1	<u>Case Study</u>
2 3	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 22	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.

CONCLUSION: Less addictive analgesic should be considered 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

35 **INTRODUCTION**

Sickle cell disease (SCD) is a heterogeneous group of disorder, with a highly variable clinical spectrum. It is an autosomal recessive structural haemoglobin disorder.¹ The most prevalent form is sickle cell anaemia (HbSS), which is due to inheritance of the sickle cell gene in a 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 HbC in HbSC, β thalassaemia in HbS β thalassaemia among others.^{1,2}

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 estimated 20 - 30% of her populace carry the sickle cell gene with a normal haemoglobin 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 state in Benin City. Inyama et al⁴ reported a prevalence of 3.7% in a multi-centre study in Nigeria.

The pathophysiology of Sickle cell anaemia is the substitution in the sixth position amino 49 acid of β globin gene or also the substitution of GAG for GTG at chromosome 11.⁵ This 50 51 substitution results 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 glutamic acid which is hydrophilic with a less polar hydrophobic, neutral amino acid valine. 53 During hypoxic condition, this abnormal valine amino acid causes intraerythrocytic 54 hydrophobic interaction of affected haemoglobin tetramers, thereafter causing their 55 precipitation and finally polymer formation, leading to the loss of potassium and water 56 resulting in cellular dehydration which also worsens the whole process⁵. Other contributing 57 factor include Nitric oxides depletion, endothelia activation with increase expression of 58

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 for this disease the mechanism of vaso-occlussive crisis remain so vast that it cannot be completely avoided thereby predisposing many of this patient to recurrent recalcitrant, unbearable bone pain crisis.

Opioid are group of potent analgesic with mixed receptor activities. Opioid is said to be absorbed from the gastrointestinal tract and metabolized in the liver, gastrointestinal tract and kidney. There are four types of opioid receptors (Mu, Kappa, Delta, Nociceptor-OR) with a major analgesic effect and a subtype nociceptor-OR which is termed the MOP.⁶ Most opioid

tend to cause a reduction in consciousness and euphoria predisposing them to abuse.⁶

Recurrent bone pain crisis represent the most common reason patient with SCD seek acute 69 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 must have had intermittent exposure to opioids. Opioids are potent analgesic associated with 73 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 77 There have been several report in substance abuse by SCD patients with a prevalence of less than 10% worldwide,¹⁰ but varies from one region to another in Nigeria. Ahmed et al¹¹ 78 reported a prevalence of 17.8% of opiate dependence among patient with SCD in Maiduguri, 79 North East Nigeria with a male preponderance. Similarly, in a study by Mabayoje et al^{10} an 80 incident of less than 10% was reported in the South West. Furthermore, Iheanacho et al¹² also 81 82 reported a less than 18.2% with male preponderance. From the various studies, it could be said that the incidence varies with geographical location with a more prevalence of male sex 83

84 CASE REPORT

85 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 86 the 4th of January 2017 with a 2 years history of self-medication of DF118 and a self-87 medication of Tramadol. She said she got addicted to these drugs about 2 years ago while she 88 was admitted at government hospital in Calabar on account of sickle cell bone pain crisis 89 90 affecting her upper and lower limb which was so severe with a pain score of 9/10 (based on numerical pain rating scale) and lasted for about 48hours despite administration of several 91 analgesic such as Diclofenac and Pentazocin. Pain began to subside on administration of oral 92 93 DF118 at 60mg to alternate with Tramadol 100mg which was given for a week. Patient said 94 while she was on admission she enjoyed the feelings of the quick relief of the pain and 95 sedative effect that allows her to sleep comfortably following the administration of DF118 96 and Tramadol. Patient on account of this improvement sought to know the name of the medication that could give such a wonderful relief and also because of fear of reoccurrence of 97 the pain. She also noticed that both medication become drug of choice each time she has 98 99 severe bone pain and present to the same health centre. She said on account of the 100 psychological burden of the disease on her parents, who were worried of the repeated bone 101 pain crisis with frequent hospital visits and was also discovered that both medication give 102 their daughter relief and reduce their hospital visit, therefore decided to purchase a card of each medication weekly for her. Administering 30mg of DF118 twice daily initially but after 103 5 months increased the dosage to 60mg twice daily for a year because the initial dosage could 104 105 not control the pain and she was very uncomfortable. She started with the new dose in the absence of pain because she was enjoying the euphoric effect. Patient revealed she was 106 107 purchasing the drug on her own and even exaggerates her pain to get the drug prescription 108 from her physician and at most time she gets it without prescription from a private pharmacy

109 whose identity she does not want to disclose. Patient said she spends about N300 (approximately \$1) to purchase a card, which she finances with her pocket money, selling her 110 111 belonging, borrowing and buying on credit. Patient said after a year of self-medication of oral 112 DF118 at 60mg twice daily she discovered she was not getting the relief she used to get. 113 Patient said she got depressed and decided to change to another potent oral opioid (Tramadol) not the injectable because she reacts to the injectable, with nausea and continuous vomiting. 114 115 She said she started with 50mg of Tramadol twice daily, got relief and also enjoyed the euphoric effect and later increased the dose to 100mg then 200mg twice daily which she took 116 117 every day for 1 year even in the absence of pain. She gets the drug from a pharmacy and each 118 card costs between ₩1700 - ₩2000 (approximately \$7). She also gets prescription from a 119 doctor who she refuse to mention the name or address. She also claims that anytime she tries 120 to stop the medication she is being thrown into withdrawal symptoms which include lack of 121 sleep, restlessness, sweating, dizziness, blurred vision, headache, joint pain and abdominal cramping, depression, agitation and craving for the drugs. Thus, these made her to seek help. 122

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 was referred to the psychiatric for further evaluation and possible detoxification and rehabilitation.

The following were the full blood count; PCV was 27%, Hb 9g/dl, WBC 11.2 x $10^{9}/L$, Neutrophiles 68%, Lymphocyte 32%, and Platelet 452 x $10^{9}/L$

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133 **DISCUSSION**

134 This is a case study of a SCA patient who is dependent and addicted to tramadol and DF118.

BPC is the most commonest presentation among SCD,¹⁴ which our index patients suffers 135 about 10-12 episodes annually necessitating her to seek treatment from an health practitioner 136 137 who prescribed Tramadol and DF118. It was also noticed that the patient was on these prescribed drug (DF118 & Tramadol) for too long with prescription note not properly 138 139 controlled, which made her to have access to this prescription note. Due to the quick analgesic relief and euphoric effect derived from both medications, patient has to feign pain 140 after genuine pain had subsided, in order to continue getting the prescription¹⁴. Based on this 141 it is pertinent to say patient is addicted to both drug and the primary aim of both drugs is now 142 143 being abused. Lack of proper orientation and counselling of the parents of the patient also 144 contributed to the abuse of the above medications. At this juncture clinical expertise and 145 judgement of the physician is highly needed to distinguish genuine pain from feigned pain in 146 patient with SCD with DF118 & Tramadol abuse. There is paucity of information on DF118 and Tramadol abuse among sickle cell disease patient. Alao et al¹³ reported the case of a 38 147 year old female sickle cell anaemia patient, though the drug of choice in this instance was 148 149 cocaine.

The immediate pain assessment and frequent reassessment at 15min, 30min, 1hour then 2hours with appropriate application of medication until pain relief, are very important to prevent drug abuse.^{15,16} Therefore the less addictive analgesic should be administered 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} The psychiatrist made an impression of opoid abuse and addiction in a known SCD patient. Patient was initially managed on outpatient basis because patient had full insight of her problem and also has the desire to stop but does not wish to be admitted.

On mental state examination, patient was calm with good hygiene, cooperative and appears motivated and emotionally stable. Her perception was normal, thoughts well collected with normal cognition.

162 On physical examination, the patient was a young slim tall lady, afebrile, anicteric, acyanose with long limbs. Patient was gradually tapered off tramadol with a 50mg weekly reduction 163 for about 6weeks until she suddenly developed an episode of bone pain crisis. She was then 164 admitted for five weeks where she was treated with NSAID (Arthrotec) 75mg which was 165 166 alternated with paracetamol 1000mg. Patient was also given diazepam 10mg and was 167 carefully observed all through the period of admission with total avoidance of opoid and was 168 discharged and placed on a routine medication of folic acid, paludrine and was given 2 weekly clinic appointment to ensure proper follow up. The patient was also counselled to 169 adopt pain tolerance. 170

171 CONCLUSION

It is suggested that regular orientation of health worker on the use of opioid particular DF118 172 173 and Tramadol among opoid naive SCD, a careful objective assessment of sickle cell patient presenting with painful episodes should be carried out by an experienced health caregiver 174 175 with each case taken on its own merit. A non-opioid analgesic should be commenced first and 176 if an opioid should be used, it should be used for a short duration. Prescription note of opioid 177 analgesic should be properly controlled; there should be a drug unit established and also 178 legislation against sales of this controlled drug. Opioid addictive patient should be taught how to tolerate pains and referred to a psychiatrist for detoxification and rehabilitation. 179

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