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Khat and oral cancer

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Abstract
Oral cancers in the Asir region of Saudi Arabia have been observed to occur mostly among patients who have been long-term khat users. In a survey that reviewed cancers for the past two years there were 28 head and neck cancer patients, 10 of whom presented with a history of having chewed khat. One of these was a case of metastatic cervical lymph node and unknown primary, one was a parotid tumour, and the remaining eight presented with oral cancers. All were non-smoking khat chewers and all of them had used it over a period of 25 years or longer. We conclude that this strong correlation between khat chewing and oral cancer warrants attention.

Introduction

Khat (*Catha Edulis Forsk*) a plant or shrub which grows wild or cultivated on hillsides in East Africa and Yemen, has been known for thousands of years for its stimulating and reinforcing qualities. It is endemic in the areas where it grows. In addition to its sympathomimetic stimulating amphetamine-like effects (Kalix and Khan, 1984), long-term khat use also manifests with tell-tale signs such as mouth ulcers and stained teeth. When khat is chewed phenylpropanolamine is identified in the urine.

All ten patients were treated at the central referral hospital of the Asir area in south west Saudi Arabia. The hospital serves small towns and more than 7,000 villages (over one million inhabitants). Some of these villages border Yemen; one of them called Fifa, nicknamed the 'capital of khat'.

Khat contents

The alkaloid (+) norpseudoephedrine present in khat leaves is an active ingredient with most of its effects being peripheral. However (−) cathinone [S-(−)-alpha-aminopropiophenone] has been regarded as the major important active compound of khat since it was identified and synthesized. Beside the two phenylalkylamines the khat leaves also contain 'more than 40 alkaloids, glycosides, tannins, terpenoids' (Elmi, 1983). Among the lipid fraction of khat which is 'rich in fatty acids, of the identified *esters, hexanoate, heptanoate and octanoate are the most prominent', and the presence of five flavonoids together with triterpanes, tannins and alkaloids in powdered khat have been phytochemically screened (Al-Meshal *et al.*, 1983). Khat leaves contain 'small amounts of ethereal oil, sterols and triterpenes, rich in flavonoids, and have high tannin content' (Kalix and Braendon, 1985).

How khat is used

Khat is chewed while the juice is swallowed. The active substance is best obtained from the youngest and freshest leaves and shoots of the plant. Chewing, especially among men, is frequently practiced in a group led by a host where talk and socialization goes on with khat group members who discuss topics of interest or listen to music or poetry. In the meantime, light drinks are served to treat dryness of the mouth, 'while a wad of chewed leaves in the cheek starts forming and may be kept there for hours all through the afternoon, evening or night' (Soufi *et al.*, 1989). The chewing habit may be practiced on one side of the mouth or the individual user had never noticed a side preference. Most of the patients in our sample said they have always chewed on the side affected by cancer.

Long-term use of khat

Long-term use of khat may lead to malnutrition of the users and their families, as khat consumes 50 per cent of the income of those who abuse it or become dependent on it. Chronic personality and behavioural changes were described by Tariq *et al.* (1984a) affecting occupation and productivity.

Material and method

A two-year review was undertaken of the cases that presented with oral, oropharyngeal and other head and neck malignancies, all seen at the Asir Central hospital, the main and only referral hospital of the area.

Results

Of 28 cases of head and neck carcinomas, oral cancers accounted for eight cases; parotid tumours, 15 cases;

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TABLE I

Case No.	Clinical Presentation	Clinical Staging	Histo-pathology	Duration of disease	Age	Sex	Duration (approx) Khat use	Final Treatment
1	Ca. floor of mouth	$T_2N_0M_0$	Squamous cell carcinoma	4 months	54	M	35 years	Radiotherapy and surgery
2	Ca. tongue ant ⅔ and floor of mouth with metastatic cervical lymph node	$T_2N_1M_0$	Squamous cell carcinoma	2 months	60	F	30 years	R.T. & surgery
3	Ca. tongue ant ⅔ and floor of mouth with metastatic cervical lymph node	$T_3N_1M_0$	Squamous cell carcinoma	2 months	49	F	25 years	Surgery & RT
4	Ca. tongue ant ⅔ and floor of mouth with metastatic cervical lymph node	$T_2N_1M_0$	Squamous cell carcinoma	4 months	62	M	40 years	R.T & surgery
5	Ca. cheek and gingivo buccal sulcus with fixed metastatic cervical lymph nodes	$T_3N_3M_0$	Squamous cell carcinoma	1 year	62	F	>30 years	Refused
6	Cancer tongue ant ⅔ and floor of the mouth with unilateral metastatic cervical lymph node	$T_3N_1M_0$	Squamous cell carcinoma	3 months	56	F	30 years	R.T. & Surgery
7	Cancer cheek and gingivo buccal sulcus extending to mandible	$T_3N_1M_0$	Squamous cell carcinoma	4 months	60	F	40 years	R.T. & surgery
8	Cancer tongue with metastatic cervical lymph node	$T_2N_1M_0$	Squamous cell carcinoma	3 months	50	M	25 years	R.T. & surgery
9	Parotid tumour	–	Adeno ca.	3 months	50	F	25 years	surgery
10	Occult primary with metastatic cervical lymph node	$T_0N_1M_0$		5 months	58	F	30 years	Surgery

and laryngeal/laryngopharyngeal cancer, five cases.

Table I shows the breakdown of cases which gave a history of long-term khat use.

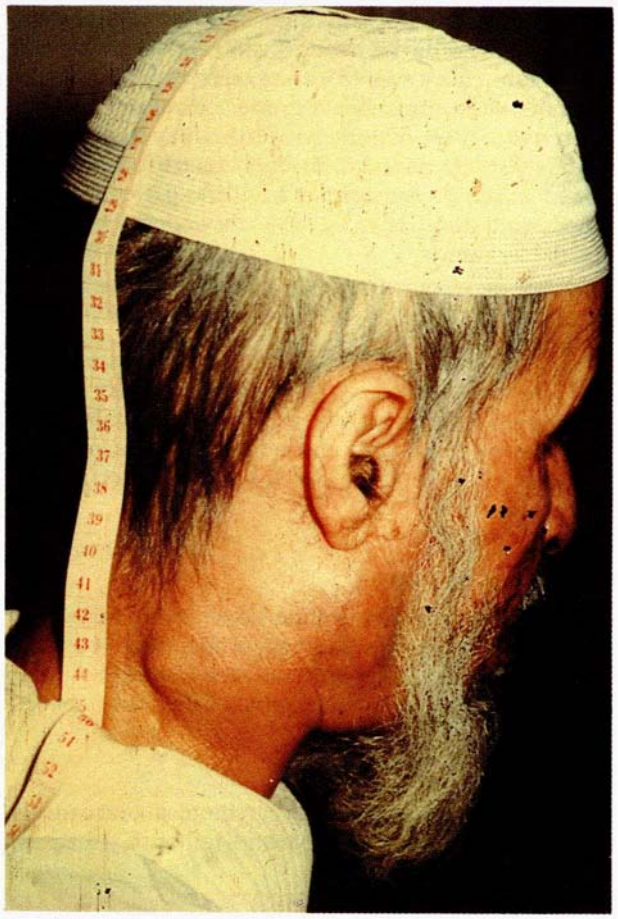

FIG. 1

Discussion

In spite of the reported works on khat concerning the biological effects at the cellualr level in different areas observed mostly in animal experiments, there has been a paucity of literature regarding cancers in man.

Investigation on the teratogenic effects in chick embryo, has been reported (Hammouda, 1971) as also were changes in DNA content (Hammouda, 1972). Cytotoxic effects that might have been the result of the inhibition of de novo RNA synthesis has been reported (Al-Ahdal *et al.*, 1988). Also noted at cell level were the effects on the spermatogenic activity of dietary khat on Gallus domesticus with a potential for genotoxicity, low production or cessation of sperms (Hammouda, 1978; Tariq *et al.*, 1984a). Impaired sexual activity in man has also been reported (Al-Meshal *et al.*, 1985). Hannan *et al.* (1985) discussed mutagenic agents in khat. In the stomach 'anti-ulcer effects' have been described (Tariq *et al.*, 1984b). Regarding khat effects on pregnancy, reduced placental blood flow was found to lead to

FIG. 2

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reduced mean birthweight by 7 per cent (Jansson *et al.*, 1988a,b).

Though the habit of chewing khat is described as 'compulsive' (Kalix and Khan, 1984), there are limits to taking increased amounts, imposed by the bulky leaves and by the traditional way of use mostly in groups. In the long run, of greater concern is the duration of khat use, which can continue for the lifetime of the individual.

Conclusion

There is a lack of literature on the clinical effects of khat on the incidence of malignancy. However, review of oral cancers presenting over a two-year period show strong circumstantial evidence linking the long-term use of khat with increased oral malignancies. Out of eight cases presenting with oral malignancies, all gave a history of khat chewing over many years and in some instances were also emphatic about keeping the khat bolus on the same side as the lesion. By contrast, only one of the 15 parotid tumour cases analyzed over the same period gave a history of long-term khat use. Similarly, none of the laryngeal or laryngopharyngeal malignancy cases analyzed during the same period had a history of khat chewing. This, in our view underlines the importance of the local effects of the khat bolus on the oral mucous membrane, especially since the contact may be for hours at a time.

References

Al-Meshal, I. A., Tariq, M., Hifnawy, M. S., Mekkawi, A. G., Muhtadi, F. J. (1983) Characterization and evaluation of Saudi Arabian Khat. Abstracts, First International Conference on Khat, ed. by International Council on Alcohol and Addictions, Lausanne, Switerland, p 110–134.

Al-Meshal, I. A., Ageel, A. M., Parmar, N. S., Tariq, M. (1985) Catha edulis (Khat): use, abuse and current status of scientific knowledge. *Fitoterapia,* **56:** 131–152.

Al-Ahdal, M. N., McGarry, T. J., Hannan, M. A. (1988) Cytotoxicity of khat (Catha edulis) extract on cultured mammalian cells: effects on macromolecule biosynthesis. *Mutation Research [NNA],* **204:** 317–322.

Elmi, A. (1983) The chewing of khat in Somalia. *Journal of Ethnophamacology,* **8:** 163–176.

Hammouda, E. (1971) Effect of khat extract, D-cycloserine and thalidomide on ribonucleic acid (RNA) of the neurons of 7 and 19 days chick embryo. *Bulletin of the Faculty of Science, Riyadh University,* **3:** 99–112.

Hammouda, E. M. (1972) Effect of khat extracts, D-cycloserine and thalidomide on deoxyribonucleic acid (DNA) of the neurones of 7 and 19 days chick embryo. *Bulletin of the Faculty of Science, Riyadh University,* **3:** 63–76.

Hammouda, E. M. (1978) Effects of dietary khat extract on the testis of the white leghorn Gallus domesticus. *Bulletin of the Faculty of Science, King Abdulaziz University, Jeddah,* **2:** 17–22.

Hannan, M. A., Aboul-Enein, H. Y., Dakan, A. A. (1985) Histidine reversion in ames' salmonella strains induced by extracts of 'khat'—a substance of abuse. *Research Communications in Substances of Abuse,* **6:** 179–188.

Jansson, T., Kristiansson, B., Qirbi, A. (1988a) Effects of khat on maternal food intake, maternal weight gain and fetal growth in the late-pregnant guinea pig. *Journal of Ethnopharmacology [K8T],* **23:** 11.

Jansson, T., Kristiansson, B., Qirbi, A. (1988b) Effects of khat on uteroplacental blood flow in awake, chronically catheterized, late-pregnant guinea pigs. *Journal of Ethnopharmacology [K8T],* **23:** 19–26.

Kalix, P., Khan, I. (1984) Khat: an amphetamine-like plant material. *Bulletin of the World Health Organization [C80],* **62:** 681–686.

Kalix, P., Braenden, O. (1985) Pharmacological aspects of the chewing of khat leaves. *Pharmacological Reviews, American Society for Pharmacology and Experimental Therapeutics,* **37:** 149–163.

Soufi, H. E., Afifi, M .M., Alshehry, M. R. G. (1989) Catha edulis abuse with a case report. In VIII World Congress of Psychiatry Abstracts, Psychiatry Today (Stefanis, C. N., Soldatos, C. R., Rabavilas, A. D., eds.) Excerpta Medica International Congress Series 899 Amsterdam, 542.

Tariq, M., Ageel, A. M., Parmar, N. S., Al-Meshal, I. A. (1984a) The pharmacological investigation of the Saudi Arabia variant of Catha edulis (Khat). *Fitoterapia,* **55:** 195–199.

Tariq, M., Parmer, N. S., Ageel, A. M., Meshal, I. A., Abu-Jayyab, A. (1984b) The gastric anti-ulcer activity of khat (Catha edulis Forsk): Investigations on its flavonoid fraction. Research Communications in Substance Abuse. Vol. 5, PJD Publications Limited, New York, USA, 157–160.

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