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HEAT SHOCK PROTEIN 27 IN LARYNGEAL SQUAMOUS CELL CANCER TREATMENT

Білок теплового шоку 27 при лікуванні плоскоклітинного раку гортані

Abstract

Heat shock protein 27 (HSP27) belongs to a family of ATP-independent chaperones and plays a fundamental role in cell physiology in various disease states, including cancer. So, it was found that serum HSP27 levels were significantly increased in patients with various tumors, but their significance in laryngeal carcinoma is not well defined.

Purpose of the study. Determination and comparison HSP27 serum levels at different stages of special treatment methods in laryngeal cancer patients.

Materials and methods. The studies were conducted in 31 patients of laryngeal cancer of T2–3 N0 M0 categories before treatment and at its various stages. The serum HSP27 levels analysis was carried out using the «ELISA» diagnostics test system by enzyme immunoassay.

Results. The serum HSP27 levels in patients before treatment and with various types of special treatment are statistically significantly higher than the control values. There was a decrease in serum HSP27 levels in patients after removal of the neoplasm and a slight increase in serum HSP27 levels after completion of radiation therapy.

Comparison of initial serum HSP27 values in patients with subsequent relapse of the disease with initial serum HSP27 levels in patients with positive treatment outcomes did not reveal statistically significant differences.

Conclusion. The serum HSP27 levels in laryngeal cancer patients are elevated and remain so at all treatment stages. Initial level of serum HSP27 cannot predict tumor recurrence.

Keywords: laryngeal cancer, HSP27.

Резюме

Білок теплового шоку 27 (HSP27) належить до сімейства АТФ-незалежних шаперонів і відіграє фундаментальну роль у фізіології клітин при різних захворюваннях, включаючи рак. Так, було встановлено, що рівень HSP27 у сироватці крові значно збільшувався у пацієнтів з різними пухлинами, але їх значення при раку гортані недостатньо визначено.

Мета дослідження. Визначення та порівняння рівня HSP27 у сироватці крові на різних етапах спеціальних методів лікування у хворих на рак гортані.

Матеріали та методи. Дослідження проводилися у 31 хворого на рак гортані категорії T2–3 N0 M0 до лікування та на різних його етапах. Аналіз рівнів HSP27 у сироватці крові проводили за допомогою тестової системи діагностики «ELISA» методом імуноферментного аналізу.

Результати. Рівень HSP27 у сироватці крові пацієнтів до лікування та при різних видах спеціального лікування статистично достовірно перевищує контрольні показники. Спостерігалось зниження рівня HSP27 у сироватці крові пацієнтів після видалення новоутворення та незначне підвищення рівня HSP27 у сироватці крові після завершення променевої терапії.

Порівняння початкових значень HSP27 у сироватці крові у пацієнтів з подальшим рецидивом захворювання із початковим рівнем HSP27 у сироватці крові пацієнтів із позитивними результатами лікування не виявило статистично значущих відмінностей.

Висновок. Рівень HSP27 у сироватці крові у хворих на рак гортані підвищений і залишається таким на всіх стадіях лікування. За початковими показниками HSP27 не можна передбачити рецидиви пухлини.

Ключові слова: рак гортані, HSP27.

INTRODUCTION

Heat shock proteins (HSPs) are a protein family produced in cells by stressors and their primary role is to maintain cellular homeostasis, promoting their (cells) survival. HSPs are classified based on their molecular weight and promote recognition of tumor cells by the immune system but at the same time HSPs are involved in the proliferation, differentiation, invasion and metastasis for tumor cells. Determined that HSP levels are elevated in most cancers, and overexpression of HSP indicates a negative or insufficient response to treatment and poor prognosis of survival [1–5]. So, levels of serum heat shock protein 27 (sHSP27) have been studied in numerous cancer types, e.g. esophageal, bladder, hepatocellular, gastrointestinal and colorectal carcinoma [6–10], but their potential relevance at treatment in patients with laryngeal carcinoma are not adequately sufficient defined [10–14].

PURPOSE OF THE STUDY

The HSP27 serum levels comparison at different stages of special treatment methods of laryngeal cancer patients.

MATERIALS AND METHODS

Studies were performed in patients with laryngeal cancer categories T2–3 N0 M0. Histological characteristics of neoplasms are keratinizing squamous cell cancer.

The patients were divided into next groups:

Group 1 – 31 patients before the start of treatment (initial data);

Group 2 – 22 patients – 2–3 days after surgery;

Group 3 – 18 patients which completion of combination treatment (surgery and postoperative radiation therapy – 40 Gy);

Group C – control group (12 patients).

The age of the patients ranged from 34 to 65 years. The control group consisted of practically healthy people of the same age.

The serum HSP27 levels analysis was carried out using the «ELISA» diagnostics test system (Sandwich-ELISA principle) by enzyme immunoassay.

Comparisons of the studied skewed variables (determined by the criterion of Kolmogorov-Smirnov's agreement), was carried out with using the Wald-Wolfowitz Runs Test and Wilcoxon Matched Pairs Test, with a significance level of 0,05. The analyzed data are presented as «median and interquartile interval»: Me (RQ = UQ–LQ). Statistical processing of the received data was made using computer programs of the STATISTICA package (Stat Soft Statistica v.7.0).

RESULTS AND DISCUSSION

The first stage of the study was a comparative analysis levels of sHSP27 in patients in the first and control groups (Group C), and then, sequentially in the control group with indicators in 2, 3th groups. On next stage we compared the values between of initial levels of sHSP27 (Group 1) with its indicators changes in patients at the various treatment stages (table 1).

Table 1

The serum HSP27 levels in control group and its indicators in patients with laryngeal cancer at special treatment

HSP27 (ng/ml)	Me (RQ = UQ–LQ)	Group C vs 1–3 Groups Wald-Wolfowitz Test	Group 1 vs 2, 3 Groups Wilcoxon Test
Group C (n = 12)	16,42 (18,42 – 14,18 = 3,62)	p-level*	p-level**
Group 1 (n = 31)	39,22 (44,29 – 35,43 = 8,86)	< 0,05	
Group 2 (n = 22)	36,55 (42,38 – 30,27 = 12,11)	< 0,05	0,367
Group 3 (n = 18)	38,33 (45,18 – 29,42 = 15,76)	< 0,05	0,372

Note: p-level* for Group C vs groups 1, 2, 3; p-level** for Group 1 vs groups 2, 3

The data presented in the table indicate an unconditional, more than twofold, increase in sHSP27 levels in patients before treatment, as well as at different stages and with various types of special treatment. Furthermore, statistically significant differences were no noted in the serum HSP27 levels at various stages of special

treatment, relative to the initial data (Group 1 vs groups 2, 3). At the same time, there was a slight (39,22 → 36,55 ng/ml; 6,8%), but a statistically significant decrease in sHSP27 levels in patients 2–3 days after removal of the neoplasm, and an increase in sHSP27 levels (≈ 37,9 ng/ml) in patients of 3th groups, can be explained by the

aggressive nature of radiation therapy.

During the observation period (about 2,5 years), in six patients were diagnosed with a relapse of the disease and else in one case a second primary neoplasm (lung cancer). However, while comparing the levels of sHSP27 with its initial values in these patients – 41,66 (44,18 – 36,67 = 7,51) and 35,95 (38,64 – 29,83 = 8,81), there was no statistically significant difference revealed ($p = 0,762$).

It should be noted that a comparison of sHSP27 values in patients of the first group with subsequent relapse of the disease with initial indicators of sHSP27 levels in patients with positive treatment

results did not reveal a statistically significant difference (41,66 (44,18 – 36,67 = 7,51) and 39,22 (44,29 – 35,43 = 8,86), $p = 0,623$).

CONCLUSION

1. The sHSP27 levels in laryngeal cancer patients are elevated and remain so at all treatment stages, which, obviously, can be explained by the aggressiveness of both surgical interventions and radiation therapy performed by the patient.

2. The sHSP27 level at relapsing tumors exceeds its initial values, but the magnitude of the latter cannot serve as a predictor of tumor recurrence.

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