. Flexure deformities of the digits

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