RETROSPECTIVE ANALYSIS OF NON-NARCOTIC ANALGESIC DRUG USE AMONG SICKLE CELL DISEASE PATIENTS WITH AND WITHOUT DOUDENAL ULCER

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ABSTRACT

Objective: To study the pattern of use and effect of non-narcotic analgesics among sickle cell disease patients.

Methods: A total of 109 patients with Sickle Cell Disease (SCD) were studied with respect to duodenal ulceration and number of prescription days of non-narcotic analgesics by a retrospective analysis of prescriptions documented in case notes.

Result: Sixteen out of the 109 SCD patients had duodenal ulcer, giving a prevalence of 14.7% among out SCD patients. The number of prescription days of non-narcotic analgesics for these patients with duodenal ulcer was compared with that of a control group (16 SCD patients without duodenal ulcer). The overall number of prescription days for all non-narcotic analgesics among SCD patients with duodenal ulcer was 148 days, which was significant ($p<0.05$) higher than 91 days among the control group. Analyzing the data with respect to individual drugs, it was found that the number of prescription days for Paracetamol, Diflunisal and Dipyrone in the duodenal ulcer group were 28, 14 and 8, which did not differ significantly ($p>0.05$)from 30, 13 and 9 days respectively in the control group. However, the number of prescription days for Aspirin (9 days), Piroxicam (23 days), Indomethacin (16 days), Diclofenac (25 days), Ibuprofen (10 days and Ketoprofen (15 days) in the duodenal ulcer group, were significantly ($p<0.05$) higher than 4, 11, 5, 12, 3, and 4 days for the respective drugs in the control group.

Conclusion: The results suggest that salicylates and other NSAID could be important aetiological co-factors in the pathogenesis of duodenal ulceration in SCD patients. Clinicians should therefore exercise caution while prescribing such drugs for SCD patients.

INTRODUCTION

The hallmark of sickle cell disease is the recurrent vaso-occlusive events caused by polymerization of deoxygenated Haemoglobin-S[1,2]. This results in the pathognomonic change in shape of erythrocytes to the sickle shape, which is stiff, deforms poorly and adheres to the vascular endothelium[3]. Further more, sickling causes endothelial damage that leads to exposure of sub-endothelial structures resulting in platelet activation and aggregation within the micro-vasculature[4]. More over, recent studies suggest that sickled erythrocytes induce endothelial cell production of adhesion molecules that favour the adherence of sickled erythrocytes on to endothelial cells resulting in stasis and prolongation of micro-vascular transit time which increase the chances of micro-thrombi formation[5]. These events finally lead to blockade of small blood vessels resulting in tissue infarctions that present clinically as the painful vaso-occlusive crisis, which is a characteristic feature of sickle cell diseases. While bone pain crisis remains the most spectacular manifestation of SCD, it must be appreciated that no organ of the body, including the gastro-intestinal tract, is immune to infarction due to sickling. The increased tendency of patients with SCD to develop duodenal ulcers was reported to be due to mucosal hypoxia and infarction associated with sickling[1]. That was supported by studies which showed that duodenal ulcers were less common than expected in patients with low levels of irreversibly sickled cells (ISC) and more common in patients with high levels of ISC[6]. However, it is a common knowledge that patients with SCD frequently use Non-Steroidal Anti inflammatory Drugs(NSAID) to obtain relief from recurrent painful episodes throughout their life times. Further more, it is well established that NSAID are commonly associated with gastro-intestinal side effects including bleeding and peptic ulceration[7]. In this report, we retrospectively analyze the pattern of non-narcotic analgesic drugs, including NSAID, used for analgesic purposes among SCD patients with and without duodenal ulcer. The aims are to discern any significant difference in the levels of NSAID used between SCD patients with and without duodenal ulcers, and deduce any possible role of NSAID as co-factors in the actiology of duodenal ulcers in SCD patients seen at the University of Maiduguri Teaching Hospital (UMTH) Maiduguri, North East Nigeria.

Methods : A total of 109 patients (aged 12-42 years) with sickle cell diseases (98 cases of Hb SS and 11 cases of Hb SC) registered with the Haematology Clinic of the UMTH, Maiduguri were included in this study.

Patients with clinically active and radiologically confirmed (with barium meal studies) duodenal ulcers being managed at our clinic as at the 31st of December 2000 were identified and enumerated. The prevalence of duodenal ulcer among our patients with SCD was then determined as a percentage of the overall SCD patient population of the clinic.

The pattern of non-narcotic analgesics use among SCD patients with duodenal ulcers was studied by a retrospective review of prescription information as documented in case notes during a period of 3 years from 1998-2000. The types of non-narcotic analgesic drugs prescribed were identified in each case and the number of prescription days was determined for each drug. Equal number of age and sex matched control group (SCD patients without duodenal ulcer) were similarly analysed. The number of prescription days for non-narcotic analgesics found among the SCD patients with duodenal ulcer was then compared with corresponding figure found among the control group (SCD patients without duodenal ulcer).

The data was analysed using the Chi-square test and a probability level of $p<0.05$ was taken as significant.

Result: Out of the 109-registered SCD in our clinic, 16 had duodenal ulcer at the time of this study, which which accounted for 14.7% among our patients. The case notes of these patients were then reviewed alongside that of equal number of control subjects (SCD patients without duodenal ulcer), from 1998-2000. The types of non-narcotic analgesics encountered in this review included Paracetamol, Aspirin, Piroxicam, Indomethacin, Diclofenac, Diflunisal, Ibuprofen, Ketoprofen and Dipyrone. The overall prescription days for all these drugs were 148 days in the duodenal ulcer group, which were significantly ($p<0.05$) higher than 91 days in the control group as shown on Table 1. analyzing the data with respect to individual drugs, it can be seen that the number of prescription days for Paracetamol, Diflunisal and Dipyrone in the duodenal ulcer group were 28, 14 and 8, which did not differ significantly ($p>0.05$) from 30, 13 and 9 days respectively in the control group. However, the number of prescription days for Aspirin (9 days), Piroxicam (23 days), Indomethacin (16 days), Diclofenac (25 days), Ibuprofen (10 days) and Ketoprofen (15 days) in the duodenal ulcer group, were significantly ($p<0.05$) higher than 4, 11, 5, 12, 3 and 4 days for the respective drugs in the control group as shown on Table 1.

TABLE 1: NUMBER OF NON-NARCOTIC ANALGESIC PRESCRIPTION DAYS AMONG SCD PATIENTS WITH DUODENAL ULCER AND CONTROL GROUP, 1998-2000

TYPES OF ANALGESIC	NUMBER OF PRESCRIPTION DAYS DUODENAL ULCER GROUP (N=16)	NUMBER OF PRESCRIPTION DAYS CONTROL GROUP n=16)
PARACETAMOL	28a	30a
ASPIRIN	9a	4b
PIROXICAM	23a	11b
INDOMETHACIN	16a	5b
DICLOFENAC	25a	12b
DIFLUNISAL	14a	13b
IBUPROFEN	10a	3b
KETOPROFEN	15a	4b
DIPYRONE	8a	9b
TOTAL	**148a**	**91b**

N= Number of subjects studied Ab Figures with different superscripts in the same row are significantly different ($p<0.05$)

DISCUSSION

The prevalence of duodenal ulcer among patients with SCD in this study was 14.7% which is comparable to the prevalence rate of 14% reported among SCD patients in southwestern Nigeria(1).

The result of this study revealed that the total number of prescription days for non-narcotic analgesics during the period of study was significantly higher among SCD patients with duodenal ulcer (148 days) as compared with the control group (91 days), as shown on Table 1. Analyzing the result with respect to individual drugs, there was no significant difference ($p>0.05$) in the number of prescription days for Paracetamol between SCD patients with duodenal ulcer and the control group (Table 1). This result showed that Paracetamol was the most commonly prescribed non-narcotic analgesic for both the duodenal ulcer and control groups. However, Paracetamol has little anti-inflammatory effect and is not associated with significant gastric irritation or peptic ulceration(7,8). Considering individual drugs that have significant anti-inflammatory effects, the result on Table 1 revealed that SCE patients with duodenal ulcer had significantly ($p<0.05$) higher number of prescription days for Aspirin and other NSAID, including Piroxicam, Indomethacin, Diclofenac, Ibuprofen and Ketoprofen, with the exception of Diflunisal and Dipyrone for which there was no significant ($p<0.05$) difference in the number of prescription days in the duodenal ulcer and control group. This result would suggest a significantly higher frequency of Aspirin and other NSAID consumption among SCD patients with duodenal ulcer as compared with the control group. Salicylates and other NSAID are injurious to the gastric mucosa and have been directly associated with peptic ulceration(7,8). Under normal circumstances, the gastric epithelium presents a barrier to the passage of ions from the lumen to the blood, thereby restricting the rate of back diffusion of hydrogen ions and limiting the diffusion of sodium ions in the opposite direction(7). However, this barrier is disrupted by salicylates and other NSAID resulting in an increased rate of hydrogen ions back diffusion, which leads to mucosal damage and ulceration(7,8,9). In addition to peptic ulceration, salicylates and other NSAID are capable of further increasing the risk of gastrointestinal

bleeding by acetylating platelet cyclo-oxygenase and inhibiting the synthesis of thromboxane A2, thereby impairing platelet aggregation(10,11). In fact, the role and significance of NSAID in the pathogenesis of peptic ulceration had been earlier reported in patients with rheumatic diseases on chronic NSAID therapy(12). This is further supported by a recent study that reported a case of Aspirin induced duodenal ulcer perforation in a Nigerian patient with SCD(13).

CONCLUSION

The higher number of prescription days for salicylate and other NSAID among SCD patients with duodenal ulcer, as compared with control group, in this study would suggest a possible role of these drugs as co-factors in the aetiopathogenesis of duodenal ulcers in our patients. Therefore, there is the need to exercise caution while prescribing NSAID for analgesic purposes for patients with SCD.

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