When the Nutritional Supplements Stop: Evidence from a Double-blinded, HIV Clinical Trial at Mengo Hospital, Kampala, Uganda

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Introduction

Last year, in this journal,[1] the authors reported on the results obtained in a prospective randomized, double-blinded clinical trial, involving 310 HIV-infected outpatients of Mengo Hospital, Kampala, Uganda. In this registered trial (International Standardized Randomized Controlled Trial Number 42274642), patients with baseline CD4 cell counts above 200, who were not receiving antiretroviral drugs, were placed randomly into Groups A and B. The medications given to patients in Group B consisted of 30 nutrients with a filler of organic sugar. This combination of nutrients had been found, in small open trials, to stimulate appetites in HIV-positive patients.[2] The logic behind this approach was to establish whether greater appetite was sufficient to encourage HIV-positive individuals to increase their consumption of local foods to a point at which enough selenium and amino acids were digested to normalize glutathione peroxidase levels. Serious loss of appetite is a common symptom of HIV/AIDS.[3]

The capsules taken by Group A patients contained the same thirty appetite stimulating supplements, but also included an additional seven nutrients. The latter nutrients were designed to directly promote the body's production of glutathione peroxidase and, in addition to amino-acid rich desiccated beef liver, included L-selenomethionine, N-acetyl cysteine, L-glutamine, hydroxytryptophan, alpha lipoic acid and ascorbic acid. Patients receiving this mixture of supplements did not have to rely on their own diet to provide the selenium, cysteine, tryptophan and glutamine thought necessary to boost body glutathione peroxidase levels.[4]

Results of Initial Trial

The year long study[1] examined the effects of these two combinations of nutrients on biochemical and immunologic parameters, that is, serum glutathione peroxidase levels and CD4 cell counts as the study's primary endpoint. Secondary endpoints were weight changes and patient assessed quality of life.

The mean/median serum glutathione peroxidase levels in Group A (37 nutrients) increased from 3825/3628 IU/L (International Units) at baseline to 8894/8575 IU/L at the trial's end ($p<0.000$). Similarly, patients in Group B (30 nutrients) had an increase in mean/median serum glutathione peroxidase levels from 3862/3602 to 9839/9203 IU/L over the length of the trial ($p<0.000$). The mean/median CD4 cell counts rose from 400/347 mm^3 to 446/388 in Group A and from 400/335 to 446/394 mm^3 in Group B ($p<0.000$). Mean weight increases over 52 weeks were 1.0 kg in Group A and 1.4 kg in Group B, while Karnofsky scores in Group A rose from 81 to 85 and in Group B from 82 to

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86. Wilcoxan Signed Ranks Test and the Sign Test both indicated that all these measured increases within both groups were statistically significant ($p<0.01$). Indeed, for both glutathione peroxidase levels and CD4 cell counts $p<0.000$ in all cases. There were, however, no statistically significant differences between the measured parameters, (serum glutathione peroxidase, CD4-cell counts, weight and Karnofsky scores) in Group A compared with those of Group B ($p>0.05$), or between males and females ($p>0.05$).

Post-Trial Results

The year-long double-blinded clinical trial was funded by the Canadian charity, The Friends of Mengo Hospital. This allowed information on serum glutathione peroxidase levels, body weights and Karnofsky scores to be assessed six months after the trial had formally ended. CD4 cell counts were also measured at the same time, as part of normal hospital procedures.

This additional data allowed an assessment of the health implications of discontinuing nutritional supplementation in HIV-positive patients. To illustrate, the initial double-blinded closed year long trial began with 310 patients, 263 of whom completed it (84.8%). At the end of the six month open, post-trial study, CD4 cell counts were available for 213 of these patients and serum glutathione peroxidase levels from 122. Karnofsky quality of life scores also had been collected for 191 of the former participants in the closed trial and body weight for 166.

Six months after the formal closed trial had ended, the mean/median serum glutathione peroxidase levels of the 124 assessed patients had fallen by 7117/5184 IU. ($p<0.001$). During this time period, of course, former members of Group A and Group B had not been provided with any nutritional supplements. This decline in serum glutathione peroxidase levels in this group was almost universal.

Similarly, in the 213 patients for whom CD4 cell counts were available at the end of the six month post-trial period, mean/median levels had fallen by 155/151 mm^3 respectively. ($p<0.001$). Similarly, in the 191 patients that had their mean/median Karnofsky quality of life scores assessed six months after the closed trial had ended, these had fallen by 5.5/5.0 respectively ($p<0.001$).

It is clear that dramatic falls in serum glutathione peroxidase levels, CD4 cell counts and Karnofsky scores had occurred during the six months in which nutrient mixtures A and B were no longer available to former closed-trial patients. Unfortunately, these losses during the post-trial period had more than negated all the gains in quality of health indicators that most patients had achieved during the nutritional trial itself. Additional analyses indicated that such declines had occurred in the post-trial period, regardless of the nutrient group to which the patient had formerly belonged. Similarly, gender difference made no statistically significant difference ($p>0.05$).

The only exception to this generalization involved body weight. During the six month period nutrient supplements were not provided, former trial participants had lost relatively little weight. In the 166 patients for whom this measure was available, mean/median weight had only fallen by 0.61/0.00 kilograms ($p>0.05$).

Conclusions

The initial prospective randomized, double-blinded clinical trial demonstrated that two nutrient mixtures taken for 52 weeks by HIV-positive patients who were receiving no anti-retroviral drugs, significantly slowed their decline into AIDS. The improvement was associated with increases in serum glutathione peroxidase levels, CD4 cell counts, body weight and improvements in quality of

life scores. In contrast, the post-trial data demonstrated that if such supplementation stops, HIV-positive patients suffer a rapid health decline. This involves highly statistically significant drops in serum glutathione peroxidase levels, CD4 cell counts and Karnofsky quality of life scores ($p<0.001$). These results are very consistent with those of smaller open trials using nutritional supplement which have been conducted elsewhere in Sub-Saharan Africa.[5] It seems clear that inadequate nutrition plays an extremely important role in the progression of HIV-infected patients into AIDS. These results also are consistent with Foster's model[6] of the development of AIDS which suggests that deficiencies of glutathione peroxidase play a key role in the process.

Acknowledgements

The authors would like to thank the Canadian charity, The Friends of Mengo Hospital (Canada) for funding the initial clinical trial and the counsellors and nurses of the AIDS Clinic, Mengo Hospital, Kampala, Uganda who made this study possible. They are also indebted to monitors Natalie Ward, Peter Hunt, Alan Lingwood, Magnus McNab, Matthew King, Josh Lam and Emily Skelton. All the glutathione peroxidase analyses were undertaken at the Mengo Laboratory under the supervision of Raymond Woods. Staff at the Hematology Laboratory at Mulago Hospital established patient CD4T lymphocyte counts. Statistical calculations and tests were carried out by Dr. Nicholas Karlson, Coordinator, University of Victoria Statistical Consulting Centre. His help is greatly appreciated.

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