Volume flow controlled targeted intra-arterial chemoinfusion for laryngeal cancer chemoradiotherapy

Poster No.: C-0645
Congress: ECR 2015
Type: Scientific Exhibit
Authors: M. S. Olshansky¹, N. A. Znatkowa¹, T. A. Mashkova¹, J. Konstantinova²;¹Voronezh/RU, ²Moscow/RU
Keywords: Outcomes, Haemodynamics / Flow dynamics, Drugs / Reactions, Chemoembolisation, Catheters, Arterial access, Catheter arteriography, Oncology, Interventional vascular, Head and neck
DOI: 10.1594/ecr2015/C-0645
Aims and objectives

The aim of this study was to evaluate effectiveness and safety of volume and flow controlled targeted intra-arterial (i.a.) procedure for locoregional laryngeal cancer treatment with low cisplatin dose then it usually applied in RADPLAT (RADiation and PLATinum) protocol. The RADPLAT protocol combining rapidly i.a. delivery of cisplatin to the tumor bulk with systemic neutralization by intra-venous (i.v.) sodium thiosulphate and concurrent radiotherapy may potentially be an alternative to surgery in selected patients with resectable tumor, allowing for preservation of organ and it function without compromising locoregional control and survival (1). This method based on the "decadose" effect of cisplatin described by KT Robbins et al (2). The intensity of this treatment is at the upper limit of human tolerance of acute toxicites. It may contribute to additional mortality due chemotherapy and further research into relevant factors and possibly reducing treatment intensity may be needed (3).

From one side some changing in delivering technique is sufficient to improve results. Delivery of chemotherapeutic agent based on classical RADPLAT technique well written bellow: "Transaxial placement of the micro-catheter is accomplished under fluoroscopic guidance and allows rapid intra-arterial infusion of cisplatin (150 mg/m2 over 3-5 minutes) with simultaneous i.v. sodium thiosulphate (9 g/m2 over 15-20 minutes, followed by 12 g/m2 over 6 hours). This allows the tumor bed to receive the maximum dose of cisplatin before thiosulphate, while the systemic organs receive protection by thiosulphate prior to cisplatin" (1).

Another point of view we describe as individual physiological approach to i.a. delivery of chemotherapeutic agent to the tumor. It may lead to possible reducing potential risk related to chemotherapy without compromising locoregional control and survival.
Methods and materials

The ability to deliver cisplatin with volume and flow rate controlled technique was examined in one center study. From December 2010 to December 2014 consecutive previously untreated 56 patients with stage III $T_3N_{0-1}M_0$ laryngeal cancer were enrolled in this study and all 56 (100%) patients were evaluated.

In all cases selective angiography of the right and left superior thyroid arteries with standard JR 5F catheter were carried out via right femoral approach. Then 5F catheter was placed in proximal segment of each superior thyroid artery (STA) to evaluate individual regional blood flow velocity rate in each patient. Nonionic contrast media was injected manually under fluoroscopy control and force applied to a syringe was assessed to avoid contrast medium reflux to non targeted vascular pools. Measured flow velocity rate in STA ranged from 0.3ml/s to 0.6ml/s, and mean was 0.45 ml/s.

It should be noted that 5F catheter occlude almost 2/3 of inner vascular lumen of STA (Fig.1). Theoretically it is clear that in case then infusion flow velocity is higher then blood flow velocity in STA almost all blood cells will be flashing from this vascular pool as it shown on (Fig.2).

Practically this fact was determined. It can be illustrated during infusion of 0.9% saline potassium chloride in STA with a flow velocity more then 0.75 ml/s (Fig.3).

White skin spots or figure as "a pale medusa" on the patients neck often appears after infusion of 3-4 ml of 0.9% potassium chloride solution in STA during this regime. It may be a good mark of targeted infusion in all part of region feeding from this STA. So it is not necessary to use micro-catheter to targeted delivery of cisplatin in all patients with locoregional laryngeal cancer.

Pulsating infusion of cisplatin concentrate 75mg in each STA was managed with the same volume and flow velocity rate as it was established individually in each patient during angiography. The duration of cisplatin injection was no less then 20 minutes in one STA. If one of STA was dominant 2/3 of total cisplatin dose was injected in this STA.

In all patients multi-fractional radiotherapy (1,1Gy/fraction/2xday, 5x weekly, 74-78Gy over 8 to 9 weeks) was started in 13-24 hours after i.a. chemotherapy. The same i.a. procedures were carried out in all patients then total radiation dose achieved 26-30Gy and 50Gy, respectively. The average follow-up time was 26 months.
**Fig. 1:** Then catheter JR 5F placed in STA it occlude almost 2/3 of inner vascular lumen.

© endovascular surgery and angiography, Voronezh State Medical Academy, Voronezh Regional Oncology Clinic - Voronezh/RU
Absence of blood flow in upper thyroid artery then intra-arterial infusion started

Volume flow rate of infusion \[
\geq \quad \text{Blood volume flow rate}
\]

ml/s

Fig. 2: In case then infusion flow velocity rate is higher then blood flow velocity rate in STA almost all blood cells washout from this vascular pool.

© endovascular surgery and angiography, Voronezh State Medical Academy, Voronezh Regional Oncology Clinic - Voronezh/RU
Results

The volume and flow controlled targeted i.a. procedure for locoregional laryngeal cancer treatment was safe and feasible at all patients. A mean dose of cisplatin concentrate was 75 mg/m$^2$. A white skin marks during procedure were observed in 54 (96%) patients (fig.3). In 2 patients without these marks micro-catheter technique was needed.

Adverse III stage toxic effects were observed in 4 (7.1%) patients (gastrointestinal toxicities in 3 patients and hematologic toxicities in 1 patient) and IV stage toxic effects were not observed. It should be noted that toxicities were relevant to duration of i.a. injection. In all cases it appears then injection time was about 20 minutes.

Simultaneous i.v. sodium thiosulphate infusion for systemic cisplatin neutralization was not conducted at all. One patient required a radiotherapy break because of severe mucositis.

The 1 and 2-year overall survival rates were 100% and 98.8%, with disease-free survival rates of 96.4% and 92.9%, respectively. Laryngectomy was carried out in two patients (3.6%) who had partial response.
Fig. 2: In case then infusion flow velocity rate is higher then blood flow velocity rate in STA almost all blood cells washout from this vascular pool.

© endovascular surgery and angiography, Voronezh State Medical Academy, Voronezh Regional Oncology Clinic - Voronezh/RU
Fig. 1: Then catheter JR 5F placed in STA it occlude almost 2/3 of inner vascular lumen.

© endovascular surgery and angiography, Voronezh State Medical Academy, Voronezh Regional Oncology Clinic - Voronezh/RU
Fig. 3: White skin spots or figure as "a pale medusa" on the patients neck often appears after infusion of potassium chloride solution in STA then infusion flow velocity rate is higher then blood flow velocity rate.

© endovascular surgery and angiography, Voronezh State Medical Academy, Voronezh Regional Oncology Clinic - Voronezh/RU
Conclusion

We believe this chemoradiation protocol is feasible and safe for all patients with locoregional laryngeal cancer. It appears high rates of loco-regional control and organ preservation with acceptable rate of treatment-related adverse effect. This treatment protocol probably is more safe than RADPLAT procedure.
References

