REPRINT

BENHA MEDICAL JOURNAL

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Published by
Benha Faculty of Medicine

Volume 12 Number 1
Jan. 1995

Benha M. J.
Vol. 12 No 1 Jan. 1995

THE EFFECT OF DIFFERENT TREATMENT MODALITIES ON NK CELLS IN CANCER PATIENTS

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Abstract

The aim of this study is determination of NK-cells% in cancer patients and its affection by various types of treatment (Radical surgery, radical radiotherapy and 3 courses of chemotherapy.

125 patients of various malignancies were Involved in the study (25 cases of cancer breast, 25 cases of lymphoma, 25 cases of skin and soft tissue malignancies, 25 cases of GIT malignancies and 25 cases of G.U. malignancies) in addition to 25 control healthy adults. For whom determination of NK c'ells in PBL was done before and after any type of treatment by direct solid-phase heterogenous immuno fluorescence assays using anti-leu-lla monoclonal antibody (and anti-leu-7 FITC, (Becton ickinson, CA, USA).

This study found that the mean NK cells % is insignificantly decrease in cancer patients. The study also found that NK cells% is insignificantly decrease in early post operative cases.

Our study also reported that surgical treatment and short courses of chemotherapy produce insignificant decrease in the NK cells %. On the other hand radiotherapy produce significant decrease in the NK cells%.

Functional assay should be performed in cases of solid tumours because of impaired NK function has been reported even in the presence of normal or high number of NK cells.

Introduction

NK cells seem to have the ability to destroy tumor cells without previous exposure to their antigens (Somers and Guillou, 1991).

Many experiments have clearly shown that NK cells are effective in vivo and can destroy tumour cells (Habu et al.,1981). Inhibition of tumour growth by IFN is associated with marked. Augmentation of NK cell - mediated cytotoxicity (Fresa and Murasko; 1986). In Familial melanoma, relatives of the patients, who have an increased risk of developing the tumours. Also showed a depressed NK cell. Cytotoxic activity suggesting a possible role of NK cells resistance to tumour growth (Hersey et al., 1979). In addition the recurrence of melanoma distant metastases has been found to be signifiedntly lower in patients with high NK cell activity thdn in those with low activity (Hersey et al., 1981).

In patients with advanced cancer, NK cell cytotoxic dctivity is usually depressed this depression appears to be secondary to tumour invasion at one hand and due either to interaction of NK cells with tumour cells or to the presence of suppressor cells on the other hand (Herberman et al., 1979).

In conclusion, the antitumour role of NK cells are likely to be in nature of first line of defence against a tumour nidus before. The development of adaptive immune response and in the early stages of tumour growth and prevent, to a limited extent, the metastatic spread of tumour cells. However they have no impact on established cancers (Roit et al., 1988).

So this work is done to study the level of NK cell percent in patients before and after different treatment modalities.

Material and Methods

125 cases of various malignancies (25 cases of cancer breast 25 cases of lymphoma, 25 cases of skin and soft tissue sarcoma, 25 cases of GIT malignancies and 25 cases of GU malignancies), in addition to 25 Healthy adults control, matching with age and sex were classified into 6 groups.

NK cells % were determined in P. B. L. of the above groups:

* Before any type of treatment.
* After radical surgery
* After radical radiotherapy.

* After 3 courses of chemotherapy.
* In control group.

By direct solid-phase heterogenous immunofluorescence assays by using anti-leu-lla, leu-7 monoclonal antibody (Becton Dickinson, CA USA).

Results

* Mean N cells % in control group = 16 + 3.16 %.
* The group of Cancer breast including 25 patients with median age 41 ± 7.919 cases and M/F ratio of 4, in this group NK cells % are insignificant decrease in patients with Cancer breast in comparison to control. Also surgery and courses of CMF produce insignificant decrease in the NK cells % while radiotherapy produce significant decrease in NK cells % (Table l).
* Lymphoma group including 25 patients with median age 35 + 11.2 Y. and M/F ratio of 3/2 NK cells % is insignificantly decrease in patients with lymphoma also surgery and 3 courses of chemotherapy produce insignificant decrease in the NK cells % while radiotherapy produce significant decredse in the NK cells % (Table 2).
* The group of skin and soft tissue malignancies including 25 patients with median age 44 + 11.5 Y. and M/F ratio of 2.6/1. In this group NK cells% are insignificant decrease in patients with skin and soft tissue malignancies. Also surgery and 3 courses of chemotherapy produce insignificant decrease in the NK cells %. While radiotherapy produce significant in the NK cells % (Table 3).

GIT malignancies group (25 pt. with median age 50 + 12.29 an M/l- ratio ot 2.11) shows insignificant decrease in NK cells % in patients with GIT malignancies surgical treatment produce insignificant decrease in the NK cells % while radiotherapy

produce highly significant decrease in the NK cells % also 3 cources of 5FU or CCNU produce moderately significant in the NK cells % (Table 4).

* The group of GU malignancies including 25 pt. with median age 51 + 5.6 Y. and M/F ratio of 1 : 2 in this group NK cells % are insignificant decrease in patient with GU nlalignancies. Also surgical treatment and 5FU Adriamycin chemotherapy decrease it insignificantly. While Radiotherapy produce moderately significant decrease in the NK cells (Table 5).

Table 1 : Effects of cancer breast and various treatment modalities on NK cells %.

	Control	pre Treatment	Post Operative	Post Radiotherapy	Post Chemotherapy
Number	15	15	7	4	4
Mean NK %	16	14	13	12*	12*
S. D. ±	3.16	1.94	2.10	2.38	2.38
t-value		1.56	1.09	1.75	1.75
P-value		0.06	0.14	0.04	0.04

* Sifnificant.

Table 2 : Effects of lymphomat and various treatment modalities on NK cells %.

	Control	pre Treatment	Post Operative	Post Radiotherapy	Post Chemotherapy
Number	15	15	3	4	4
Mean NK %	16	15	15	12*	14*
S. D. ±	3.16	1.48	2.65	2.82	4.24
t-value		1.51	1.11	1.45	0.83
P-value		0.13	0.13	0.04	0.20

* Sifnificant.

Table 3 : Effects of skin and soft tissue mal malignancies and various treatment modalities on NK cells %.

	Control	pre Treatment	Post Operative	Post Radiotherapy	Post Chemotherapy
Number	15	15	10	2	3
Mean NK %	16	15.60	15	12*	13
S. D. ±	3.16	1.99	2.12	1.00	1.73
t-value		0.41	0.71	7.24	5.19
P-value		0.34	0.23	0.05	0.12

* = Sifnificant.

Table 4 : Effects of GIT malignancies and various treatment modalities on NK cells %.

	Control	pre Treatment	Post Operative	Post Radiotherapy	Post Chemotherapy
Number	15	15	10	2	3
Mean NK %	16	15.8	15	10***	11.67**
S. D. ±	3.16	2.77	3.66	2	3.69
t-value		0.18	0.62	2.89	1.99
P-value		0.42	0.26	0.01	0.03

**= Moderately Sifnificant.
*** = Highly Sifnificant.

Table 5 : Effects of GU malignancies and various treatment modalities on NK cells %.

	Control	pre Treatment	Post Operative	Post Radiotherapy	Post Chemotherapy
Number	15	15	10	2	2
Mean NK %	16	15	15	10***	14
S. D. ±	3.16	2.37	3.16	1	0
t-value		0.89	0.90	2.12	1.86
P-value		0.16	0.18	0.02	0.20

**= Moderately Sifnificant.

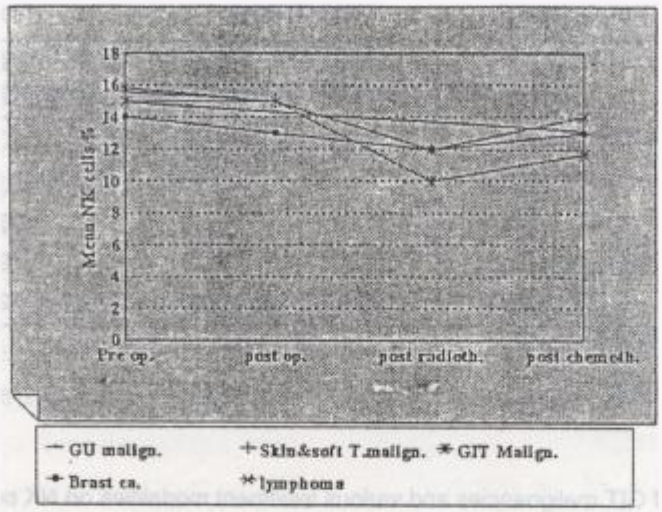

Fig. 1 : Effects of GU, skin & soft tissues tumours GIT malignancies, Breast cancer, lymphoma and various treatment modalities on NK cells %.

Discussion

The aim of this study is determination of NK cells % in cancer patients and its affection by various treatment modalities.

Our study found that the mean NK leu-lla cells% in normal control was 16 + 3 % of PBP. (Goh and Zarraloi, 1988) stated that NK cells comprise 14-15% of human peripheral blood lymphocytes.

In patients with cancer breast NK cells % are insignificantly decrease in comparison to control. Roitt et al. (1988) stated that NK cell activity is slightly decrease in early cases of cancer and as the tumour progresses much reduction in NK cell activity occurs. This depression may be due to either interaction of NK cells with tumour cells or the presence of suppressor T-cells (Miller, et al., 1991).

We also found that NK cells% insignificantly decrease in early post operative cases (13 + 2.1%) , also CMF chemotherapy produce insignificant decrease in the NK cells % on the other hand radiotherapy produces significant de-

crease in the NK cells %.

In patients with lymphoma NK cells % is insignificantly decrease (15 + 1.48%) in comparison to control (16 + 3.16%).

Surgery and chemotherapy produce insignificant decrease in the NK cells% while radiotherapy produce significant decrease in the NK cells %. As large dose of irradiation produce a profound decrease in the level of NK cells (Ghossein and Bosworth, 1988).

In patient with skin and soft tissue malignancies NK cells% are insgnificantly (15.6 + 1.99%) in comparison to control (16 + 3.16%). Surgery and chemotherapy produce insignificant decrease in the NK cells %. Roitt et al. (1986) reported that the effect of chemotherapy on NK activity varied with pretreatment NK status, patients with normal NK function prior to chemotherapy demonstrated a progressive decline in NK function throughout the post-treatment weekly assessment period. In contrast, chemotherapy appeared to potentiate NK activity in the peripheral blood of those patients who had significantly depressed NK function prior to chemotherapy. This effect may be due to chemotherapy, Induced suppressor cells capable of reducing NK function. On the other hand our study reported that radiotherapy produces significant decrease in the NK cells %.

In patient with GIT malignancies, our study found that NK cells % are insignificantly decreas in patients with GIT malignancies (15.8 + 2.77%) in comparison to control (16 + 3.16%) . Our study also found that surgery decrease it insignificantly this can be explained by the stress of anaesthesia and surgery which may stimulate the release of hormones including glucocorticoids, as well as the synthesis of acute phase reactants suppressor cells may also be stimulated in response to, the products of tissue necrosis, all these factors lead to decrease In the NK cells % (Jubert et al., 1983). On the other hand our study reported that radiotherapy produce highly significant decrease in the NK cells%, as NK

cells are among cells that undergo interphase death within hours of radiation (Goh and Zarraloi, 1988). Also SFU/CCNU produce moderately significant decrease in the NK cells% . As most cytotoxic drugs are immunosuppressive.

In cases with G.U. malignancies we found that NK cells are insignificantly decrease in patients with G.U. malignancies (15 + 2.37%) in comparison to control (16 + 3.16%) and NK activity in patients with ovarian malignancies was much lower than those of cancer cervix. Also the study reported that surgery and 5F.U./ Adriamycin chemotherapy decrease it insignificantly, as the NK activity ascends Nearly to normal level. After eradication of malignancies. While radiotherapy produce moderately significant decrease in the NK cells%.

Conclusion

* Nk cells % are insignificantly decrease in cancer patients in comparison to control.

* Surgical treatment and short courses of chemotherapy produce insignificant decrease in the NK cells %.

* Radiotherapy pruduce significant decrease in the NK ells %.

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