ON THE INFLUENCE OF "KOHA", A PHOTSENSITIZING DYE, AGAINST ANEMIA CAUSED BY IRRADIATION

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The destructive effects on the human body, especially on the haematopoietic tissues caused by heavy irradiation of ionizing rays have already been acknowledged by many previous investigators, while effective treatments of general irradiation injuries are not well known except the blood transfusion showing temporary improvement.

To the irradiation anemia we administered the "Koha" that reacts as a stimulant to reticuloendothelial tissues, and obtained good results on clinical anemia human cases caused by radiation therapy, and on experimental anemia of animals as well.

(I) Clinical observations

Among 21 cases which showed so-called crapulence clinically and leucopenia under the level of 4000 per cmm, 2 mg of Koha solved in 40cc physiological saline solution was administered to 15 cases intravenously per day, and 1 mg of Koha in 20 c.c. to 3 cases, until leucocyte count has risen to the normal level of 5000. In another 3 cases put aside as controls, 50 c.c. of hypertonic glucose solution adding 6 mg of Vitamin B, and 50 mg of Vitamin C was intravenously injected every day.

In the cases administered 2 mg of Koha, the crapulence was seen to be completely disappeared within 1-4 days, and in 3 cases administered 1 mg of Koha, the recoveries of crapulence were seen after 5, 9, and 12 days respectively.

Blood findings.

Erythrocyte count, hemoglobin value and blood sedimentation rate showed no remarkable changes after the administration of Koha. Therefore Koha seems to have almost no recovering effect on these fields.

On the contrary, the Koha showed marked reaction against leucocytes, as shown in Figure 1.

* "Koha" was a cipher name of ex-army for cryptocyanin O. A., which was synthesized by Dr. T. Ogata for sensitizing the photoplate to infrared rays. Thereafter many physiological studies concerning allied substances were carried out and wide applications were found in medical and agricultural field through the World War II.

Fig. 1
The reaction of Koha against the leucocyte count

In the cases administered 2 mg Koha the increases of leucocytes count to the level of 5000 appeared within 11 days and in the cases administered 1 mg within 15 days, while in the non-administered cases only a little increase was shown during a month.

When investigating the 2 mg administered cases more minutely, we found all but groups (6 of 7 cases) of more than 3000 leucocyte counts recovered within 7 days and the groups (6 of 8 cases) of leucocyte counts less than 3000 recovered within 10-11 days.

So we can see the fact that the administration of proper dose of Koha has a marked effect on the recovery of leucocyte count, and the slighter the leucopenia is, the more rapidly it recovers.

Percentage of leucocyte count.

In the group administered Koha appeared at first the shifting of the nucleus to the right, such as an increase of neutrophil segmental leucocytes and a decrease of unripe or unlobed-nuclear cells, with the increase of total leucocyte count. Then, a little later or almost simultaneously, a rapid increase of eosinophil cells, and still later a remarkable increase of lymphocytes were observed, and gradually normal cell percentage were obtained. In the cases of controls, on the contrary, were few changes of neutrophil or eosinophil leucocytes, and was only a gradual increase of lymphocytes seen. There were no specific changes of monocytes, basophil cells and plasma cells. (Fig. II).

Fig. 2

Blood findings of clinical anemia treated with Koha

(1) 2 mg Koha per day

(2) 1 mg Koha per day

(3) control group
(hypertonic glucose solution)

(II) Animal experiments

We used the rats of 1—5 months old in our experiments. After enclosing 4—8 rats in groups into a paper box and irradiating under the same condition, we administered Koha to the half of them and compared with the rest half.

i) Blood findings.

The result is classified in two groups as follows.

(A) In the group irradiated by a great amount—almost lethal dose—of X-ray, the rats that were not administered Koha, were died of an extreme decrease of both erythrocytes and leucocytes. The others, administered Koha, whose erythrocytes were decreasing gradually in spite of a slow increase of leucocytes, died a little later. But it aroused our interest that two of them lived out after the decrease of erythrocytes had stopped.

(B) In the group which had a moderate amount of irradiation (a group irradiated only by X-ray, and recovering their leucocyte-count to the level of 5000 after about 1 month), the Koha administered cases all regained their normal leucocyte-count more rapidly than the non-administered cases. (Koha administered cases after 14 days in average, non administered cases 25 days in average).

On the other hand, there were few differences in erythrocyte counts between the administered and non-administred cases, and they began to increase generally after 1 month.

(C) Percentage of leucocyte counts.

Immediately after the irradiation all over the body, there occurred a rapid decrease of total leucocyte count with marked lymphopenia, and at almost the same time, eosinophil leucocytes remarkably decreased or often disappeared. Then a decrease of neutrophil segmental lucocytes and the shifting of nucleus to the left were observed.

And by the administration of Koha, an increase of total leucocytes and neutrophil segmental cells appeared first. Then a little later, eosinophil leucocytes appeared or increased rapidly, lymphocytes also increased and thus the total leucocyte count recovered to the normal level, with an almost normal constitution.

In the non-administered cases, the processes were about the same, but their recoveries were much slower than in the administered cases. No specific changes were seen with monocytes, basophil leucocytes and plasma cells.

ii) *Pathological-anatomical and histological findings.*

All of the rats used in the experiment were put to death and anatomized, and their various organs investigated pathological-anatomically and histologically. The results were classified in four stages of their death as follows.

- (1) 1st Stadium: Stadium of maximal diminution of leucocytes after the irradiation.
- (2) 2nd Stadium: Stadium when in the Koha-administered groups the recovery of leucocyte count reached the 5000 level, and in the non-administered

groups not get reached so high as that.

(3) 3rd Stadium: Stadium when the leucocyte-count exceeds the 5000 level in both groups.

(4) 4th Stadium: Stadium when more than 1 month has passed after the recovery of normal leucocyte-count.

A) Macroscopic findings.

In the macroscopic findings most common changes were anemia and edema of various organs. Between the administered and non-administered animals, there was almost no difference except one in spleen of the 2nd and 3rd stadium in which the grade of atrophy was a little higher in the non-administered than in the administered.

B) Pathological-histological findings.

In the 1st stadium there were few differences between the administered and non-administered cases in all organs.

In the 2nd stadium there were marked differences between the two groups in the hematopoietic organs, such as spleen, bone-marrow, lymphnodes and liver, but few differences in other organs.

In the group which had a great amount of irradiation, the lymph-follicles in spleens and lymphnodes of the Koha administered cases showed some omens of regeneration, but those of the non-administered cases had the symptoms of degeneration only. And only the administered cases showed findings of blood formation in the pulp of spleen and bone-marrow.

In liver, the administered cases showed only an evidence of atrophy, but the non-administered ones accompanied a moderate degree of degeneration. However, in the group with a moderate amount of irradiation, lymph-follicles in spleen and lymph glands of the Koha-administered cases showed a remarkable regeneration, while those of the non-administered stayed still in a condition of severe degeneration. As for the findings of blood formation in bone-marrow and pulp of spleen, the administered cases showed an extreme improvement as compared with the non-administered. In the administered cases, atrophy of the liver was slight and the type of fatty degeneration was on the whole regular and peripheral, but in the non-administered, atrophy was much prominent and the fatty degeneration was mainly of irregular and diffuse forms.

In the 3rd Stadium was seen a great difference between the two groups too. Namely, in the group irradiated by a moderate amount, the spleen, bone marrow and lymph glands of the Koha-administered group almost resumed its normal con-

dition, and those organs of the non-administered showed the evidences of both degeneration and regeneration in the same degree.

In the 4th Stadium there seemed to be no marked difference between the two groups, both being restored almost to normal.

After all, it may well be said that the administration of Koha has a good therapeutic effect on the disturbances caused by irradiation, according to the clinical observations and animal experiments stated above.