شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأفلام قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار

في درجة حرارة من ١٥-٢٥ مئوية ورطوبة نسبية من ٢٠-٤٠%

To be Kept away from Dust in Dry Cool place of 15-25- c and relative humidity 20-40%

بعض الوثائـــــــق الاصليـــــة تالفـــة

بالرسالة صفحات لم ترد بالاصل

In Vitro sensitivity profile of some new chemotherapeutic agents in bilharzial related bladder cancer

THESIS
Submitted in partial Fulfillment
For The Degree Of M.Sc.
In Zoology
Cytology, Histology and Genetics

By

Ayman Mohamed Metwally

National Cancer Institute
Cairo University

To
Zoology Department
Faculty Of Science
Cairo University

2000

APPROVAL SHEET

Title of the M. Sc. Thesis

In vitro sensitivity profile of some new chemotherapeutic agents in bilharzial related bladder cancer

Name of Candidate

Ayman Mohamed Metwally

Submitted to the faculty of Science,
Cairo University
Zoology Department

Supervision Committee

1)Prof. Dr. Mohamed Akmal Abd El – Rehiem El – Ghor .

2)Prof. Dr. Hussein Mostafa Khaled.

3)Prof. Dr. Mostafa Raafat Mahmoud.

Head of Zoology Department

Prof. Dr. Kamal S. Al – Badry

ACKNOWLEDGEMENT

To begin with, I feel always indebted to Allah the most kind and merciful.

For **Prof. Dr. Akmal Abd El-Rehim El-Ghor**, Prof. of genetics, Zoology Department, Cairo university, no words can satisfy and explain my deep feeling of gratitude for his help, suggestions and encouragement throughout the work.

My very special to **Prof. Dr. Hussein Mostafa Khaled,** Prof. Dr. in the National Cancer Institute, for his suggestions and valuable help in this work.

I would like to express my deepest gratitude and thanks to **Prof. Dr. Mostafa Rafaat Mahmoud**, Prof. Dr. in the National Cancer Institute, for his careful supervision and his advise.

ABSTRACT

The present study demonstrated the in vitro effect of gemcitabine, taxotere, navelbine and their combination against bilharzial related bladder cancer. Tumors were explanted using the three dimensional in vitro histoculture assay with the MTT end point. All drugs were tested at their peak plasma levels. No tumor sensitivity could be detected to any of the 28 samples tested for gemcitabine with an overall in vitro response of 0 %. Among 21 samples tested for taxotere only 3 samples showed in vitro sensitivity with an overall in vitro response rate 14.28 %. Navelbine has demonstrated in vitro activity in 2 samples among 17 tested samples with an overall in vitro response rate 11.76 %. Among 14 samples tested for simultaneous application of the 3 drugs, the sensitivity of the combination was demonstrated in 1 sample and the overall in vitro response rate was 7.14 %.

There was no significant correlation between the tumor percent reduction using the different treatment and any of the clinical parameters including age, sex bilharzial affection, pathologic grade, stage and lymph node status. By comparing the tumor percent reduction among the 4 treatment groups taxotere was significantly more effective in vitro than gemcitabine. Bilharzial related bladder cancer might be more sensitive in vitro to single agents that attack microtubules than those inhibit the DNA synthesis.

The three dimensional in vitro histoculture assay with the MTT end point is a suitable in vitro chemosensitivity test that can be used if applied by others for the evaluation of the in vitro effect of different anticancer drugs singly or in combination on the bilharzial related bladder cancer.

Table Of Contents

List Of Tables

List Of Figures

INTRODUCTION

&

AIM OF THE WORK

INTRODUCTION

Carcinoma of bilharzial bladder is the most common cancer among Egyptian patients accounting 32% of all malignant cases presenting at the National Cancer Institute, Cairo university ***(Sherif and Ibrahim, 1987).***

Radical cystectomy with urinary diversion is considered as the only curative modality so for available ***(El- Sebai, 1983)***. However, the overall 5 - year survival rates range only between 27%, and 39%. Also, about 25% of the cases at first presentation are advanced and not amenable to surgery.

These cases in addition to patients with non-resectable, recurrent and/or metastatic disease are potential candidates for chemotherapy.

Because bilharzial related bladder cancer is different in etiology, biology and response to chemotherapy when compared to that reported in Western countries, phase II clinical trials have been conducted since 1976 and aimed at screening various chemotherapeutic agents singly or in combination in patients with inoperable, metastatic, or recurrent bladder cancer. However, response rates and survival data are not yet satisfactory ***(Gad El–Mawla et. al., 1989).*** So, new ideas are still clearly needed to help in management of the most common cancer in Egypt.

At the same time, the perfection of a practical test to evaluate the efficacy of different antineoplastic drugs in the treatment of human cancer prior to the initiation of clinical chemotherapy has been an elusive goal for many investigators since the early 1950s. Recent clinical correlations of 60% accuracy for predicting a positive clinical response and 90% accuracy for predicting a lack of response to chemotherapeutic agents suggest promising clinical usefulness. There have been many attempts to design in vitro systems to determine drug response of tumors. The most widely used system is the clonogenic assay, adopted by ***Salmon et al. (1984).*** However,

the recent development of the collagen gel assay permitted its use for malignant tissue samples rather than tumor cell suspensions ***(Shimoyama et al., 1989).***

Aim of work

This work was designed to check the efficacy of some new chemotherapeutic agents against bilharzial related bladder cancer in vitro in an attempt to recommend their clinical application .