EVALUATION OF THE EFFECT OF LOW MOLECULAR WEIGHT HEPARINS ON THE OUTCOMES OF CONCURRENT CHEMORADIO THERAPY FOR LOCALLY ADVANCED CERVICAL CANCER PATIENTS

Olga P Matylevich, MD, DSc, Ludmila V Mirilenko,
Oleg G Sukonko, MD, DSc, prof.

NN Alexandrov National Cancer Center of Belarus, a/g Lesnoy-2, Minsk, Belarus, 223040

Objectives: To investigate the efficacy of low molecular weight heparins (LMWH) on the outcomes of concurrent chemoradiotherapy for locally advanced cervical cancer patients.

Methods: 85 stage IIB-IVB locally advanced cervical cancer patients were treated at the Gynecologic Oncology Department in 2011-2013 years. Patients were randomized into two arms. The control patient arm received the conventional chemoradiotherapy course, in the study arm it was supplemented with LMWH.

Results: Hemorrhagic complications associated with the using of LMWH were not detected. The immediate results of chemoradiotherapy in the study and control groups were the same ($p = 1.0$): according to RECIST criteria 47% in each group were recorded in complete regressions, 42% in partial regressions, 11% in the stabilization of the disease, and the progression of the disease to the end treatment was not recorded in any of the studied groups. The 5-year cancer-specific survival of patients in the study arm was 68.2% (SE 7.9%), in the control arm it was 66.4% (SE 7.1%), $p=0.80$ (Figure 1). The 5-year overall survival was 63.3% (SE 8.1%) and 64.4% (SE 7.2%) respectively, $p=0.94$ (Figure 2). The 5-year progression-free survival was 63.3% (SE 8.1%) and 64.4% (SE 7.2%), respectively, $p=0.93$.

Conclusions: Thus, despite the theoretical data, as a result of a clinical study, the effect of using LMWH on the primary cure of a tumor has not been established. The analysis of long-term treatment outcomes found no effect of LMWH on the cancer-specific survival, overall survival and progression-free survival in locally advanced cervical cancer patients treated by concomitant chemoradiotherapy.

Figure 1: Adjusted survival patients in control and study arms

Figure 2: Overall survival of patients in control and study arms

REFERENCES

1. Lal I., Dittus K., Holmes C.E. Platelets, coagulation and fibrinolysis in breast cancer progression. *Breast Cancer Research*. 2013; 15: 207.
2. Y.W. van den Berg, S. Osanto, P.H. Reitsma, Versteeg H.H. The relationship between tissue factor and cancer progression: insights from bench and bedside. *Blood*. 2012; 119 (4): 924–932.
3. J.E. Bluff, N.J. Brown, M.W.R. Reed, Staton C.A. Tissue factor, angiogenesis and tumour progression. *Breast Cancer Research*. 2008; 10: 204–214.
4. Quinlan D.J., Mc Quinlan A., Eikelboom J.W. Low-molecular-weight heparin compared with intravenous unfractionated heparin for treatment of pulmonary embolism: a meta-analysis of randomized, controlled trials. *Ann. Intern. Med.* 2004; 140 (3): 175–183.
5. Castelli R., Porro F., Tarsia P. The heparins and cancer: review of clinical trials and biological properties. *Vasc. Med.* 2004; 9: 205–213.
6. Lazo-Langner, A., Goss, G.D., Spaans, J.N., and Rodger, M.A. The effect of low-molecular-weight heparin on cancer survival. A systematic review and meta-analysis of randomized trials. *J Thromb Haemost.* 2007; 5: 729–737.
7. Kuderer, N.M., Khorana, A.A., Lyman, G.H., and Francis, C.W. A meta-analysis and systematic review of the efficacy and safety of anticoagulants as cancer treatment: Impact on survival and bleeding complications. *Cancer*. 2007; 110: 1149–1161.
8. Falanga, A., Marchetti M. Heparin in tumor progression and metastatic dissemination. *Semin. Thromb. Hemost.* 2007; 33 (7): 688–694.
9. Sanford D., Naidu A., Alizadeh N., Lazo-Langner A. The effect of low molecular weight heparin on survival in cancer patients: an updated systematic review and meta-analysis of randomized trials. *J Thromb Haemost.* 2014; 12: 1076–1085.
10. Che D.H., Cao J.Y., Shang L.H., Man Y.C., Yu Y. The efficacy and safety of low-molecular-weight heparin use for cancer treatment: a meta-analysis. *Eur J Intern Med.* 2013; 24: 433–439.