Calcium Ribonate and Vitamin C (Nu 240-10) in the Treatment of Tuberculosis

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The object of this paper is to show that the use of calcium ribonate and vitamin C in the treatment of tuberculosis is definitely indicated. The total serum calcium concentration varies normally from 9 to 11 mg. per 100 cc. It is important to note that the absorption of calcium is governed by these factors: 1) The hydrogen-ion concentration within the intestines. 2) The relative proportion of other substances in the diet. 3) Vitamin D.

Calcium metabolism is easily altered in febrile tuberculous patients because of poor nutrition, of deficiency in free hydrochloric acid, of depressed digestive processes, of reduced alkalinity of the blood and of increased elimination of calcium on account of exudative inflammatory processes.

It is a known fact that in all exudative lesions there is an increase of H-ion concentration in the affected tissues with a relative decrease of calcium. It has also been shown that patients with exudative lesions eliminate more calcium than is ordinarily eliminated under normal conditions. As the result of inflammation, the capillaries become dilated and more permeable, hence serum and its constituents pass into the paravascular spaces. In acute inflammatory conditions this exudate is readily re-absorbed and the tissues involved are restored to their normal state. In chronic inflammation however, some of the exudate remains stagnant and the blood cells found there are eventually disintegrated.

In the presence and action of calcium, the exudate of the paravascular spaces is converted into two histological elements, 1) the matrix, and 2) the fibrils. Eventually these fibrils unite through a process of fusion and later form white waxy bundles of non-elastic fibres. Without the action of calcium the formation of fibrils and fibrous tissue would not take place any more than the

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coagulation of blood in the absence of calcium. Therefore, calcium deficiency is to be considered as a serious handicap for tuberculous patients, inasmuch as it plays such an important part in the formation of fibrous tissue, the forerunner to the healing of some tuberculous lesions.

Since calcification of a pulmonary lesion is considered to be an indication that the process is healed, numerous attempts have been made to promote calcification of these lesions by some form of calcium therapy. Gordon and Cantarow administered parathormone, 20 units every 48 hours, and calcium lactate, 30 grains three times daily, to 14 patients with pulmonary tuberculosis for periods of one to six months. Roentgenographic studies failed to reveal any change in calcification of the lung fields or bones of the hand. They maintained that calcium may exert a beneficial effect upon certain symptoms. Excessive bronchial secretion may be lessened, with consequently diminished cough; the pain of acute pleurisy may be relieved by intravenous or intramuscular injections of calcium gluconate or by parathormone; serofibrinous pleurisy may be benefited.

Menkin noted that approximately 10 times as many calcified areas were found in rabbits injected with calcium chloride than in the control animals. Spies demonstrated that repeated administration of viosterol caused calcification of tubercles. Scholtz gave intramuscular injections of calcium gluconate every second day to 22 patients with exudative tuberculous lesions. This therapy exerted a marked influence on exudation for in 80 per cent of the patients the quantity of sputum decreased rapidly. In many cases the night sweats were favorably influenced. He concluded that the effect of calcium therapy is not due to a specific influence upon the tuberculous process but rather to its vascular action, diminishing capillary permeability and inhibiting inflammatory exudation.

Many writers have recommended the use of calcium in patients with pulmonary tuberculosis, particularly those receiving pneumothorax and those with intestinal tuberculosis. Pisani and Smekal reported favorably on the prevention of pleural effusions by the use of calcium.

Calcium is of undeniable value in the treatment of diarrhea in intestinal tuberculosis. Brown and Sampson said it was about the best remedy for this purpose. Cantarow suggested that calcium therapy for the diarrhea of intestinal tuberculosis is beneficial because of its inhibitory action on peristalsis and general dehydrating effect. In any event, it has a tendency to relieve abdominal pain, intestinal bleeding and diarrhea in most cases. Pisani in his treatment of 43 cases of intestinal tuberculosis with
intramuscular injection of calcium gluconate found that 20 were definitely improved. Calcium therapy in the majority of cases can bring about changes which tend to rectify the disturbed physiological activity of the intestines.

According to Pisani, the use of calcium for intestinal tuberculosis is of importance because it restores the normal calcium ion concentration of the tissues, it stimulates phagocytosis, stimulates fibrosis and it counterbalances the existing vagotonia through stimulation of the sympathetic filaments. The importance of an early diagnosis of intestinal tuberculosis cannot be overestimated. We doubt if far advanced tuberculous intestinal lesions are amenable to any treatment.

It is generally agreed that the most important function of vitamin C is control of the intercellular cement substance in connective tissue. In this connection, it is of vital importance to tissues of mesodermal origin such as collagen, vascular endothelium, cartilage, and the matrices of bone. Most authors maintain that there is a deficiency of vitamin C in tuberculous patients. Some have shown a rough parallelism between the severity of the tuberculosis and the degree of vitamin C deficiency. In normal individuals the blood-serum level of ascorbic acid is between 0.7 and 2.5 mg. per 100 cc. Elimination of vitamin C from the diet is followed by a gradual fall in the blood level of the vitamin until it reaches a value as low as 0.2 mg. per 100 cc. The urinary excretion of vitamin C in the normal healthy subject is dependent upon the dietary intake.

Faulkner and Taylor have shown that there is an increased demand for vitamin C in infection. Patients with tuberculosis required more than 200 mg. of ascorbic acid a day to keep the plasma level normal. This is to be compared with 25 to 60 mg. which is considered to be the daily requirement of a normal adult. Kaplan and Zonnis have shown that the vitamin C concentration in the blood can be raised in most patients to normal levels by the oral administration of synthetic vitamin.

Singer and Van Bark report that the ordinary balanced hospital diet in itself is adequate in maintaining a vitamin C equilibrium in a large percentage of tuberculous children studies. Controlled feedings of 50 to 100 mgm. of vitamin C daily were followed by a rise in the ascorbic acid values of blood plasma to normal or high levels. Bumbalo and Jetter have shown a comparison of the excretion of vitamin C between tuberculous and nontuberculous children. In the first place, the average basic level of the urinary excretion of vitamin C in the two groups varied considerably. The tuberculous group consistently excreted less than 10 mg. per 24 hours. On the other hand, the control...
groups of healthy children excreted on the average of 30 to 35 mg. per 24 hours. As far as could be ascertained, the vitamin C intake of this latter group was approximately similar to that of the tuberculous group, showing that such a diet in a healthy child is adequate, but in one with a chronic infection such as existed in the tuberculous group, it was insufficient.

In consideration of the above-mentioned factors, we have employed at the Boston Sanatorium a combination of calcium ribonate and vitamin C on a series of 50 cases. The preparation was supplied in ampules of 10 cc. containing a 10 per cent solution of calcium ribonate buffered with sodium ascorbate. This new calcium salt is water-soluble to the extent of approximately 70 per cent. It is ionized slowly, and it is believed that in metabolism the acid radical is probably oxidized. Maddock has shown that the intravenous administration of this product on parathyroidectomized and normal dogs, possesses a more prolonged hypercalcemic effect than calcium gluconate. All of our patients received 10 cc. of calcium ribonate intravenously, three times weekly for a period of three months (Table I).

**Intestinal Tuberculosis**

Our first group consisted of 11 patients, ranging from 18 to 56 years of age, with intestinal tuberculosis. Eight of the patients were females and three were males. The main symptoms presented by this group were diarrhea, abdominal pains, dyspepsia, occasional vomiting, loss of appetite and weight. Four patients failed to respond to ultraviolet therapy. We were able to note a definite improvement in five patients after three months' treatment with calcium ribonate. There was no change in one case and there were five deaths.

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Case 1: S.C., a 48 year old, white, married female was admitted with a positive sputum and far advanced pulmonary tuberculosis. Roentgenograms of the chest revealed infiltration and moderate broncho-pneumonic reaction involving the entire left lung with a large cavity in the left apical area. The patient was admitted with a two-months' history of cough, expectoration, night sweats, loss of appetite, and 17 lb. in weight. After one week's hospitalization the patient began to complain of abdominal pains, nausea, and diarrhea ranging from 6 to 10 bowel movements a day. Roentgenograms of the gastro-intestinal tract revealed the presence of intestinal tuberculosis. The patient was placed on calcium ribonate therapy and after 6 weeks' treatment her diarrhea, nausea, and abdominal pains had disappeared. At the end of three months' treatment, the patient had gained 22 lbs. A left thoracoplasty is to be performed in the future.

Pleural Effusion Following Pneumothorax

Our next group consisted of 10 patients ranging from 16 to 42 years of age, who had developed a pleural effusion during the course of their pneumothorax. Six of the patients were females and four were males. The pleural effusion had existed anywhere from 2 months to 9 months. On calcium ribonate therapy, we were gratified to note that the fluid disappeared in 9 cases and there was no change in one case which required thoracentesis.

Case 2: N.B., a 16 year old, single, white school girl, was admitted with a positive sputum and moderately advanced pulmonary tuberculosis. Roentgenograms revealed infiltration and moderate broncho-pneumonic reaction involving the upper half of the right lung. The patient was admitted with a 6 weeks' history of cough, expectoration, loss of appetite and 10 lbs. in weight. A right artificial pneumothorax was instituted and a good collapse was obtained. Three weeks following the initial pneumothorax, the patient developed a right pleural effusion. The patient was placed on calcium ribonate therapy and the pleural effusion completely cleared after 5 weeks treatment. The patient has since been discharged from the sanatorium.

Pre pneumothorax

We selected for our next group 10 patients ranging from 18 to 38 years of age, who were to be given pneumothorax therapy. Seven of the patients were females and three were males. Calcium ribonate was administered one month prior to pneumothorax and continued for 2 months during their refills. We noted that only 2 of the 10 patients developed fluid. In a control group of 10 cases, six patients developed fluid.

Case 3: C.C., a 20 year old, white, single student nurse, was admitted with a positive sputum and minimal pulmonary tuberculosis. Roentgenograms revealed infiltration and moderate broncho-pneumonic reaction in the region of the 1st right interspace. The patient was admitted with a 7 weeks history of slight cough, fatigue and 5 lb. weight loss. A right pneumothorax was advised. One month prior to receiving pneu-
mothorax, the patient was placed on calcium ribonate therapy and this was continued for two months. She has been receiving right pneumothorax for 16 months with no evidence of fluid in the pleural cavity.

**Tuberculous Empyema**

Our next group consisted of 6 patients, ranging from 21 to 39 years of age, with tuberculous empyema. Four of the patients were male and two were female. These patients had thoracenteses on the average of every 2 weeks. After three months of calcium ribonate therapy, we noted that there was definite improvement in three patients, in that the fluid became less viscid and the amount of fluid decreased requiring less frequent thoracenteses. No change was seen in two cases and one patient died.

*Case 4*: T.C., a 21 year old, white, single female was admitted with a positive sputum and moderately advanced pulmonary tuberculosis. Roentgenograms revealed infiltration and small cavity in the right upper lobe. The patient was admitted with a 2 months' history of cough, expectoration, weakness, and loss of 17 lbs. in weight. A right pneumothorax was instituted and after 5 weeks' treatment the patient developed a tuberculous empyema. The patient was tapped on the average of once every 2 weeks for a period of 3 months. On each thoracentesis from 20 to 30 oz. of greenish-yellow fluid was obtained. The patient was placed on calcium ribonate therapy and after 3 months' treatment the fluid practically disappeared. She has not been tapped for 4 months and has since been discharged from the Sanatorium with a negative sputum and partial atelectasis of the right lung.

**Far Advanced Pulmonary Tuberculosis**

Our next group consisted of 13 patients ranging from 27 to 52 years of age with far advanced pulmonary tuberculosis. Nine of the patients were males and four were females.

The majority of these cases had been in the sanatorium from 6 months to 2 years. None of these patients were considered suitable for collapse therapy. After 3 months treatment on calcium ribonate we found that 9 patients were definitely improved. Decrease in night sweats, lessening of cough, and improvement in appetite were especially noted. In 2 patients there was no change and 2 patients died.

*Case 5*: H.P., a 31 year old, white, married male was admitted with a positive sputum and far advanced pulmonary tuberculosis. Roentgenograms revealed soft infiltration and moderate bronchopneumonic reaction with multiple small cavities involving both upper lobes. The patient was admitted with a 4 months' history of cough, expectoration, weakness, loss of appetite and 12 lbs. in weight. Due to the patients' clinical condition and extensive disease, no collapse therapy could be undertaken. After 3 months' treatment on calcium ribonate a definite improvement in the patients' cough, strength, and appetite was noted. He gained 20 lbs. in weight. The patient has recently been started on pneumоперитонеum treatments.
No ill effects or untoward symptoms were noted in the intravenous administration of calcium ribonate.

In view of the findings of many workers in tuberculosis and our own experience, we believe that the use of calcium ribonate and vitamin C has a definite place in the treatment of tuberculosis particularly intestinal tuberculosis and pleural effusion.

SUMMARY

1) The writer's observations as well as other investigators' have revealed that there is a definite use for calcium and vitamin C therapy in the treatment of tuberculosis.

2) In a series of 50 cases at the Boston Sanatorium a combination of calcium ribonate and vitamin C was administered intravenously three times weekly for a period of three months.

3) The results obtained justify the continued use of calcium ribonate and vitamin C in the treatment of tuberculosis, especially intestinal tuberculosis and pleural effusions.

4) No ill effects were encountered in the intravenous administration of calcium ribonate in any of our cases.

RESUMEN

1) Las observaciones del autor, lo mismo que las de otros investigadores, han revelado que existe un uso bien definido para la terapia con calcio y vitamina C en el tratamiento de la tuberculosis.

2) En una serie de 50 casos en el Sanatorio de Boston se administró una combinación de ribonato de calcio y vitamina C por la vía intravenosa tres veces a la semana por un período de tres meses.

3) Los resultados obtenidos justifican el uso continuado del ribonato de calcio y vitamina C en el tratamiento de la tuberculosis, especialmente tuberculosis intestinal y derrames pleurales.

4) La administración intravenosa del ribonato de calcio no causó efectos contraproducentes en ninguno de nuestros casos.

REFERENCES


