1	<u>Case Study</u>
2	Case Report: Successful Management of Opioid Abuse and Addiction in a
4	Known SCD Patient at the University of Calabar Teaching Hospital,
5	Calabar, Nigeria
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7	ABSTRACT
8 9 10	BACKGROUND: Opioids are group of potent analgesic with mixed receptor activities. Pain related symptom accounts for the main reason for substance dependence among sickle cell disease (SCD) patients.
11 12 13	AIMS: The report aims to elucidate the adverse effects of opioid and it's complication (abuse, dependency and addiction) and provide management strategy for health practitioners to curtail the dependency of SCD patients to opioid use.
14 15 16 17 18 19 20 21	PRESENTATION OF CASE: The patient was a 27 years old lady that was diagnosed with sickle cell disease at the age of two. She presented with a two years history of oral self-medication of DF118 and Tramadol. She became dependent on the opioid on the account of sickle cell bone pain crises affecting both her upper and lower limbs with a pain score of 9/10. Other anagelsic like Diclofenac and Pentazocin couldn't ameliorate her excruciating pain but administration of 60mg of oral DF118 provided her with quick relieve. The sedative effect of Tramadol and DF118 allows her sleep comfortably and hence the beginning of her dependency. On review, patient's system was essentially intact and she was further referred for psychiatrist evaluation and possible rehabilitation.
23 24 25 26 27 28	DISCUSSION: Recurrent bone pain crisis represent the most common reason patient with SCD seek acute medical care. Due to the quick analgesic relief and euphoric effect derive from both medication, patients feign pain after genuine pain had subsided in other to continue getting the prescription. The immediate pain assessment and frequent reassessment at 15min, 30min, 1hour then 2hours with appropriate application of medication until pain relief is very important to prevent drug abuse.
29 30 31	CONCLUSION: Less addictive analgesic should be consider first after observing the nature of the pain before moving to stronger analgesic that have high potential for abuse and when stronger analgesic is to be used it should be for a short duration.
32	Keywords: Opioid Abuse, Sickle Cell Disease, Dependency, Addiction, UCTH

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INTRODUCTION

Sickle cell disease (SCD) is a heterogeneous group of disorder, with a highly variable clinical 36 spectrum. It is an autosomal recessive structural haemoglobin disorder. The most prevalent 37 38 form is sickle cell anaemia (HbSS), which is due to inheritance of the sickle cell gene in a 39 homozygous state. Other forms of SCD include the compound heterozygous forms in which the sickle beta globin gene is co-inherited with another abnormal haemoglobin gene such as 40 HbC in HbSC, β thalassaemia in HbSβ thalassaemia among others.^{1,2} 41 42 SCD is the most common genetic disorder in Sub-Sahara Africa. Nigeria is bearing a high disease burden with an estimated 1 - 2% of its population affected by the disease. An 43 estimated 20 - 30% of her populace carry the sickle cell gene with a normal haemoglobin 44 45 gene (carrier state). The disease burden differ slightly from one geographical region to another. Nwogoh et al³ reported the prevalence rate of SCD to be 2.4% and a 23% carrier 46 state in Benin City. Inyama et al⁴ reported a prevalence of 3.7% in a multi-centre study in 47 Nigeria. 48 The pathophysiology of Sickle cell anaemia is the substitution in the position sixth amino 49 acid of β globin gene or also the substitution of GAG for GTG at chromosome 11.5 This 50 51 substitution result in the broad clinical spectrum of the disease that extend beyond the red 52 cell, as a result of the tactoid formation which is due to the effect of the substitution of the hydrophilic nature of the haemoglobin with hydrophobic haemoglobin with aggregation of 53 tactoid forming polymer that will lead to vascular obstruction.⁵ The loss of potassium and 54 55 water resulting in cellular dehydration which also worsen the whole process. Other 56 contributing factor include Nitric oxides depletion, endothelia activation with increase 57 expression of adhesion molecule, inflammation and activation of coagulation system all play a vital role in the pathophysiology of this disease.⁵ Despite understanding the molecular basis 58

for this disease the mechanism of vaso-occlussive crisis remain so vast that it cannot be 59 completely eluted thereby predisposing many of this patient to recurrent recalcitrant, 60 unbearable bone pain crisis. 61 Opioid are group of potent analgesic with mixed receptor activities. Opioid is said to be 62 63 absorbed from the gastrointestinal tract and metabolized in the liver gastrointestinal tract and 64 kidney. Opioid is said to have four different type of opioid receptor (Mu, Kappa, Delta, 65 Nociceptor-OR) with a major analgesic effect or a subtype of nociceptor-OR which is termed 66 the MOP, because of the mixed against effect of opiod in other sub type Nociceptor OR such as DOP and KOP.6 Most opioid tend to cause a reduction in consciousness and euphoria 67 predisposing them to abuse.⁶ 68 69 Recurrent bone pain crisis represent the most common reason patient with SCD seek acute medical care. In a study among sickle cell anaemia patient that are substance dependent, pain 70 related symptom accounted for about 88% of all symptom.⁷ Opioid analgesic are the 71 mainstay of therapy for bone pain crisis in SCD, thus before adulthood most SCD patients 72 73 must have had intermittent exposure to opioids. Opioids are potent analgesic associated with decrease hospitalization.⁸ The management of bone pain crisis has been an issue of debate 74 among physician. Some physician advocate minimal use of these drug for fear of addiction, 75 while others believe that inadequate analgesia predisposes patients to pseudoaddiction.⁹ 76 There have been several report in substance abuse by SCD patients with a prevalence of less 77 than 10% worldwide, 10 but varies from one region to another in Nigeria. Ahmed et al 11 78 79 reported a prevalence of 17.8% of opiate dependence among patient with SCD in Maiduguri, North East Nigeria with a male preponderance, similarly, in a study by Mabayoje et al¹⁰ an 80 incident of less than 10% was reported in the South West. Furthermore, Iheanacho et al 12 also 81 reported a less than 18.2% with male preponderance. From the various studies, it could be 82 83 said that the incidence varies with geographical location and more of male predominance.

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CASE REPORT

Miss EO is a 27 years old Nigerian Female graduate with sickle cell anaemia. That was diagnosed when she was 2 years old using Haemoglobin electrophoresis. She presented on the 4th of January 2017 with a 2 year history of oral self-medication of DF118 and Tramadol Iyear respectively. She said she got addicted to these drug about 2 years ago while she was admitted at government hospital in Calabar on account of sickle cell bone pain crisis affecting her upper limb & lower limb which was so severe with a pain score of 9/10 and lasted for about 48hours despite administration of several analgesic such as Diclofenac and Pentazocin, but said pain began to subside on administration of oral DF118 at 60mg to alternate with Tramadol 100mg which was given for a week, patient said while she was on admission she enjoyed the feelings of the quick relief of the pain and sedative effect that allows her to sleep comfortably following the administration of DF118 and Tramadol. Patient on account of this improvement she anxiously decided to know the name of the medication that could give such a wonderful relief and also because of fear of reoccurrence of the pain. She also noticed that both medication become drug of choice each time she has severe bone pain and present to the same health centre. She said on account of the psychological burden of the disease on her parents, who were getting so worried of the repeated bone pain crisis with frequent hospital visits and was also discovered that both medication give their daughter relief and reduce their hospital visit, therefore decided to purchase a card of each medication weekly for her, which she said she took 30mg of DF118 initially twice daily but after 5months increased the dose to 60mg twice daily for a year due to that the initial dosage could not control the pain and she was very uncomfortable and continue on the new dose in the absence of pain because she was enjoying the euphoric effect. Patient revealed she was purchasing the drug on her own and even exaggerate her pain to get the drug prescription from her physician and at most time she gets it without prescription from a private pharmacy whose identity she does not want to

UNDER PEER REVIEW

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disclose. Patient said she spends about ₹300 to purchase a card, which she often finance on with her pocket money, selling her belonging, borrowing and buying on credit. Patient said after a year of self-medication of oral DF118 at 60mg twice daily she discovered she was not getting the relief she used to get. Patient said she got depressed and decided to change to another potent oral opioid (Tramadol) not the injectable because she react to the injectable, reaction such as nausea and continuous vomiting. She said she started with 50mg of Tramadol twice daily, got relief and also enjoyed the euphoric effect and later increases the dose to 100mg then 200mg twice daily which she took every day for 1 year even in the absence of pain. She gets the drug from a pharmacy which she opt not to disclose and each card cost between ₹1700 - ₹2000, and also get prescription from a doctor who she refuse to mention the name or address. She also claimed that anytime she tries to stop the medication she is being thrown into withdrawal symptoms which include lack of sleep, restlessness, sweating, dizziness, blurred vision, headache, joint pain and abdominal cramping, depression, agitation and craving for the drugs. Thus the patient is not aware of these symptoms and she is seeking for help. On examination, a young lady, pale, anicteric, conscious, alert and coherent, well oriented in person, time and place, well groomed with good motor function with intact both long and short term memory, sense of judgement was mildly impaired. A review of her system were essentially intact, patient is to be referred to the psychiatric for further evaluation and possible detoxification and rehabilitation. Full blood count; PCV= 27%, Hb= 9g/dl, WBC= 11.2 x 10⁹/L, Neutrophiles= 68, Lymphocyte= 32%, Platelet= $452 \times 10^3/L$

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DISCUSSION

The case in study revealed that the patient, was exposed to both DF118 and tramadol, which is as a result of the unfortunate condition she found herself (sickle cell anaemia). BPC is the most commonest presentation among SCD, 14 which our index patients suffers about 10-12 episodes annually necessitating how to seek treatment from an health practitioner that will invariably prescribe Tramadol of DF118, predisposing to abuse of these drugs. 14 It was also noticed that the patient was on these prescribed drug (DF118 & Tramadol) for too long with prescription note not properly controlled, which made her to have access to this prescription note. Due to the quick analgesic relief and euphoric effect derive from both medication, patient has to feign pain after genuine pain had subsided, in other to continue getting the prescription¹⁴. Base on this it is pertinent to say patient is addicted to both drug and the primary aim of both drug is now being abuse. Also lack of proper orientation and counselling of the parents of the patient also contributed to the abuse of the above medications. At this juncture clinical expertise and judgement of the physician is highly needed to distinguish genuine pain from feigned pain in patient with SCD with DF118 & Tramadol abuse. There are paucity of information on DF118 and Tramadol abuse among sickle cell disease patient. Alao et al¹³ reported the case of a 38 year old female sickle cell anaemia patient, though the drug of choice in this instance was cocain. The immediate pain assessment and frequent reassessment at 15min, 30min, 1hour then 2hours with appropriate application of medication until pain relief, this is very important to prevent drug abuse. 15,16 Therefore the less addictive analgesic should be consider first after considering the nature of the pain before moving to stronger analgesic that have high potential for abuse and when stronger analgesic is to be used it should be for a short duration. 15,16

157 The psychiatrist made an impression of opoid abuse and addiction in a known SCD patient. 158 Patient was initially managed on outpatient basis because patient has full insight of her problem and also has the desire to stop and does not wish to be admitted. 159 160 On mental state examination, patient was calm with good hygiene, cooperative and appears 161 motivated and emotionally stable. Her perception was normal, thoughts well collected with 162 normal cognition. 163 On physical examination, the patient was a young slim tall lady, afebrile, anicteric, acyanose 164 with long limbs. Patient was gradually tapper off tramadol with a 50mg weekly reduction for 165 about 6weeks until she suddenly develop an episode of bone pain crisis. And was then 166 admitted for five weeks where she was treated with NSAID (Arthrotec) 75mg which was 167 alternated with paracetamol 1000mg. Patient was also given diazepam 10mg and was 168 carefully observed all through the period of admission with total avoidance of opoid and was 169 discharged on her routine medication folic acid, paludrine and was declared stable with 170 follow up every two weeks and counselling of caregiver and managing physician on opoid

CONCLUSION

use in this patient.

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It is suggested that regular orientation and re-orientation of health worker on the use of opioid particular DF118 and Tramadol among opoid naive SCD, a careful objective assessment of sickle cell patient presenting with painful episodes should be carried out by an experience health care-givers with each case taken in it own merit. A non-addictive analgesic should be commenced first and if an opioid should be use it should be alternated with an NSAID and should be for a short duration. Prescription note of opioid analgesic should be properly controlled, there should be a drug unit established and also legislation against sales of this

- 180 controlled drug for opioid addictive patient should be referred to a psychiatric for
- detoxification and rehabilitation.

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