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Survey of Pentazocine Addiction and Opioid Use in Adult Sickle Cell Anaemia Patients: The Perspective of Healthcare Providers

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Abstract

Background: Sickle cell anaemia (SCA) is characterized by episodes of bone pain creating a major role for analgesic therapy in the emergency management of this condition. Opioids, including pentazocine, is used in some cases and may be addictive with prolonged use.

Aim: This study aims to assess the scope of opioid use; pentazocine addiction and availability of resources for its management.

Materials and Methods: This study was conducted using a 10-item pre-tested and pre-validated questionnaire which was administered to medical doctors working in haematology units across Nigeria.

Results: 55 doctors involved in SCA patient care in 25 Nigerian health institutions with 13,314 registered SCA patients responded. The 5-year prevalence rate of pentazocine addiction was 2.9%. In managing pain in these patients, pentazocine ranked 2nd (21.2%) as the drug of choice after NSAIDs (26.9%). Majority of the physicians (48.1%) frequently prescribed DF118 while about 80% of them rarely prescribed morphine. Most of the doctors (61.8%) routinely counselled their patients on the dangers of opioid use, 88.9% believed there was need to adopt a guideline for opioids use and 89.1% agreed that pentazocine addiction was a major health challenge. 90.9% of the participants had neuropsychiatry units in their institutions, 71.2% of them accepted to have adequate neuropsychiatry staff and facilities.

Conclusion: Pentazocine addiction in was thought to be a major heath challenge by majority of the managing physicians. They also agreed that there was a need to provide guidelines/ policies for opioid use as well as restriction of access to opioids by unauthorized persons while encouraging multidisciplinary approach in the management of pain.

Keywords: Sickle cell; Doctors' perspective; Analgesia; Haemoglobinopathy

Abbreviations: SCA: Sickle Cell Anaemia; WHO: World Health Organization; SPSS: Social Sciences.

Introduction

Sickle cell anaemia is marked by acute exacerbations of bone pain secondary to vaso-occlusion and ischaemia [1,2]. Analgesia and fluid therapy are key aspects of sickle bone pain crisis management [3]. Choice of analgesia usually includes opioids or non-steroidal anti-inflammatory drugs either alone or in combination [4]. The prolonged use of NSAIDs is discouraged due to their effect of inhibiting cyclo-oxygenase 2 (COX-2) and consequent vaso-constriction of the vasculature including the renal parenchyma [5]. With prolonged use this may cause chronic kidney disease in sickle cell anaemia coupled with the already existing background predisposition to develop nephropathy [5,6]. In SCD, pentazocine is usually prescribed in the management of acute pain, chronic pain or a combination of both [3,7]. The use of pentazocine in combinations containing an antihistamine (Tripelaminne) as a recreational drug was quite frequent due to its synergistic sedative action hence the choice of naloxone in most combinations available in Europe and America [8]. Pentazocine lactate, the intramuscular/intravenous injectable form is largely available in Nigeria and most African countries and is still widely used for pain control. Opioids act by binding to mainly kappa, mu and delta (α, μ & δ) receptors in the sensori-neural system and other tissues [8,9]. Pentazocine is a syntheticopioid kappa receptor agonist of the benzomorphan family [10].

Other treatment modalities for chronic pain in SCD include nerve block, physiotherapy, orthopaedic intervention or surgery, and cognitive behaviour therapy [3,11]. The doctor has an obligation to ensure effective pain relief and at the same time be mindful not to exceed the medical needs of the patients [3]. It is worthy of note that in the current world health organization (WHO) analgesic ladder and guidelines in pain control, pentazocine and pethidine were omitted due to their tendency to cause dependence as well as other notable adverse effects [12-14]. It is noteworthy that phenotypic and genotypic differences exist in among individuals with sickle and even occur over time in the same patient. This may present challenges over time with regards management of bone pain crisis.

Opioid addiction is defined as a psychological dependence on opioids with associated craving, loss control of drug use or compulsive drug use aimed at achieving psychic effects despite obvious harm [15]. This persistent abuse may lead to deleterious consequences associated with inordinate craving despite adequate dosing and pain control with other non-opioid drugs [16,17]. The use of opioids as a sole agent in the treatment of chronic pain has been identified as a cause of addiction [18]. Pentazocine addiction may present as intense craving for the drug, excessive sweating, body (not bone) pains, signs of needle pricks on the body and poor academic performance [19,20]. Some personality disorders resulting from opioid dependence reflective of dysfunction in the limbic system and higher centres are loss of productivity at work, truancy and criminal tendency ostensibly to raise funds for crave satisfaction. Ultimately, job loss, premature school attrition and other socio-economic are untoward effects of pentazocine abuse [20,21]. It has also been associated with stealing [20,21] and other corrupt practices (to raise money for its purchase) as well as loss of job following associated physical deformity [21].

Pentazocine addiction is underreported in Nigeria probably due to low index of suspicion especially in cases where the patients do not easily divulge information [22]. In Nigeria, despite regulation, pentazocine is still being purchased "over the counter" in many places [21]. Clinical experience has indicated a rising prevalence of addiction to pentazocine in the Nigerian population in people living with sickle cell disease [20,21]. This study is designed to determine the extent of the problem, assess the prescription pattern of the attending physicians as well as evaluate the necessity for guidelines in the prescription of opioids.

Materials and Methods

This was a descriptive study carried out among Physicians involved in sickle cell patients' care in Nigeria who were in attendance at the annual general meeting of the Nigerian Society of Haematology and Blood Transfusion in October 2016. The participants were consenting consultants and resident doctors include resident doctors in different stages of residency of training. Physicians in attendance who did not manage sickle cell anaemia were excluded. The instrument of assessment was a 10-item self-administered questionnaire pre-validated by doctors working in the UNTH, Enugu Haematology unit. Information sought for included the name of institution of practice, number of registered adult sickle cell patients in those institutions, number of cases of pentazocine addiction recorded in the past 5 years, first choice and other types of analgesics prescribed, counselling practices, need for guidelines, personal view of the problem of addiction and availability of neuropsychiatric units in the different centers.

Statistical Analysis

On completion, the questionnaires were retrieved from these doctors and the information obtained was transferred to an excel sheet where frequency tables were derived and data analyzed using the Statistical Package for Social Sciences (SPSS) software version 20. The data obtained was analyzed and expressed as rates and frequencies.

Results

Responses were obtained from 55 out of 76 doctors who correctly completed the questionnaire. These were doctors from 25, out of the 53 tertiary health institutions across Nigeria. The number of registered sickle cell patients in these institutions ranged from10 to 3000, with a median of 100. The number of pentazocine addiction cases seen in the past 5 years ranged from 0 to 50 with a median value of 4 patients per health institution. The total number of patients observed to have had pentazocine addiction in the past 5 years was 386 out of 13,314 registered sickle cell patients across these health institutions. This gives an estimated 5 year prevalence rate of 0.029 or 2.9%.

Table 1 shows the frequency of use of the various analgesic agents by the respondents. With regards to dihydrocodeine (DF118), majority of the physicians 48.1% used this drug very often, while an additional 28.8% used it often. Cocodamol, a combination of acetaminophen and codeine, was prescribed sparingly and once in a while by 35.1% and 29.7% of them. About 53.2% of the responding physicians sparingly prescribed oral morphine while 29.8% of them agreed to only prescribe it once in a while see Table 1. This implies that more than 80% of the Physicians managing sickle cell pain rarely used morphine.

Drug	Frequency of prescription			
	Very often	Often	Once in a while	Sparingly
Tramadol	26(47.3%)	22 (40%)	4 (7.3%)	2 (3.6%)
Dihydro-Codeine (DF-118)	26 (47.3%)	14 (25.5%)	9 (16.4%)	3 (5.5%)
Morphine	6 (10.9%)	3 (5.5%)	13 (23.6%)	25 (45.5%)
Codeine/Acetaminophen (Cocodamol)	8 (14.5%)	5 (9.1%)	11 (20%)	13 (23.6%)
Pethidine	3 (5.5%)	5 (9.1%)	16 (29.1%)	26 (47.3%)

Table 1: Prescription pattern of analgesics for sickle cell by Nigerian haematologists

Routine counselling on dangers in opioid use was done always by majority (61.8%) of these doctors while 23.6% only counselled these patients sometimes. About 88.9% of the managing physicians believe guidelines need to be put in place to restrict or modify clinical use of opioid analgesics. 89.1% of them agree that pentazocine addiction is a major health challenge in the Nigerian sickle cell patient population. The responses to questions on opioid use and availability of neuropsychiatry teams and facilities in the centers are recorded in Table 2.

Questions	Yes	No	Not Sure
1. Do you routinely counsel patient on the possible addiction with opioids?	34	13	8
	61.80%	23.60%	14.50%
2. Do you think a guideline restricting/modifying use of opioids in sickle cell is necessary?	48 (88.9%)	4	2
		7.40%	3.70%
3. Do you think pentazocine addiction is a major problem in the Nigerian sickle cell population?	49	5	1
	89.10%	9.10%	1.80%
4. Does your center have a neuropsychiatric unit?	50	5	0
	90.90%	9.10%	
5. Is the neuropsychiatric unit in your centre equipped with the accommodation and staff to handle drug addiction cases?	37	7	8
	71.20%	13.50%	15.40%

Table 2: Responses to questions on opioid use and addiction management.

Majority (90.9%) of the doctors managing sickle cell patients across the country had neuropsychiatry units within their health facility. Approximately 71.2% of them felt their neuropsychiatry units had adequate facilities and personnel to handle addiction cases while 15.4% were uncertain.

Discussion

Regulation of opioid use aimed at averting addiction should be an important aspect of pain care in people living with sickle cell. Evaluation of the prescription pattern of analgesics as well as a definition of the extent of the problem was the focus of this survey. Fifty five out of 76 doctors who were in attendance were included in this survey. This represents an adequate proportion of haematologists in the country. These doctors predominantly worked in teaching hospitals, federal medical centers and general hospitals from across the country. However, all the respondents filled their questionnaires on-the-spot and this might account for some recollection bias. The significance of this bias is however difficult to estimate in this occasion as in any other on-the-spot questionnaire-based study where specific figures are needed. These facilities are tertiary health institutions and referral centers and may be involved in handling a different spectrum of patients at variance with those seen in the primary and secondary health facilities. The obvious consequence is that majority of the patients seen here may be those with complicated disease. However, experience has shown most patients choose to be attended to in these facilities due to paucity of manpower and facilities at other levels of healthcare. Therefore this study, albeit tertiary-based, still provides a true representation of the situation amongst doctors involved in handling this condition.

This study showed that the prevalence of pentazocine addiction among people living with sickle cell is 2.9%. This is lower than the findings of Ahmed [22] which reported prevalence of 9.6%. The difference in prevalence may be due to shorter duration of our study compared to that of Ahmed. Another reason may be due to improved medical services that are available now with reduction in episodes of painful crisis that may necessitate treatment with opioids unlike what the situation was over a decade ago when Ahmed et al conducted their study. Repeated painful crisis with long term exposure to opiates may lead to addiction [23]. The high prevalence may also be due to pseudo-addiction caused by under-treatment of pain [7]. It has been suggested that suboptimal treatment of painful episodes could be an important contributing factor to the development of drug abuse through self medication [7,15,24]. In some instances of under treatment patients in pain may exhibit some features which ceases once adequate therapeutic doses are given.

This study also found that the first choice analgesic in managing painful episodes in sickle cell disease patients is non-steroidal anti-inflammatory drugs (NSAIDs), followed by pentazocine, tramadol, paracetamol, dihydrocodeine and morphine in that order. Common use of NSAIDs in management of pain associated with sickle cell disease was also reported by Jimoh, et al. [25]. Non-steroidal anti-inflammatory drugs have been reported to be effective in relieving the inflammatory component of vaso-occlusive bone pain in addition to analgesic effect [3]. Its popularity may also be due to its availability in different preparations including the suppository form and the fact that it may be conveniently used in both in-patient and out-patient setting. However, nephropathy, gastritis and anti-platelet effect associated with its long term use is a limitation [1]. The most commonly used opioid among the

respondents was pentazocine. Previous studies have also reported that pentazocine is commonly used in the treatment of pain associated sickle cell disease [4,21]. This may be due to its wide availability, easy accessibility and low cost [21]. There is also a possibility that it is used as the sole option for management of chronic pain disregarding other possible potent treatment options like nerve block, physiotherapy, orthopaedic intervention or surgery, and cognitive behaviour therapy [3].

Acetaminophen, though a relatively weak analgesic, can be effective for some pain episodes in sickle cell disease. It can be used either singly or in combination with other analgesics in management of mild to moderate pain. Apart from the dose-dependent hepatotoxicity, side effects of acetaminophen are less than those of the other NSAIDs [2]. Morphine was rarely used by respondents in this study for pain management in sickle cell disease. This may be due to the unavailability of a parenteral preparation of the drug in Nigeria [26] and its multi-organ toxicity including respiratory depression as reported by previous study.

There is dearth of data on pentazocine addiction as a major health challenge among people living with sickle cell in Nigeria [27]. Lack of guidelines of opioid use and ease of procurement of the drug in Nigeria could possibly contribute to pentazocine addiction as had been reported in other environments [23]. There is a great need to increase awareness on WHO guidelines on pain control and the use of the analgesic ladder in patient evaluation, analgesic prescription and monitoring. Morphine, which apart from Tramadol and dihydrocodeine is the predominant opioid on the guideline, should be made readily available for the management of severe pain. Counselling for dangers in opioid abuse is a very important aspect of patient care [28].

Management of addiction of any kind is usually specialized and requires trained and dedicated personnel. Adequate accommodation and security is also central in the success of treatment and optimal rehabilitation. This study also showed that majority of our institutions had neuropsychiatric units while a lower percentage accepted that these units in their center were well equipped to handle addiction cases. This pre-supposes that the respondents were aware of the demands of an addiction rehabilitation unit in terms of personnel and staff. Further studies will be needed to assess the capacity of the several neuropsychiatry units in most centers to handle addiction cases. A multi-disciplinary approach involving the psychiatrist, palliative and pain care specialists and anesthetists in-pain management of sickle cell disease in our institutions is critical and may help to reduced cases of addiction.

The limitations of this study include the survey of doctors who were in attendance at the annual meeting of haematologists as this did not offer them the opportunity to access their hospital data. Some of the responses therefore might not be precise thus affecting data quality and thus introducing some recall bias, the significance of which is difficult to estimate. The survey did not include the psychiatrists who may have a different experience as they also manage opioid addicts who do not live with sickle cell. New areas of study would involve investigating the views and opinions of people living with sickle cell who have pentazocine addiction with the aim of defining the factors, causes and challenges of this peculiar patient group.

Conclusion

Pentazocine addiction, with a prevalence rate of 2.9% is a major health challenge among people living with sickle cell in Nigeria. It was the most the most frequently used opioid in treatment of pain in SCA. Most of the respondents accepted that there is a need to provide guidelines for opioid use in these patients. Tertiary health institutions in the country were deemed fit to handle cases of opioid addiction.

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