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Analgesic Use by Leprosy Patients[1]

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Analgesic nephropathy (AN) is a form of renal disease characterized by renal papillary necrosis (RPN) and renal failure and is associated with the excessive consumption of analgesic compounds, commonly containing aspirin, phenacetin and caffeine. The primary lesions in AN include RPN, chronic interstitial nephritis with secondary glomerular changes, analgesic microangiopathy, and uroepithelial tumors ([6]).

Many patients with leprosy develop severe pain in the extremities as a result of peripheral neuritis, and consequently may have to consume analgesics. It has been stated that RPN may then occur. However, in reviewing the literature we could find no published data on RPN or AN associated with leprosy. We, therefore, undertook the present study to determine if patients with leprosy do consume excessive amounts of analgesics and if RPN and AN do occur in these patients.

MATERIALS AND METHODS

Inpatients of the Sungai Buluh Leprosarium, which is the Malaysian center for the treatment of patients with leprosy, were questioned as to whether they consume analgesics and, if so, the type, quantity, frequency, duration, and reasons for the consumption of analgesics were ascertained. Subjects were interviewed by medical students using a standardized questionnaire. Analgesic abuse was defined as an overall total intake of at least 2 kg of analgesics. Hematological, renal, and liver profiles were done on these patients. Urine samples were collected for microscopic examination and culture and sensitivity. An intravenous urogram (IVU) was also performed on each subject.

RESULTS

The study population of inpatients consisted of 174 males and 61 females, ranging in age from 20 to 90 years. Of this group, 28.9% had consumed a total of more than 1 kg of analgesics, and 19.5% (46) of the subjects had consumed more than 2 kg (Table 1). Of those who had consumed more than 2 kg of analgesics, there were 38 males and 8 females, and the majority of the patients (37) were in the age group of 51 to 80 years. The duration of intake of analgesics ranged from 2 to more than 20 years (Table 2). The major reason for consuming analgesics was neuritic pain (58.7%) (Table 3).

Paracetamol (acetaminophen) was the most common analgesic consumed (Table 4); 45.7% consumed paracetamol alone and 82.8% consumed paracetamol either alone or in combination with other analgesics. The average amount consumed was 1.3 g daily. Chap Kaki Tiga and Chap Harimau were the next most commonly consumed drugs; 8.6% took them alone and 36.9% took them either alone or in combination with other drugs. The average amount consumed was 2 g daily.

Chap Kaki Tiga and Chap Harimau both contain aspirin (597 mg and 540 mg, respectively); phenacetin (385 mg and 175 mg, respectively); and caffeine (226 mg and 185 mg, respectively). Since 1981, phenacetin has been replaced with acetaminophen (307 mg) in Chap Kaki Tiga and by salicylamide (175 mg) in Chap Harimau.

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TABLE 1. *Amount of analgesics consumed.*

Amount (kg)	No. patients	% of total[a]
0.25–0.50	24	10.2
0.51–1.0	22	9.4
1.1–2.0	22	9.4
2.1–5.0	28	11.9
5.1–10.0	7	3.0
10.1–15.0	5	2.1
15.1–20.0	2	0.8
>20.0	4	1.7

[a] Total refers to the 235 leprosy patients questioned. Of these, 46 (19.5%) had consumed >2 kg of analgesics.

TABLE 2. *Duration of consumption of analgesics by subjects taking >2 kg.*

Duration (yrs)	No. patients	% of total[a]
0–1	0	0
2–5	7	3.0
6–10	16	6.8
11–15	4	1.7
16–20	7	3.0
>20	12	5.0
Total	46	19.5

[a] Total here refers to the 235 leprosy patients questioned.

Of the 46 patients who had consumed more than 2 kg of analgesics, only 28 patients consented to have the IVU and other tests performed. Of these, only three patients had impaired renal function (serum creatinine ranging from 134 to 343 μmol/l). Microscopic examination of the urine was essentially normal in 21 of the 28 patients. Three patients had a trace of albuminuria and one had 2+ albuminuria. Only one patient had microscopic hematuria. Four patients had pyuria, and one patient had granular casts in the urine. Urine cultures demonstrated mixed growth in three patients. IVUs demonstrated normal kidneys in 25 patients, horseshoe kidney in 1 patient, and changes consistent with pyelonephritis in 2 patients. None of the 28 IVUs demonstrated RPN.

DISCUSSION

Of the population surveyed, 19.5% had consumed more than 2 kg of analgesics, an amount sufficient to meet the criteria of analgesic abuse as well as to cause severe renal impairment. The commonest cause for consumption of analgesics was neuritic pain, followed by multiple aches and pains. The most common analgesic consumed was paracetamol (acetaminophen) (45.7%–82.8%), followed by Chap Kaki Tiga and Chap Harimau (8.6%–36.9%). Both of these two drugs are local proprietary compound analgesics containing aspirin, phenacetin, and caffeine. As mentioned earlier, the phenacetin has now been replaced by acetaminophen in Chap Kaki Tiga and by salicylamide in Chap Harimau.

Paracetamol is the immediate major metabolite of phenacetin. When animals are fed phenacetin, it is paracetamol that is concentrated in the renal papilla ([1]). The nephrotoxicity of phenacetin may be related, therefore, to the concentration of paracetamol, its major metabolite, in the renal papilla ([1]). Recently, cases of RPN due to the consumption of paracetamol alone have been reported ([9]). Hence, although paracetamol (and not phenacetin) was the most common analgesic consumed by subjects in this study, it might have been anticipated that RPN might have occurred in these subjects.

Surprisingly, in spite of the long-standing leprosy with its attendant renal complications, as well as the large amounts of analgesics consumed, only 3 subjects had impaired renal function, only 1 patient had significant proteinuria, 1 patient had microscopic hematuria, and 4 patients had pyuria. No patient demonstrated RPN in the IVUs. This lack of significant renal impairment, abnormal urinary sediment, and RPN is difficult to explain when one considers the large amounts of analgesics consumed by these patients. Four patients had consumed more than 20 kg of analgesics and 1 of these 4 patients had consumed a total of 50 kg of analgesics.

We postulate three reasons which might account for the lack of RPN: a) There may be genetic factors involved. AN is noted to occur in patients with HLA-B12 antigen ([5]), while leprosy is noted to occur in patients with HLA-DR2, -DR3, and MTI antigens ([10]). b) There may be interactions between the drugs used for the treatment of leprosy and the analgesics consumed. c) Although the chronic interstitial nephritis in AN is believed to be secondary to RPN ([7]), it may

TABLE 3. *Reason for consumption of analgesics for subjects taking >2 kg.*

Reason	No. patients	% of total[a]
Headache	3	6.5
Neuritic pain	27	58.7
Joint pain	2	4.4
Multiple pains[b]	6	13.0
Pain (other)[c]	5	10.9
Heaviness in the head	1	2.1
Unspecified	2	4.4
Total	46	100.0

[a] Total here refers to the 46 leprosy patients taking >2 kg of analgesics.
[b] Includes neuritic pain.
[c] Includes bone, chest, and tendon pain.

TABLE 4. *Type of analgesic consumed by subjects taking >2 kg.*[a]

Type	No. patients	% of total[b]
Paracetamol only	21	45.7
Chap Kaki Tiga only	3	6.5
Chap Harimau only	1	2.1
Multiple types	21	45.7
Predominantly paracetamol	8	17.4
Predominantly Chap Kaki Tiga	1	2.1
Predominantly Chap Harimau	3	6.5
Equal amounts of latter two	9	19.7
Total	46	100.0

[a] Paracetamol (total) = 82.8%; Chap Kaki Tiga/Harimau (total) = 36.9% of the 46 subjects.
[b] Total here refers to the 46 leprosy patients taking >2 kg of analgesics.

occasionally occur in the absence of RPN, and this may be due to direct chronic aspirin toxicity ([6]). There are patients who give a history of significant analgesic abuse who have no radiologic evidence of RPN, but they show chronic nephritis on renal biopsy ([6]). Interstitial nephritis is a significant autopsy finding in patients with leprosy ([3]). It has been ascribed to the prolonged disease state unrelated to reactive episodes ([2]) and, possibly, prolonged chemotherapy ([4, 8]). Excessive ingestion of analgesics may also be a contributory factor in the development of interstitial nephritis.

In conclusion, we have demonstrated that patients with leprosy consume a considerable amount of analgesics, the main reason being neuritic pain. Although the amount of analgesics consumed is sufficient to cause RPN, we have been unable to demonstrate radiological evidence of RPN. Excessive ingestion of analgesics may be a contributory factor in the development of interstitial nephritis in patients with leprosy.

SUMMARY

We questioned 235 subjects with leprosy regarding the consumption of analgesic preparations, and 46 subjects (19.5%) admitted to having consumed more than 2 kg of analgesics; the main reason for consumption was neuritic pain. The commonly consumed analgesics are paracetamol (acetaminophen) and local proprietary compound analgesics containing aspirin, phenacetin, and caffeine. Intravenous urograms were done on 28 of the 46 subjects, but none showed evidence of renal papillary necrosis. The reasons for this lack of renal papillary necrosis are postulated. Excessive ingestion of analgesics may be a contributory factor in the development of interstitial nephritis in patients with leprosy.

RESUMEN

Se interrogó a 235 pacientes con lepra respecto a su consumo de analgésicos. Cuarenta y seis individuos (el 19.5%) admitieron haber consumido más de 2 kg de analgésicos. La razón principal del consumo fue el dolor neurítico. Los analgésicos más comunmente consumidos fueron el paracetamol (acetaminophen) y analgésicos de fuentes locales conteniendo apsirina, fenacetina y cafeina. En 28 de los 46 pacientes se hicieron urogramas intravenosos pero en ninguno de ellos se encontró evidencia de necrosis papilar renal. Se postulan las razones de esta falta de necrosis papilar renal. La excesiva ingestión de analgésicos puede ser un factor contribuyente al desarrollo de nefritis intersticial en los pacientes con lepra.

RÉSUMÉ

On a questionné 235 malades de la lèpre quant à la consommation de préparations analgésiques. Parmi ces malades, 46 personnes (19, 5%) ont reconnu avoir pris de 2 kg d'analgésiques, le motif principal pour la consommation étant les douleurs nerveuses. Les analgésiques les plus constamment utilisés étaient le paracetamol (acetaminophène), et des composés analgésiques locaux contenant de l'aspirine, de la phénacétine, et de la caféine. Des urographies intraveineuses ont été pratiquées chez 28 des 46 sujets. Aucun signe de nécrose rénale papillaire n'a été notée. On commente les raisons qui pourraient expliquer cette absence de nécrose rénale papillaire. Une injection excessive d'analgésiques peut contribuer au développement d'une néphrite interstitielle chez les malades atteints de lèpre.

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