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Key words:
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Large doses of ascorbate

Prolongation of Survival Times of Terminal Cancer Patients by Administration of Large Doses of Ascorbate

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Summary: Clinical trials administering supplemental ascorbate to terminal cancer patients were conducted at two hospitals in Japan. During the period 1973–1977 there were 99 patients with terminal cancer at the Fukuoka Torikai Hospital. The average times of survival after the date of designation as terminal were 43 days for 44 low-ascorbate patients and 246 days for 55 high-ascorbate patients. Three of the high-ascorbate patients were still alive, their average survival being 1550 days, on April 1, 1980.

Similar effectiveness of ascorbate was also observed at the Kamioka Kozan Hospital. There were 31 patients with terminal cancer during the period 1975–1979. The average survival times were 48 days for 19 control patients and 115 days for 6 high-ascorbate patients. One of the high-ascorbate patients was still alive, his survival being 215 days.

In addition to the increase in survival times, the administration of large doses of ascorbate seemed to improve the quality of life.

Introduction

There are a number of reports in the literature, beginning around 1938, on treatment of cancer patients with ascorbate, sometimes together with vitamin A and other nutrients. The dosage of ascorbate was usually small, often less than 1 g per day, and these early clinical reports attracted little attention at their time and have since been largely forgotten. The early work has been reviewed by STONE [1], by CAMERON and PAULING [2] and by CAMERON, PAULING and LEIBOVITZ [3].

During the past ten years, a considerable understanding of the modes of action of ascorbate in helping cancer patients has been achieved, and several studies by CAMERON and PAULING [2, 4, 5] have shown that large doses of ascorbate increase survival times and improve symptoms of patients with advanced cancer.

In 1974 one of us, MORISHIGE, began administering his cancer patients large doses of ascorbate in the Fukuoka Torikai Hospital, and the first report on this clinical trial was published in 1978 by MORISHIGE and MURATA [6]. YAMAGUSHI started to follow this clinical trial in the Kamioka Kozan Hospital, in 1977.

This paper describes the results of the clinical trials conducted at the Fukuoka Torikai Hospital and the Kamioka Kozan Hospital.

The Fukuoka Torikai observations. Patients and Methods

The Fukuoka Torikai Hospital is a 220-bed general hospital located in Fukuoka, a city with a million inhabitants. There were 296 patients with the diagnosis of cancer during the years 1967–1977, as shown in Table I. Tumor characteristics for the 296 patients are listed in Table II. Thirty-five per cent of the patients were those with cancer of the stomach. As shown in Table III, until the end of 1973, fifty-three of these patients received no supplementary ascorbate, 90 received 0.5 g per day and 18 received 1 g per day. In 1974, MORISHIGE began administering his cancer patients larger doses of ascorbate, and later on other physicians with cancer patients in the hospital began to follow his example, until in 1977 all cancer patients in the hospital were

Tab. I: Annual number of new patients admitted to Fukuoka Torikai Hospital with diagnosis of cancer

Year	No.
1967	7
1968	22
1969	25
1970	20
1971	31
1972	31
1973	25
1974	36
1975	29
1976	33
1977	37
All	296

The hospital was opened in August 1967.

Tab. II: Distribution by

Primary site
All sites
Stomach
Lung and bronchu
Uterus
Liver
Rectum
Breast
Pancreas
Thyroid
Colon
Esophagus
Malignant lympho
Bladder
Brain
Ovary
Thymus
Other sites

Tab. III: Change of dosa

Year	0	0.5	1	D
1967	4	3		
1968	7	15		
1969	11	13	1	
1970	5	14	1	
1971	8	19	4	
1972	13	16	2	
1973	5	10	10	
1974	3	6	7	
1975	1		5	
1976			1	
1977				
All	57	96	31	

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en achieved, and several studies by
that large doses of ascorbate increase
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No.
7
22
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296

d in August 1967.

Tab. II: Distribution by primary site for all cancer patients

Primary site	No.	%
All sites	296	100
Stomach	104	35
Lung and bronchus	35	12
Uterus	26	9
Liver	20	7
Rectum	18	6
Breast	14	5
Pancreas	7	2
Thyroid	6	2
Colon	5	2
Esophagus	4	1
Malignant lymphoma	4	1
Bladder	4	1
Brain	3	1
Ovary	3	1
Thymus	2	1
Other sites	41	14

Tab. III: Change of dosages of ascorbate to cancer patients

Year	No. of patients								
	Daily dose of ascorbate, g								
	0	0.5	1	2	3–4	5–6	7–9	10–29	30–60
1967	4	3							
1968	7	15							
1969	11	13	1						
1970	5	14	1						
1971	8	19	4						
1972	13	16	2						
1973	5	10	10						
1974	3	6	7	5	4	5	6		
1975	1		5	6	6	6	2	3	
1976			1	1	1	6	2	11	11
1977						1		10	26
All	57	96	31	12	11	18	10	24	37

receiving at least 5 g per day. Especially administering 30 g per day or more was begun with 33+ of the patients in 1976 and extended to 70% of the patients in 1977. Large doses of ascorbate were administered orally (usually 6 to 12 g, sometimes 30 g) and by intravenous infusion of ascorbate solution (10 or 20 g per 500-ml bottle). Table IV shows the outcome of these patients (on May 1, 1978). Of the 296 patients, 235 (80%) died and 41 (14%) were still alive.

During the five-year period from January 1, 1973, to December 31, 1977, there were 112 patients with apparently terminal cancer. The patients with terminal cancer indicate those being regarded as untreatable by any conventional forms of cancer therapy. Of the 112 patients, 4 were excluded because of failure of follow-up, 8 were excluded because of death from some cause other than their cancer, and 1 was excluded because of discontinuing ascorbate treatment. No patient was excluded because of short survival time. Therefore, 99 of the 112 patients were considered to be evaluable.

Of the 99 patients, 2 received no supplementary ascorbate, 42 received 4 g per day or less and 55 received 5 g per day or more (average 25 g per day). Because there were but very little control patients, we compared low-ascorbate patients (44 patients receiving 4 g per day or less, including 2 patients receiving no ascorbate) with high-ascorbate patients (55 patients, receiving 5 g per day or more). We believe that the assignment of patients to the low-ascorbate and high-ascorbate group was essentially random, although no formal randomization process was carried out. Characteristics of the patients are listed in Table V. The average age was 63.8 years (range 39 to 87 years) for the low-ascorbate group and 57.5 years (range 26 to 86 years) for the high-ascorbate group, and the sex distribution was 23 male, 21 female, and 25 male, 30 female, respectively. The site of the primary tumor was stomach for 17 (39%) and 17 (31%), lung and bronchus for 6 (14%) and 9 (16%), uterus for 4 (9%) and 8 (15%), and others for 17 (39%) and 21 (38%), respectively.

The Fukuoka Torikai observations. Results

Table VI shows the individual survival times after the date of designation as terminal (to April 1, 1980, for those still alive), together with the average survival times of patients receiving various doses of ascorbate in each kind of cancer. None of the low-ascorbate patients survived more than 174 days, whereas 18 (33%) of the high-ascorbate patients survived more than 174 days; their average being 620 days. Three (6%) of the high-ascorbate patients were still alive: one with cancer of the uterus (1561[1]+ days), one with cancer of the breast (1419+ days), and one with cancer of the thymus (1671+ days). These 3 patients were clinically well, but with no significant progression or regression in tumor; that is, the patients survived in symbiotic existence with their tumors.

[1] The sign + indicates that the patient was still alive on April 1, 1980

There were no patients with cand
thymus in the low-ascorbate grou
terminal cancer patients (during the
patients received no or little ascorb
the breast, 51 days for 4 with cance

Tab. IV: Ou

Outcome	
All	
Died in hospital	
Died after discha	
Alive	
Unknown	
on May 1, 1978	

Tab. V: Characterist

Characteristic	Lo
	N
No. of patients	
Age, years	
Under 45	
45–54	
55–64	
65–74	
75 and over	
Sex	
Male	2
Female	2
Site of primary tumor	
Stomach	1
Lung and bronchus	
Uterus	
Liver	
Breast	
Rectum	
Pancreas	
Esophagus	
Malignant lymphoma	
Brain	
Other sites	1

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the patients survived in symbiotic exis-

ve on April 1, 1980

There were no patients with cancer of the breast, the rectum, the pancreas and the thymus in the low-ascorbate group. The average survival times for the historical terminal cancer patients (during the period 1967–1972, a great majority of the cancer patients received no or little ascorbate, see Table I) were 100 days for 3 with cancer of the breast, 51 days for 4 with cancer of the rectum, 51 days for 2 with cancer of the

Tab. IV: Outcome of all cancer patients

Outcome	No.	%
All	296	100
Died in hospital	191	65
Died after discharge	44	15
Alive	41	14
Unknown	20	7

on May 1, 1978

Tab. V: Characteristics of patients with terminal cancer

Characteristic	Low-ascorbate group		High-ascorbate group	
	No.	%	No.	%
No. of patients	44	100	55	100
Age, years				
Under 45	3	7	11	20
45–54	6	14	11	20
55–64	15	34	15	27
65–74	10	23	9	16
75 and over	10	23	9	16
Sex				
Male	23	52	25	46
Female	21	48	30	54
Site of primary tumor				
Stomach	17	39	17	31
Lung and bronchus	6	14	9	16
Uterus	4	9	8	15
Liver	5	11	1	2
Breast	0	0	5	9
Rectum	0	0	2	4
Pancreas	0	0	2	4
Esophagus	1	2	1	2
Malignant lymphoma	0	0	2	4
Brain	1	2	1	2
Other sites	10	23	7	13

Tab. VI: Individual survival times after date of designation as terminal, with average survival times of patients receiving varying doses of ascorbate

Primary site	Survival time, days						
	Daily dose of ascorbate, g						
	0	0.5	1–2	3–4	5–9	10–29	30–60
Stomach		3	17	16	48	311	223
		54	23	28	177	129	44
		72	37	(22)	148	30	34
		44	17		(124)	75	66
		57	50			30	223
		(46)	174			(115)	107
			24				55
			10				29
			43				27
			35				(90)
			(43)				
Lung and bronchus		95	33	32	244	100	13
		48	38	51	15		108
		(72)	(36)	(42)	13		84
					(91)		45
							19
							(54)
Uterus			55		838	1495	90
			36		1561+	370	666
			22		4	(933)	114
			62		(801)+		(290)
			(44)				
Liver	8	21	4	63			126
				12			
				(38)			
Breast					195	70	15
					1419+		303
					(807+)		(159)
Rectum							170
							846
							(698)
Pancreas					154		
					46		
					(100)		
Thymus						1671+	

Primary site	0	0.5
Other sites	35	127
		88
		(108)

The average survival times in each grou
The sign + indicates that some of the pa

Tab. VII: Ratios of average survival ti

Primary site	Low-ascor
Stomach	41
Lung and bronchus	50
Uterus	44
Other sites	43
All	43

The number of patients in each group are
The sign + indicates that the patient was

pancreas and 15 days for 1 with can
times for the historical terminal canc
stomach, 39 days for 9 with cancer of
and 30 days for 11 with cancer of the
increase in survival times of patients v
cancer.

The results of the study are summ
was 43 days for the 44 low-ascorbate
patients. On the average, the patients
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benefit according to tumor site. Asc
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and lung than for other kinds of can

signation as terminal, with average survival times
rying doses of ascorbate

Survival time, days				
aily dose of ascorbate, g				
-2	3–4	5–9	10–29	30–60
17	16	48	311	223
23	28	177	129	44
37	(22)	148	30	34
17		(124)	75	66
50			30	223
74			(115)	107
24				55
10				29
43				27
35				(90)
43)				
33	32	244	100	13
38	51	15		108
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				170
				846
				(698)
		154		
		46		
		(100)		
			1671+	

Primary site	Survival time, days						
	Daily dose of ascorbate, g						
	0	0.5	1–2	3–4	5–9	10–29	30–60
Other sites	35	127	40	20	188	183	60
		88	9	55		4	242
		(108)	128	8		49	93
			11	(28)		(79)	35
			36				118
			60				19
			(47)				(95)

The average survival times in each group are given in parentheses.
The sign + indicates that some of the patients were still alive on April 1, 1980.

Tab. VII: Ratios of average survival times for high-ascorbate group and low-ascorbate group

Primary site	Low-ascorbate group	High-ascorbate group	Ratio H/L
Stomach	41 (17)	103 (17)	2.5
Lung and bronchus	50 (6)	71 (9)	1.4
Uterus	44 (4)	642+ (8)	14.6
Other sites	43 (17)	286+ (21)	6.7
All	43 (44)	246+ (55)	5.6

The number of patients in each group are given in parentheses.
The sign + indicates that the patient was still alive on April 1, 1980.

pancreas and 15 days for 1 with cancer of the thymus. Further, the average survival times for the historical terminal cancer patients were 56 days for 25 with cancer of the stomach, 39 days for 9 with cancer of the lung, 64 days for 5 with cancer of the uterus, and 30 days for 11 with cancer of the liver. Evidently, large doses of ascorbate gave an increase in survival times of patients with terminal cancer, with no concern of kinds of cancer.

The results of the study are summarized in Table VII. The average survival time was 43 days for the 44 low-ascorbate patients and 246 days for the 55 high-ascorbate patients. On the average, the patients receiving large doses of ascorbate survived 5.6 times as long as the patients receiving small doses of ascorbate. There is some survival benefit according to tumor site. Ascorbate is especially effective for cancer of the uterus, whereas it gives smaller increase in survival times for cancer of the stomach and lung than for other kinds of cancer.

CAMERON and PAULING, who administered usually 10 g per day, have suggested that daily dosages of ascorbate larger than 10 g would be more effective. Our study shows no difference in results for dosages of 5 to 9 g per day and 10 to 29 g per day, and a decreased effectiveness at 30 to 60 g per day (Table VI). There is a possibility that this decrease is only apparent, resulting from the use of higher doses for patients with a poorer prognosis. However, in any case, the most effective dosage of ascorbate should be determined.

The survival curves for the low-ascorbate and high-ascorbate groups are shown in Figure 1. There is significant difference in survival between the two groups. The median survival in the high-ascorbate group was 105 days, as compared with 35 days for low-ascorbate group. This indicates that the death rate of the low-abscorbate patients is three times that of the high-ascorbate patients. In addition, a fraction of the high-ascorbate patients, about 10%, seems to have greatly extended life expectancy.

In many cancer patients, the administration of ascorbate seemed to improve the state of well-being, as measured by improved appetite, increased mental alertness, decreased requirement for pain-controlling drugs, and other clinical criteria.

The Kamioka Kozan observations. Patients and Methods

The Kamioka Kozan Hospital is a 75-bed general hospital located in Kamioka, a small town with a population of approximately 17,000. This hospital is about 800 km away from the Fukuoka Torikai Hospital, and has no relationship to that hospital. Because most of cancer patients in this town tend to be sent to hospitals in nearby larger cities, an average of less than 10 patients had been admitted to this hospital each year.

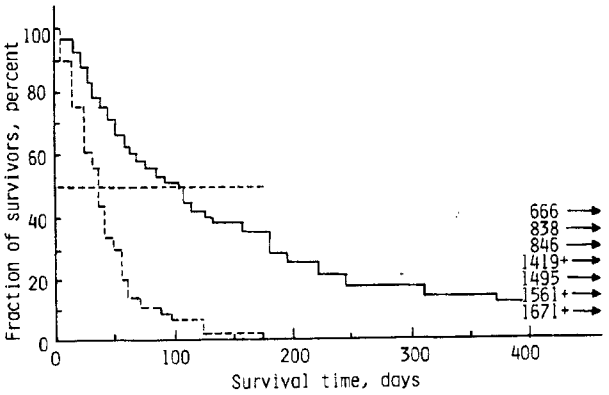

Fig. 1: Fraction of survivors at times after date of designation as terminal.
The solid line shows survival in 55 high-ascorbate patients.
The dashed line shows survival in 44 low-ascorbate patients.
The sign + indicates that some of the patients were still alive on April 1, 1980.

During the five-year period fro
were 31 patients with apparently
study. Until April 1976, all thes
YAMAGUCHI began administering
dose in 1976 and high-dose in 197
day (low-ascorbate group) and 6 r

Tab. VIII: Individual surviv
(Kan

Primary site	0
Stomach	28 25 69 61 73 26 23 26 93 47 (47)
Lung and bronchus	98 53 28 (60)
Liver	
Bile duct	
Bladder	
Colon	34
Uterus	
Other sites	25 28 72 38 56 (44)

Parentheses indicate the average survival
The sign + indicates that some of the pa

ered usually 10 g per day, have suggested
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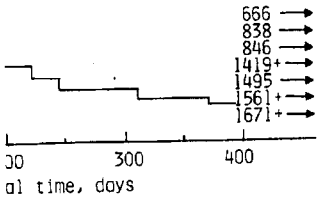

s after date of designation as terminal.
l in 55 high-ascorbate patients.
al in 44 low-ascorbate patients.
patients were still alive on April 1, 1980.

During the five-year period from January 1, 1975, to December 31, 1979, there were 31 patients with apparently terminal cancer. No patient was excluded in this study. Until April 1976, all these patients received no supplementary ascorbate. YAMAGUCHI began administering his cancer patients supplementary ascorbate, low-dose in 1976 and high-dose in 1977, and until the end of 1979, 6 received 0.5 to 3 g per day (low-ascorbate group) and 6 received 5 to 30 g per day (high-ascorbate group);

Tab. VIII: Individual survival times after date of designation as terminal (Kamioka Kozan Hospital)

Primary site	Survival time, days					
	Daily dose of ascorbate, g					
	0	0.5	1–2	3–4	5–9	10–30
Stomach	28 25 69 61 73 26 23 26 93 47 (47)			76	132 63 (98)	60
Lung and bronchus	98 53 28 (60)	171	21 30 (26)			
Liver					90	
Bile duct						127
Bladder						215+
Colon	34			150		
Uterus			56			
Other sites	25 28 72 38 56 (44)					

Parentheses indicate the average survival times in each group.
The sign + indicates that some of the patients were still alive on April 1, 1980.

19 received no ascorbate (control group). The sex distribution is 7 male and 12 female for the control group, 3 male and 3 female for the low-ascorbate group and 5 male and one female for the high-ascorbate group, and the average age was 61.2 years, 69.2 years and 70.2 years. The sites of the primary tumor are listed in Table VIII. The methods were the same as mentioned above.

The Kamioka Kozan observations. Results

Table VIII shows the individual survival times after date of designation as terminal (up to April 1, 1980, for those still alive). None of the control patients survived more than 98 days, whereas 3 (50%) of the high-ascorbate patients (receiving 5 g per day or more) survived longer than 98 days, their average being 158 days. One of the high-ascorbate patients was still alive, with a survival of 215 days. In this case repeated cytographic examinations showed the decrease in size of tumor of the bladder (tumor volume decreased from 115 to 7 in 3 months).

The results of the study are summarized in Table IX. The average survival time was 48 days for the 19 control patients and 115 days for the 6 high-ascorbate patients. The average survival time of the high-ascorbate patients was 2.4 times that of the controls. We could compare also the ratios of average survival time for high-ascorbate/low-ascorbate or low-ascorbate/control, but the value obtained would have little statistical significance because of small numbers of the subjects.

Valuable relation of ascorbate to pain control was also noted. Of the 19 control patients, 15 (79%) received narcotic drugs to control pain, whereas 3 (50%) of the 6 low-ascorbate patients and only 1 (17%) of the 6 high-ascorbate patients received those drugs.

Discussion

The results of the clinical trials conducted at the Fukuoka Torikai Hospital and the Kamioka Kozan Hospital show that large doses of ascorbate offer some degree of benefit to advanced cancer patients, even though there were some defects in the methods.

Tab. IX: Ratios of average survival times for ascorbate groups and control group (Kamioka Kozan Hospital)

Primary site	Control group	Low-ascorbate group	High-ascorbate group	Ratio H/L
Stomach	47 (10)	76 (1)	90 (3)	1.9
Other sites	48 (9)	86 (5)	144+ (3)	3.0
All	48 (19)	84 (6)	115+ (6)	2.4

For legends, see Table VII.

We have made no attempt to conc
have been quite impossible for us t
comparison within our own clinic
PAULING [4, 5] indicated that ascorb
many kinds of cancer, with no pron
who were the subjects of the studies
we felt it to be ethically wrong to wit
merely for the sake of obtaining ob
comparison.

There is good evidence that hig
system in various ways. Ascorbate m
chemical and physical carcinogens ar
in a number of other biological pr
cancer [2, 3, 7]. These can provide

Finally, no harmful long-term sid
received large doses of ascorbate.

We conclude, in agreement with CA
bate in large dosages has significant
cancer. In addition to the increase in
with CAMERON and CAMPBELL [8],
ascorbate seems to improve the qua

Acknowledgements: We thank Prof. Linus

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The sex distribution is 7 male and 12 female
for the low-ascorbate group and 5 male and
, and the average age was 61.2 years, 69.2
imary tumor are listed in Table VIII. The
)ove.

observations. Results

times after date of designation as terminal
None of the control patients survived more
-ascorbate patients (receiving 5 g per day or
r average being 158 days. One of the high-
survival of 215 days. In this case repeated
rease in size of tumor of the bladder (tumor
onths).
l in Table IX. The average survival time was
) days for the 6 high-ascorbate patients. The
e patients was 2.4 times that of the controls.
rage survival time for high-ascorbate/low-
he value obtained would have little statisti-
rs of the subjects.
control was also noted. Of the 19 control
gs to control pain, whereas 3 (50%) of the
)) of the 6 high-ascorbate patients received

ussion

d at the Fukuoka Torikai Hospital and the
ge doses of ascorbate offer some degree of
hough there were some defects in the meth-

es for ascorbate groups and control group
ozan Hospital)

bate group	High-ascorbate group	Ratio H/L
(1)	90 (3)	1.9
(5)	144+ (3)	3.0
(6)	115+ (6)	2.4

benefit to advanced cancer patients
Results of clinical trials of high dosages of ascorbate acid

We have made no attempt to conduct a double-blind trial for two reasons. It would have been quite impossible for us to obtain anything like exactly matched pairs for comparison within our own clinical practice, and the studies by CAMERON and PAULING [4, 5] indicated that ascorbate in large dosage has some effectiveness against many kinds of cancer, with no pronounced correlation with age or sex of the patients who were the subjects of the studies. Moreover, as our clinical experience increased, we felt it to be ethically wrong to withhold ascorbate in otherwise hopeless situations, merely for the sake of obtaining observations of dubious significance for statistical comparison.

There is good evidence that high intakes of ascorbate potentiate the immune system in various ways. Ascorbate may also offer some protection against a variety of chemical and physical carcinogens and against oncogenic viruses, and is also involved in a number of other biological processes believed to be involved in resistance to cancer [2, 3, 7]. These can provide theoretical bases for the clinical results.

Finally, no harmful long-term side effect was observed among the patients who received large doses of ascorbate.

Conclusion

We conclude, in agreement with CAMERON and PAULING, that supplemental ascorbate in large dosages has significant benefit for patients with advanced untreatable cancer. In addition to the increase in life expectancy, we have noticed, in agreement with CAMERON and CAMPBELL [8], that in many patients the administration of ascorbate seems to improve the quality of life.

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