

Some Factors that Influence Ascorbic Acid Retention in Psychiatric Patients

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Introduction

Few areas of psychiatric research have generated more apparently conflicting reports than that of the relationship between Vitamin C metabolism and schizophrenia. Early reports of gross plasma ascorbic acid concentration abnormalities in schizophrenics^{1,2,3} were followed by reports that these abnormalities were simply due to dietary differences.⁴ Still later reports indicated that plasma Vitamin C levels were very unreliable measurements in general.⁵ Recently, VanderKamp, using Vitamin C loading and urine concentration studies, has reported gross Vitamin C retention abnormalities in schizophrenics as opposed to normals.⁶ His methods seem to avoid many of the pitfalls of earlier Vitamin C studies, and his reported results indicate that its metabolism may be central to understanding the pathophysiology of this disease.

Our own recent research has been in the study of physiological and functional factors which modulate certain slowly changing bioelectrical phenomena—the TCDC circuit.^{7,8} Among these significant variables are capillary integrity and plasma steroid concentrations.⁹ Since both of these factors are related to ascorbic acid metabolism, it appeared reasonable to attempt a replication of VanderKamp's studies by a group relatively disinterested in the hypotheses previously tendered relating Vitamin C and schizophrenia.^{2,3} Relationships were studied between ascorbic acid retention in normal subjects, hospitalized schizophrenics and hospitalized non-schizophrenic mental patients.

In addition, the effects of the subject's sex, organic brain damage, microcirculatory abnormalities,^{9,10,11,12} wheal size response to histamine skin testing,^{13,14} cortisone administration and chlorpromazine administrations were studied. Relationships to the TCDC potential itself will be reported elsewhere.

Methods

The subjects used in these studies were divided into three groups, each approximately the same in sex and age distribution. The first consisted of seven normal subjects selected from hospital personnel. The second group of 14 consisted of un-medicated non-schizophrenic hospitalized mental patients, and the third consisted of 18 unmedicated schizophrenics.

Most of the experimental procedures are self explanatory and so only the specific techniques of histamine skin testing, nail bed capillary plexus index ratings and urinary testing after ascorbic acid loading will be detailed here. Each test was performed by experimenters who were "blind" to other test results and within-group diagnoses.

Histamine skin tests were modified after Weckowicz.^{13,14} Skin overlying the deltoid insertion was lightly cleaned with alcohol and wiped clean. One drop of 1:1000 histamine was placed on the skin after which the epidermis was gently punctured with a 25 gage needle. Longitudinal and transverse diameters were measured on the resulting wheal every minute for 10 minutes. The mean minute diameters were

determined and the approximate wheal areas computed for each minute of observation. Capillary plexus determinations were modified after Maricq.¹⁰¹¹ Each cleaned and immersion oil-coated nail bed was examined through a dissecting scope at 40x magnification. Capillary loops were ignored. The presence of transversely running microvessels only were scored. If found running up to one mm. proximal to the cuticle, the finger was scored a "one." Plexi found up to two mm. proximal were rated a "two," three mm. back a "three," and if found beyond three mm. the finger was rated a "four." Thus indices ranging from "0" to "40" could be determined by adding the scores on all ten fingers.

Ascorbic acid loading was tested in the following way. After voiding at 9 a.m. the subject ingested 4.0 gm. of Vitamin C tablets with water. Two urines were collected at 1¹/₂ hour intervals for ascorbic acid testings, by the procedure of Vander-Kamp.⁶ If both were negative, the subject ingested another 4 gm. of Vitamin C at noon and had the next two urines tested. If these were still negative, he was given 8 gm. Vitamin C the next morning after voiding. His next two urines were collected and tested. If both of these were still negative, 8 more gm. were given at noon of this second day and the subsequent urines tested. Thus total doses of 4, 8, 16 and 24 gm. of Vitamin C were administered.

Results

To simplify statistical procedures, the t-test of proportionality was generally used two tailed.

A. Ascorbic acid retention by normals and non-schizophrenic mental patients

Six out of seven normal subjects had a positive urine test on the first urine following 4 gm. of Vitamin C loading. Only four of 14 non-schizophrenic patients excreted ascorbic acid this readily. The Vitamin C retention in these patients exceeded that of normals at a 4 gm. loading cut off, $t = 3.36$, $P < .01$.

B. Schizophrenic vs. non-schizophrenic patients

None of 14 non-schizophrenic patients retained more than 16 gm. Vitamin C before showing a positive urine, but five out of 18 schizophrenics failed to show a positive urine at this point. Their Vitamin C retention exceeded that of non-schizophrenics at a 16 gm. cut off point, $t = 2.64$, $P < .025$.

C. Chlorpromazine administration

No differences in ascorbic acid retention could be found in a group of seven non-schizophrenic patients when in an unmedicated state and following administration of 50 mgm. Chlorpromazine b.i.d.

D. Cortisone administration

Five normals who showed a positive first urine after ingesting 4 gm. of Vitamin C were retested one week later by preceding the Vitamin C administration with 50 mgm. Cortisone p.o. one hour earlier. In this repeat test none showed positive first urines and two failed to show a positive second urine. Seven non-schizophrenic patients were selected who had all shown positive urines well below the 16 gm. ascorbic acid loading. When given 50 mgm. Cortisone p.o. one hour before Vitamin C loading, three out of seven failed to excrete at 16 gm. This ascorbic acid retention following



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icortisone administration was significant $t = 2.29$ $P < .05$. Thus Cortisone administration inhibited obtaining a positive urine test in both groups of subjects tested.

E. Sex differences

Five out of six non-schizophrenic male patients failed to show a positive urine after four gm. of Vitamin C while only five out of eight non-schizophrenic women were abnormal, t value for this group was $t = 0.91$, $N = 14$, $P < .33$. Six out of nine schizophrenic men showed abnormal ascorbic acid retention tests while four out of nine schizophrenic women did so, $t = 0.97$, $N = 18$, $P < .33$. Thus the co-joint occurrence was $P < .10$ two **tailed that** men retain ascorbic acid more often than do women.

F. Organic brain damage patients vs. functional non-schizophrenics

Seven out of nine organic brain damaged patients failed to show a positive urine test at 4 gm. Vitamin C loading as opposed to three out of five functional mental patients. Although this failed to reach statistical significance **it** may be due to the small number found in each group.

G. Comparison of simple vs. non-simple schizophrenics

None of five simple schizophrenics failed to show a positive urine test by the 16 gm. Vitamin C loading stage whereas five of the 13 other schizophrenics failed to show a positive urine even at this amount of ascorbic acid administration. This difference is significant at $t = 2.85$, $P < .05$. Thus simple schizophrenics appear to excrete ascorbic acid much more readily than patients with other schizophrenic classifications.

H. Vitamin C retention and histamine skin testing

This study was done only on the schizophrenics and the wheal size cut off point was selected differently for males and females due to general sex differences in wheal size responses to histamine.⁹ Of men with maximum wheal size over 15 mm.,² and women with maximum wheal of over 11 mm.,² only one out of 11 required more than 16 gm. Vitamin C to develop a positive urine. Three out of the four "small whealers" required more than 16 gm. to show a positive urine test, $t = 2.82$, $P < .02$. The factors which inhibit the histamine skin test response in mental patients may also inhibit "C" excretion.

I. Microcirculatory plexus index relationships

None of eight non-schizophrenic patients with a plexus index of 0-11 showed a positive urine at 4 gm. Vitamin C loading. Four out of the five with a plexus index of 11-40 did show a positive urine at 4 gm. loading $t = 4.46$, $P < .001$. For the schizophrenics, none of the four who had a plexus index 21-40 needed more than 16 gm. Vitamin C to show a positive urine, while five of the 14 with a plexus index of 0-20 needed more than 16 gm. of ascorbic acid to show a positive urine, $t = 2.79$, $P < .01$, $N = 18$. Thus in both groups tested, Vitamin C retention was significantly reduced in those with high plexus indices.

Discussion and Conclusion

From our results it is clear that non-schizophrenic hospitalized mental patients show gross Vitamin C retention test abnormalities as well as do schizophrenics. However, schizophrenics do differ significantly from these hospitalized controls, and there is strong evidence that the mental patient population is affected by factors over and above dietary ones. The variables selected for this study are not truly independent of each other, but those most intimately connected with the ascorbic acid test results were microcirculatory plexi, histamine wheal response and Cortisone loading. It is most doubtful that these variables are, in turn, a reflection of diet.

Although the diet factor is not tenable as a full explanation of the group test differences, the test results themselves are not unambiguous. A failure to produce a positive urine may be due 1) to a failure to absorb the ingested Vitamin; 2) to a steroid or glutathione-like substance in the plasma that pushes absorbed Vitamin C into the tissues so rapidly that renal threshold is not exceeded; 3) to an abnormality in the renal threshold itself so that little ascorbic acid enters the urine; and 4) to the presence of a reducing substance in the plasma or urine that neutralizes the excreted ascorbate, yielding a false negative test.

As frequently happens in scientific disputes, both sides mentioned in the introduction appear to be partly correct and partly incorrect. Further

investigations along these lines are warranted.

Abstract and Summary

Factors influencing Vitamin C retention as determined by the VanderKamp urine test were studied in seven normal subjects, 14 hospitalized non-schizophrenic mental patients, and 18 hospitalized schizophrenics. Both patient groups retained significantly more ascorbic acid than the normals, and the schizophrenics retained significantly more than the non-schizophrenic patients. Chlorpromazine administration had no measurable effect, but cortisone administration significantly increased Vitamin C retention in normal and patient subjects.

There was some indication that males retained more than females and organic brain damaged patients more than functional non-schizophrenics. Schizophrenics with diminished histamine skin test responses retained significantly more Vitamin C than those with normal skin tests. Simple schizophrenics excrete Vitamin C more readily than other schizophrenics, and patients with a high incidence of microcirculatory plexi in their nail beds excreted ascorbic acid significantly more readily than the low plexus group. It is concluded that the VanderKamp test is influenced by non-dietary and non-medicinal factors operating in psychiatric patients.

This study was financed by Marcy (N.Y.) State Hospital and Syracuse (N.Y.) Veterans Administration Hospital.