

ABSTRACT

The Therapeutic Effect of Amino Acids in Colorectal Cancer Patients A Case Series Study

Interim Results as of May 2006

(Not for publication: follow-up to be completed)

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Background:

- Changes in plasma amino acid patterns reflect changes in protein metabolism that occur with different pathological conditions.
- Many cancer symptoms may be the repercussion of a disturbance/irregularity in protein.
- Colorectal cancer patients demonstrate imbalances in blood plasma amino acid composition.
- Over a seven-year period in a clinical setting, hundreds of cancer patients have been administered patient-specific orthomolecular supplementation for a range of cancers.

Objectives:

- Identify blood plasma amino acid patterns in colorectal cancer patients in comparison to standardized optimal norms.
- Administer a patient-specific orthomolecular therapeutic
- Observe the symptomatic and biochemical impact of the intervention.

Conclusions:

- Colorectal cancer symptoms correlate with disturbances in the host's protein metabolism.
 - Normalization of imbalanced plasma amino acid profiles by the administration of patient-specific amino acid formulas can positively influence the clinical management of the cancer.
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Methodology:

- *Setting:*
 - Subjects were recruited during their regularly scheduled visits to a medical center in Ottawa, Ontario.
 - Study followed the ethics policy of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.
- Blood plasma concentrations of 28 amino acids were profiled using HPLC in 52 colorectal cancer patients.
- Study Participants (n=52):
 - average of 5 years since diagnosis (range 1-15)
 - average of 3.0 years on nutritional program (range 1-6)
 - total blood assays performed = 133
 - average assays/patient = 2.6
 - 87% of subjects had undergone chemo, radio &/or surgery

Participant Age Distribution

Age	Female	Male	Total
21-35	4%	12%	8%
36-40	4%	0%	2%
41-45	4%	4%	4%
46-50	4%	12%	8%
51-55	23%	8%	15%
56-60	15%	0%	8%
61-65	12%	19%	15%
66-70	8%	12%	10%
71-75	15%	15%	15%
76-80	12%	12%	12%
81-85	0%	8%	4%
	100%	100%	100%

Participant Disease Stage

Stage IV: 85%
 Stage III: 12%
 Other: 3%

Participant Prior Treatment

82.7% of participants had undergone prior treatment for their cancer.

Treatment		%age	
SRC	7	13.5%	
SC	19	36.5%	
S	6	11.5%	
SR	3	5.8%	
S		0.0%	67.3%
R		0.0%	
C	6	11.5%	
RC	2	3.8%	82.7%
Nothing	9	17.3%	
	52	100.0%	

S= Surgery C = Chemotherapy R= Radiation

- To standardize nutritional variables, subjects uniformly and daily self-administered highly bio-available, pharmaceutical grade, pathogen-free, nutritional supplements consisting of:
 - 1) multi-macronutrient, vitamin and minerals as well as a variety of nonessential nutrients, such as certain phytochemicals, antioxidants and enzymes.
 - 2) a broad-based colorectal specific supplement containing various compounds including alpha lipoic acid, betaine, epigallocatechin (green tea extract), lycopene, and other enzymes and B, C and E vitamins

- 3) essential fatty acids
- Patient-specific supplementation:
 - reflected individual circumstances compared to standard norms
 - a daily total of 10grams of protein as a general source of amino acids along with additional patient-specific supplementation of deficient amino acids, typically; taurine, histidine and occasionally leucine, lysine, thiamin.

Amino Acid Composition of Protein Supplement

Aspartic Acid	10.8%
Threonine	7.3%
Serine	4.8%
Glutamic Acid	17.2%
Glycine	1.6%
Alanine	4.8%
Valine	5.7
Isoleucine	6.6%
Leucine	10.2%
Tyrosine	2.9%
Phenylalanine	2.8%
Histidine	1.9%
Lysine	8.0%
Arginine	2.0%
Proline	7.1%
Cysteine	2.5%
Methionine	2.0%
Tryptophan	1.7%

- Therapeutic cycle was repeated for each subject while cancer and collateral medical symptoms were qualitatively and quantitatively monitored through multiple case studies.
- The case series clinical research evidence was correlated with a systematic review of cancer literature regarding metabolic and therapeutic aspects of amino acids. (Abstract note: systematic review available under separate cover on release of final Case Series review).

Results:

Post-intervention, the following observations were made in 95% of the subjects:

- (1) plasma amino acid profiles demonstrate correlative movement with intervention
- (2) subjects demonstrate significant positive response rates in disease stabilization, and improvement in quality of life without side effect or adverse events
- (3) there is beneficial management of collateral damage from radiotherapy and chemotherapy

Significant Starting/Ending Amino Acid Changes in Blood Plasma
(maximum difference during assay period)

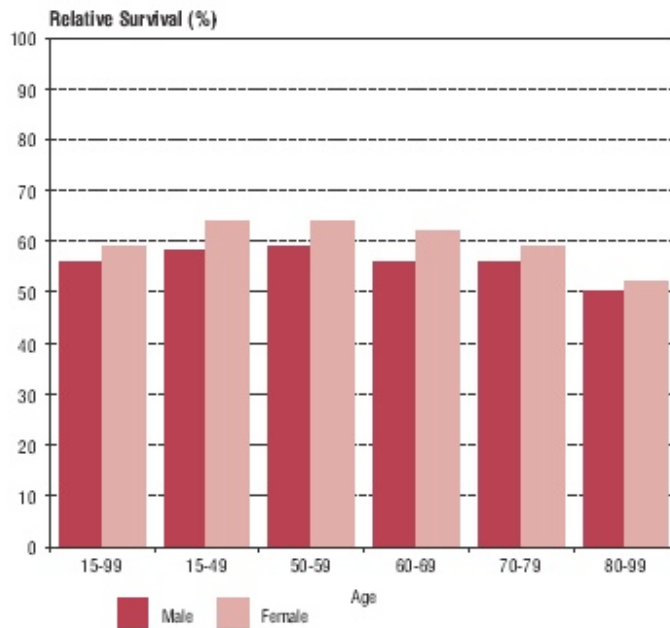
units= nmol/mL	Starting	Ending	Difference
Taurine	65.6	70	4.4
Leucine	101.91	117.2	15.3
Arginine	70.8	82.0	11.2
Histidine	63.1	70.4	7.3
Glutamine	502.5	557.4	54.9
Alanine	360.4	461.8	101.4
Glycine	212.1	253.6	41.5

Survival: During the 7-year period, patient survival appears to be ahead of that which might be typically anticipated.

Deceased:	0	21.7%
Stable:	36	78.3%
<u>Discontinued:</u>	<u>6</u>	
Total:	52	

The National Cancer Institute of Canada reports that the 5-year relative survival rate for people whose colorectal cancer is treated in an early stage, before it has spread, is greater than 90%. Only 39% of colorectal cancers are found at that early stage. Once the cancer has spread to nearby organs or lymph nodes, the 5-year relative survival rate goes down, and if cancer has spread to distant organs (i.e., the liver or lung) the 5-year survival is less than 10%.

Figure 11.3
Five-year Relative Survival from Colorectal Cancer, Canada*, 1992



* Note: NCI results are for all stages of colorectal cancer. This research analysis primarily consisted of Stage III & IV patients.

The 5-year survival rate refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Many of these patients live much longer than 5 years after diagnosis. The 5-year survival rate is a standard way of discussing prognosis (outlook). Five-year relative survival rates don't include patients dying of other diseases. Five-year relative survival rates are considered to be a more accurate way to describe the prognosis for patients with a particular type and stage of cancer.

The following colorectal cancer statistics were derived from a study published in the Journal of the National Cancer Institute. The survival rate provided is higher for stage 3A colon cancer (83%) than for stage 2B colon cancer (72%). Survival rates generally decrease with later stage cancers. In the study, the researchers explained that the discrepancy may be due to the fact that stage 3 colon cancer patients usually receive chemotherapy but stage 2 colon cancer patients don't.

O'Connell, Jessica and Maggard, Melinda. "Colon Cancer Survival Rates With the New American Joint Committee on Cancer Sixth Edition Staging." Journal of the National Cancer Institute 96.19 (Oct. 2004): 1420-1425. 20 Aug. 2006.

Stage 1:	93%
Stage 2A:	85%
Stage 2B:	72%
Stage 3A:	83%
Stage 3B:	64%
Stage 3C:	44%
Stage 4 :	8%

The 5-year crude survival rate after curative resection for colorectal cancer ranges between 40 and 60% in most studies.⁽¹⁾ Local recurrences and/or regional lymph node metastases occur in over 90% of failure cases.⁽²⁾ The prognosis of colorectal cancers is affected by a number of factors which can be broadly classified into those related to the tumor stage, clinical variables, pathologic features, and oncogenetic, molecular, and immunologic variables. The stage and factors directly or indirectly affecting the stage of the primary tumor remain the most important prognostic factors.

(1) Patel SC, Tovee EB, Langer B. Twenty-five years of experience with radical surgical treatment of carcinoma of the extraperitoneal rectum. Surgery 1977;82:460.

(2) Russel AH, Pelton J, Reheis CE, Wisbeck WM, Tong D, Dawson LE. Adenocarcinoma of the colon: An autopsy study with implications for new therapeutic strategies. Cancer 1985;56:1446.

Quality of Life: In all surviving subjects (n= 36 = 78%), participants indicated overall improvement Quality of Life. Many indicated a reduction in the side effects of conventional treatment. Similarly, despite the loss of 22% of the subjects, many survived longer than had been anticipated by their doctors and reported enjoying a higher quality of life.

Study Limitations

(A) Supplementation was self-administered by the participants. Compliance, while encouraged could not be mandated

(B) There was no control of the environmental variables for each participant (i.e., eating habits, smoking, level of activity, etc).

(C) It would be at least 10 to 15 years after the last patient was enrolled before a possible conclusion could be drawn regarding the criterion of survival.

(D) There is difficulty in quantitatively measuring endpoints such as remission, stabilization or immune response.

(E) All participants had the same base macronutrient supplementation. However, there will always be uncertainty surrounding how to assess the relative contribution of each nutritive product.

(F) Amino acid adequacy is much better defined in growing and healthy organisms than during illness.

Disclosure:

William O'Neill is the CEO and Dr Ken Lin is the Lab Director for Immune System Management Inc., the corporate entity that has sponsored this research.

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