Acta Obstet Gynecol Scand 57: 79–83, 1978

REGRESSION OF TUMOUR GROWTH AFTER ADMINISTRATION OF ALKOXYGLYCEROLS

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Abstract. A regression of tumour growth is observed when alkoxyglycerols are administered prior to radiation treatment of patients suffering from cancer of the uterine cervix. This regression has been demonstrated by a change in the quotient between the incidence of early and advanced stages.

Alkoxyglycerols occur in small quantities in many natural products. In the haemopoietic organs of mammals, particularly the bone marrow, they are relatively abundant. They are also found in relatively high concentrations in human mother's milk. They occur most abundantly in nature in the liver oil of certain species of shark (1, 8, 9). The general formula for alkoxyglycerols is $CH_2OH{\cdot}CHOH{\cdot}CH_2O{\cdot}R$, where R is a long-chain aliphatic radical.

The alkoxyglycerols have proved to be of medical interest (1–7). To some extent they prevent leukopenia and thrombocytopenia. The administration of alkoxyglycerols before, during and after radiation treatment of patients with cancer of the uterine cervix results in higher survival rates than if radiation treatment alone is given (1, 2). Furthermore, the alkoxyglycerols promote the growth of *Lactobacillus lactis* (1), the formation of antibodies (2, 4), and they reduce to a large extent (ca. 50%) the frequency of injuries following radiation therapy (5, 7, 10).

The aim with the present study has been to investigate the regression of tumour growth when alkoxyglycerols are administered before radiation treatment of patients suffering from cancer of the uterine cervix.

MATERIALS AND METHODS

The clinical experiments in this study were conducted using alkoxyglycerol preparations from the liver oil of the Greenland shark. The preparation, produced by AB Astra with the working name AT 18, is a concentrate containing 85% free alkoxyglycerols. The contents of various alkoxyglycerols from a variety of sources are given in Table I.

The alkoxyglycerols were administered orally in capsules, 2 capsules 3 times a day, each capsule containing 0.1 g of alkoxyglycerols. The total daily dose thus was 0.6 g.

The practical procedure was as follows. Immediately upon the receipt of the referral letter, the patient was given a date for the commencement of radiotherapy and at the same time a package containing the alkoxyglycerols and information regarding the dosage. At the start of

Table I. *Percentage composition (weight) of alkoxyglycerols from various sources*

Alkoxyglycerols	Human bone marrow	Human milk	Liver oil: Greenland shark
14:0			2.0
15[a]			0.7
16:0	29.4	23.9	9.1
16:1		trace	10.8
17[a]	7.6	3.6	3.6
18:0	24.6	22.8	2.8
18:1	16.7	33.8	59.4
18:2		1.4	1.6
18:3			
19[a]	6.1	2.4	1.5
20:0	2.9	1.6	
20:1	3.2	2.3	6.2
22:0	0.7	0.7	
22:1	5.1	3.4	2.2
24		2.1	

Analyses are according to Hallgren & Larsson (2, 3).
The number of carbon atoms in the first column refers to the long-chain component of the molecule. The number after the colon denotes the number of double bonds.
[a] Both branched and normal chains C_{15}, C_{17} and C_{19} are present.

Table II. *Definitions of clinical stages*

E: Early stages

Stage I
Carcinoma strictly confined to the cervix.

Stage I A
Cases of early stromal invasion.

Stage I B
All other cases of stage I.

Stage II A
The carcinoma extends beyond the cervix but has not extended onto the pelvic wall. The carcinoma involves the vagina, but not the lower third. No parametrial involvement.

A: Advanced stages

Stage II B
The carcinoma extends beyond the cervix but has not extended onto the pelvic wall. The carcinoma involves the vagina, but not the lower third. Parametrial involvement.

Stage III
The carcinoma has extended onto the pelvic wall. On rectal examination there is no cancer-free space between the tumour and the pelvic wall. The tumour involves the lower third of the vagina.

Stage IV
The carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum.

Definitions according to FIGO (International Federation of Gynecology and Obstetrics).

radiotherapy, the period of medication and the administration schedule was noted in the case report.

The total series of cases with invasive carcinoma of the uterine cervix, treated at the Department of Gynaecology, Radiumhemmet, Stockholm, during the period 1958–75, were subsequently reviewed. The patients comprised all stages (Table II) and were allotted to the following groups.

Group I

Those who adhered to the scheme of prophylactic alkoxyglycerol medication, i.e. took alkoxyglycerols for 7 days before the start of radiotherapy, during the radiation treatment, and for 1–3 months after the completion of therapy.

Period 1. From September 1, 1964 to February 15, 1966, the majority of the cases (458) had taken alkoxyglycerols prophylactically.

Period 2. A double-blind study comprising 137 patients was conducted 1970–73. This is the second prophylactic group.

Period 3. During the years 1973–75 every second patient was given alkoxyglycerols "prophylactically" (245). The cases were chosen at random.

Group II

Group II comprised all those who were given radiotherapy without any prophylactic administration of alkoxyglycerols, i.e. all patients who had not received alkoxyglycerols prior to radiation treatment.

RESULTS

The distribution according to clinical stages is given for all patients during the period 1958–75 in Tables III A and B. The patients in Table III A did not receive any prophylactic administration of alkoxyglycerols, while those in Table III B did receive such prophylactic medication.

The situation of early invasion (stage I A) was not clearly defined during the 'fifties, and during the 'sixties the percentage of I A has varied much more than for other stages which have shown a more or less constant distribution (Tables III and IV). In order to obtain a more correct comparison between the different groups of patients, stage I A has therefore been excluded in the Tables IV A and B. When comparing the figures in the Tables III and IV a shift towards early stages is observed for the prophylactic group, both when all stages are included and when stage I A is excluded.

Table III. *Distribution according to clinical stages (1958–1975): All stages*[a]

	I A		I B		II A		II B		III		IV		I–IV
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*
A. Radiotherapy													
1958–64	200	7.2	646	23.3	806	29.0	564	20.3	384	13.8	176	6.4	2 776
1966–75	174	10.7	393	24.2	408	25.1	329	20.3	225	13.8	95	5.9	1 624
Total	374	8.5	1 039	23.6	1 214	27.6	893	20.3	609	13.8	271	6.2	4 400
B. Prophylactic administration of alkoxyglycerols													
Period 1	45	9.8	159	34.7	129	28.2	71	15.5	39	8.5	15	3.3	458
Period 2	17	12.4	36	26.3	39	28.5	19	13.9	18	13.1	8	5.8	137
Period 3	16	6.5	84	34.3	78	31.8	34	13.9	26	10.6	7	2.9	245
Total	78	9.3	279	33.2	246	29.2	124	14.8	83	9.9	30	3.6	840

[a] The stage was determined at the start of radiotherapy.

Table IV. *Distribution according to clinical stages (1958–1975): Stage I A excluded*

	I B		II A		II B		III		IV		I B–IV
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*
A. Radiotherapy											
1958–64	646	25.1	806	31.3	564	21.9	384	14.9	176	6.8	2 576
1966–75	393	27.1	408	28.1	329	22.7	225	15.5	95	6.6	1 450
Total	1 039	25.8	1 214	30.2	893	22.2	609	15.1	271	6.7	4 026
B. Prophylactic administration of alkoxyglycerols											
Period 1	159	38.5	129	31.2	71	17.2	39	9.5	15	3.6	413
Period 2	36	30.0	39	32.5	19	15.8	18	15.0	8	6.7	120
Period 3	84	36.7	78	34.1	34	14.8	26	11.3	7	3.1	229
Total	279	36.6	246	32.3	124	16.3	83	10.9	30	3.9	762

Table V A. *Decrease in advanced stages after prophylactic administration of alkoxyglycerols (all stages)*

Group	No. of patients	E		A		E/A	D (%)	D_A (%)
		n	%	*n*	%			
Radiotherapy (1958–75)	4 400	2 627	59.7	1 773	40.3	1.48	12.1	30.0
Prophylactic administration (Periods 1, 2, 3)	840	603	71.8	237	28.2	2.54		

E=I A+I B+II A; A=II B+ III+IV; D=Decrease, in per cent; D_A=Decrease, in per cent, related to the number of patients with advanced stages

Table V B. *Decrease in advanced stages after prophylactic administration of alkoxyglycerols (Stage I A excluded)*

E=I B+II A; A=II B+III+IV

Group	No. of patients	E		A		E/A	D (%)	D_A (%)
		n	%	*n*	%			
Radiotherapy (1958–75)	4 026	2 253	56.0	1 773	44.0	1.27	12.9	29.3
Prophylactic administration (Periods 1, 2, 3)	762	525	68.9	237	31.1	2.22		

For a numerical evaluation of the shift in stage following prophylactic administration of alkoxyglycerols it is convenient to subdivide the stages into advanced stages: A=stage II B and higher and early stages, E=II A and lower. Based upon bimanual palpation the referral of patients to group A or E is done with a high degree of accuracy, while the differentiation between other stages often presents difficulties. The distribution of A and E (E_1=I A+I B+II A and E_2=I B+II A) for the different groups is given in Table V. The decrease in the advanced stages (D) after prophylactic administration is statistically significant ($P<0.001$).

The percentage of early and advanced stages is given for each year during 1958–75 (Table VI). *No* systematic change with time is observed for the years when the patients were treated with radiotherapy but did not receive alkoxyglycerols pro-

Table VI. *Distribution of early and advanced stages (1958–75)*

	Year	No. of pats.	E_1 I A+I B+II A		A II B+III+IV		E_1/A	No. of pats.	E_2 I B+II A		A II B+III+IV		E_2/A
			n	%	*n*	%			*n*	%	*n*	%	
	1958	428	251	58.6	177	41.4	1.42	419	242	57.8	177	42.2	1.37
	1959	436	251	57.6	185	42.4	1.36	410	225	54.9	185	45.1	1.22
	1960	356	201	56.5	155	43.5	1.30	336	181	53.9	155	46.1	1.17
	1961	401	236	58.9	165	41.1	1.43	379	214	56.5	165	43.5	1.30
	1962	426	261	61.3	165	38.7	1.58	388	223	57.5	165	42.5	1.35
	1963	348	225	64.7	123	35.3	1.83	307	184	59.9	123	40.1	1.49
	1964	381	227	59.6	154	40.4	1.47	337	183	54.3	154	45.7	1.19
Period 1	*1965*	458	333	*72.7*	125	*27.3*	*2.66*	413	288	*69.7*	125	*30.3*	*2.30*
	1966	309	190	61.5	119	38.5	1.60	266	147	55.3	119	44.7	1.24
	1967	318	200	62.9	118	37.1	1.69	285	167	58.6	118	41.4	1.42
	1968	299	171	57.2	128	42.8	1.34	279	151	54.1	128	45.9	1.18
	1969	290	168	57.9	122	42.1	1.38	259	137	52.9	122	47.1	1.12
Period 2	*1970–1972*	137	92	*67.2*	45	*32.8*	*2.04*	120	75	*62.5*	45	*37.5*	*1.67*
	1970–1972	142	88	62.0	54	38.0	1.63	125	71	56.8	54	43.2	1.31
Period 3	*1973–1975*	245	178	*72.6*	67	*27.4*	*2.66*	229	162	*70.7*	67	*29.3*	*2.42*
	1973–1975	266	158	59.4	108	40.6	1.46	236	128	54.2	108	45.8	1.19

phylactically. A shift towards earlier stages occurs however for the periods 1, 2, 3 (prophylactic administration of alkoxyglycerols).

COMMENTS

The regression of tumour growth, demonstrated by a change in the quotient between early and advanced stages, is observed as a consequence of administration of alkoxyglycerols prior to the radiation treatment. It is of importance to mention that this regression is due to a non-toxic natural substance found in the human body (1). Furthermore, the incidence of injuries following radiation therapy is markedly reduced by the administration of alkoxyglycerols. Complex injuries (due to radiation injury and tumour growth in combination) are reduced to about 1/3 in a group receiving alkoxyglycerols in prophylactic administration. A more detailed analysis of the effect of alkoxyglycerols on the incidence of injuries is published elsewhere (7).

The regression of tumour growth and the decrease in injuries following radiotherapy influences the survival rate. This dependence will be discussed in a separate paper (6).

It is evident that there are prospects of improving the effect of alkoxyglycerol therapy. Seven days of prophylactic administration of alkoxyglycerols results in a marked reduction of the advanced stages, 12–13% (30% if the decrease is related to the number of patients with advanced stages, Table V). It would be worthwhile carrying out clinical trials with a patient group receiving prophylactic administration of alkoxyglycerols during 2–3 weeks. Furthermore, some observations indicate that a prolonged administration of alkoxyglycerols after radiotherapy might be of value.

ACKNOWLEDGEMENTS

This work was supported by grants from the Knut and Alice Wallenberg Foundation and from the Sven and Dagmar Salén Foundation.

We wish to thank Prof. H. L. Kottmeier and Doc. B. Tjernberg, former and present head of the Department of Gynaecology of Radiumhemmet, Stockholm, for helpful discussions. Our thanks are also due to Prof. Ingemar Joelsson for stimulating criticism and advice.

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Submitted for publication May 16, 1977

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