Current views on the treatment and prevention of toxic alopecia and phlebitis induced by chemotherapy in patients with breast cancer

LA Sivak, GA Gubareva, SA Lyalkin, N.M. Maidanevych, O.M. Aleksyk, K.S. Filonenko, M.Y. Klimanov, A.V. Askolskyy, H .B. Kasap, K.O. Ulyanchenko

National Cancer Institute, Kyiv

Summary: This article presents a literature review on the development, diagnosis and treatment of leather toxicity, and toxic phlebitis and ekstravazatsiy chemotherapy as a result of chemotherapy, given their experiences of studying these complications in patients with breast cancer. Revealed that local complications of chemotherapy are quite frequent (15%) and serious complication of treatment, the development of which can lead to reduced effectiveness of HT and requires active treatment and prevention.

Keywords: breast cancer, alopecia, toxic phlebitis, Extravasation of chemotherapy, chemotherapy.

Malignant tumors of the breast (ZPHZ) - the most common cancer among the female population. Most patients ZPHZ receiving chemotherapy (CT): adjuvant (after surgery), the common stages and unfavorable prognostic factors of neoadjuvant (preoperative) and palliative (in the case of metastatic lymph nodes and other organs). [1] Thus, CT receive more than 80% of patients ZPHZ.

Chemotherapy-induced alopecia occurs in 65 - 100% of patients. The intensity of hair loss depends on chemotherapy (CP) and CT circuits. Thus, the frequency of alopecia at monochemotherapy anthracycline antibiotics (doxorubicin) - 60 - 100%, alkylating agents (cyclophosphamide) - 60%, antimetabolites (fluorouracil) - 10 - 50%. The combination of several CPs are usually associated with a higher probability of alopecia [2]. 74% of women consider hair loss the most traumatic side effect of chemotherapy, 8% of them reject it for fear of losing hair. Alopecia can affect the self-perception of his own body, sexuality, forcing avoid communication and oppress the lives of patients [3, 4].

Alopecia is the result of direct cytotoxic effects of CP on the cells of hair follicles, which are divided. According to recent data [5] inclusion of various mechanisms of influence in different phases of the cell cycle determines the intensity of hair loss. Most alopecia - a temporary phenomenon, hair growth is restored within 3-6 months after completion of chemotherapy. However, the known permanent form of alopecia caused by chemotherapy HIGH with allogeneic bone marrow transplantation [6].

Researchers conducted some attempts prevention and treatment of complications. One of the most promising studied and almost only applicable to the present method is scalp cooling (hypothermia). But among the more than 50 studies, only 7 - randomized [7-13]. Some researchers [14, 15] reported an increased risk of metastasis in the scalp after cooling. The authors of another publication [16] reported the presence of contraindications to the use of this method in patients receiving chemotherapy, aimed at full recovery. Patients receiving this method of preventing alopecia noted discomfort during the procedure, and complain of headache.

Patients cancer hospitals usually receive numerous infusion, which often lead to fragility, mobility disorders and vascular catheterization difficulties vessels. Comorbidity peripheral veins, cachexia, changes in tissue elasticity after radiotherapy, secondary lymphedema also contribute to the high risk of

reverse extravasation of blood vessels [17]. Damage to blood vessels in cancer patients due to repeated intravenous (v / v) intervention, sometimes - not secure the infusion equipment (infusion system, needles, catheters), sometimes - too active manipulation of the catheter [17].

The risk of phlebitis and ekstravazatsiy toxic chemotherapy depends on the properties of solutions, osmolarity, and the presence of certain components of the solution (ethyl alcohol, polyethylene glycol).

Through the mechanism of action of cytostatic drugs question their extravasation is very important. Most of them belong to vezykantiv, ie substances that cause severe damage to tissues. They directly interact with the DNA of the cell, leading to a gradual dying healthy cells, resulting appearance ulcers. [18].

Occurrence of toxic chemotherapy phlebitis and ekstravazatsiy factor affects the patient, ie the presence of comorbidities, previous radiotherapy of the zone administration of chemotherapy and social features.

The use of certain medications promotes strengthening of local complications of chemotherapy through a mechanism of action.

The development ekstravazatsiy can also affect infusion rate, which must be selected in accordance bandwidth vein, total volume infusion, especially while entering several solutions [19]. Cytostatics should enter only experienced and competent nurse who understands the toxic effects of chemotherapy and regulations for emergency medical care. Infusion solution should be prepared only by the rules specified by the manufacturer. Quality work requires constant medical staff of his training, the establishment of appropriate rules of his work.

Toxic phlebitis developing in 12-15% of infusions. According to research conducted by S. Ikeda and sang. (2004), often toxic phlebitis develop following treatment with cytarabine, doxorubicin, epirubicin, dacarbazine and taxanes. The frequency of toxic phlebitis directly proportional to the number of infusions and chemotherapy concentration in solution [20].

Tactics ekstravazatsiy chemotherapy treatment depends on the individual course. Supervision may exercise specialists from a nurse to a plastic surgeon and anesthesiologist. Particular attention should be paid to pain relief and prevention of infections [21]. A separate part on the recommendations of North Trent Cancer Network is anesthesia, which is crucial for the patient. It enables observance and performance of all doctors appointments, positive attitude towards medical personnel actions by the patient, avoiding unnecessary stress to the body [22] ..

When extravasation drug group (see Table 1), treatment begins with the application of cold / heat (only vinkaalkaloyidiv) for 20 minutes 4 times a day for 3 days, avoiding direct contact with the skin, if the patient has local manifestations. So according to the TV. Goolsby and sang. (2006) Local abrupt cooling without other therapy has an efficiency of 89% in preventing ulceration [23]. Limb is elevated position within 48 hours, limb movements have to be careful. In the presence of local symptoms using 1% hydrocortisone ointment. Typically, the only necessary treatment. Medication support is always with extravasation of large amounts of fluid. In this case, according to the developed algorithms, treatment extravasation should be in accordance with the algorithm for treatment of chemotherapy extravasation group C.

For products group (see Table 1) should additionally apply medication. If the skin is intact (no vesicles) topical solution or cream application of dimethylsulfoxide (antidote for extravasation of doxorubicin, daunorubicin, mitomycin) or compresses it (with analgesics, corticosteroids) (plotted kystochkoyu) 4 times daily for 14 days. Leave the treated area is covered. If there are vesicles, DMSO is used [22].

TABLE 1. Classification of cytotoxic agents based on their potential damaging effect

Neutral

substances

(Group A): Irrytanty

(Group A): exfoliant

(Group B): Vezykanty

(Group C):

Asparaginase Carboplatin Cisplatin carmustine

Bleomycin Docetaxel Irinotecan Dakarbazyn

Kladrybin Tenypozyd Doxorubicin

Liposomal Doxorubicin

Epirubicin Cyclophosphamide Etoposide mitoxantrone

Cytarabine 5-Fluorouracil Oxaliplatin idarubicin

Fludarabine Methotrexate topotecan mitomycin

Gemcitabine Paclitaxel

Ifosfamide vinblastine

Melphalan Vinkristyn

Rituximab Vinorelbin

Thiotepa

A significant role is also given to the use of antidotes [22]. For group C necessary Injection of hyaluronidase S / C respectively pole compass around the affected area 128 OD units in 2 ml of 0.9% sodium chloride) for 14 days [24]. Sodium thiosulfate is recommended as an antidote to mehloretaminu, mustynu, cisplatin. Use 1.6 ml of 25% solution of preparatuiy numerous installations in and around the site extravasation (n / w and w / w) [17.

According to recent research by doksorubitsynovyh ulcers using local administration granulocyte-macrophage growth factor (GM-CSF). But the tactic is understudied and needs further study. This includes the use of pyridoxine hydrochloride for treatment ekstravazatsiy mitomycin [17]. Proved successful use of local administration of saline under resolution extravasation and to prevent ulceration [17].

Materials and methods. Studied the development of local complications of chemotherapy scheme in 130 patients ZPHZ, aged 25 to 75 years (median age 50 years). Used schemes FAC (cyclophosphamide, doxorubicin, fluorouracil), AT (doxorubicin, paclitaxel), TP (paclitaxel, cisplatin), VP (vinorelbin, cisplatin)

Each patient in terms of combined treatment was from 4 to 6 courses of chemotherapy scheme.

Take into account the clinical manifestations and results of laboratory research methods (sonographic examination of the damaged veins, surgical consultation). Assessed risk factors for toxic phlebitis and ekstravazatsiy. Local toxicity of chemotherapy was evaluated on a scale NCI-CNC V.4.0.

Results and discussion. All in all, 732 courses of chemotherapy. Of these, the scheme FAC - 496 courses (68%), SC - 92 courses (13%), TR - 106 (14%) and VP (5%) - 38 courses.

Figure 1. Distribution of cancer for varieties of courses of chemotherapy

In the study of toxic manifestations of PCT in patients ZPHZ revealed toxic effects of CP on the skin, which manifested itself in the form of alopecia of varying severity, which was observed in all patients with ZPHZ who underwent chemotherapy schemes FAC, AT, RT and in 45% of patients treated scheme VP.

This complication developed already at 7 and 14 days after the first course of chemotherapy. Alopecia and degree (CTC NCIC) developed in all 130 (100%) patients after a course of chemotherapy and the scheme FAC, second degree - in 34 (85%) after the second course of chemotherapy, III degree - in 6 (15%) after the second year and in 28 (71%) after the fourth course of chemotherapy. However, this complication does not affect the conduct of CT.

In order to prevent the development of alopecia ZPHZ 42 patients were given simple advice that included avoiding adverse chemical and physical effects on hair, short hair trimming or shaving. In 21 patient ZPHZ throughout the duration chemotherapy scheme was applied topically FAC minoxidil.

In 4 patients ZPHZ who completed chemotherapy scheme FAC (4-6 courses of chemotherapy), hair growth began to recover within 1 month after cessation of chemotherapy, and the rest - in 3-6 months.

Extravasation of chemotherapy reported in 4 patients (3%). Emergence ekstravazatsiy often occurred after 4-7th cycles of chemotherapy. In 2 of these patients develop this complication has led to a decrease in the intensity of chemotherapy by dose reduction or prolongation of the interval between courses. In 3 cases observed extravasation of doxorubicin in 1 - cyclophosphamide. In 3 patients reported extravasation degree, in 1 patient extravasation of chemotherapy followed by breach of the skin.

To treat the pain and used antihistamines, topical - 1% hydrocortisone ointment, while maintaining the integrity of the skin - applications 25-50% solution dimeksida and compresses it. The process of repair lasted an average of 76 days (from 40 to 156 days). In all patients, he completed a full recovery.

Development of toxic phlebitis was found in 16 patients: 8 patients phlebitis occurred after 4 courses of chemotherapy, 2 - after 5, 6 - after the first two courses. In 11 cases has been registered and the degree of toxicity, in the remaining 5 - second degree.

In Fig. 2 shows a case of toxic phlebitis second degree N. patient after 4 courses of chemotherapy scheme FAC.

Figure 2 - Manifestations of toxic phlebitis second degree patient on N.

In case of toxic phlebitis used conservative treatments. Treatment of toxic phlebitis were performed using non-steroidal anti-inflammatory drugs, antiplatelet agents, and analgesics. Locally applied heparin and ointments of NSAIDs. The process of repair lasted from 30 to 64 days (average - 41 days). Residual changes in the form of vein wall influx detected only when vinorelbinovyh phlebitis. In all cases of toxic phlebitis had no effect on the subsequent treatment of the underlying disease.

Thus, toxic phlebitis are less severe complication of chemotherapy than extravasation. The appearance of toxic phlebitis may occur after the 1st course of chemotherapy. The number of these complications increases with the number of cycles of chemotherapy. Drugs that often cause their occurrence is vinorelbin and doxorubicin. Moreover, the introduction vinorelbinu in 100% of cases leads to toxic phlebitis. Treating them as a whole, conservative. The emergence of toxic phlebitis had no effect on the subsequent treatment of the underlying disease.

Estravazatsiyi there is a serious complication that can lead to serious consequences, like violating the intensity of treatment of the underlying disease, and in injury to the patient. They require additional financial costs of treatment, care related professionals, leading to disruption of the quality of life of patients and the functioning of organs and systems.

Conclusions:

1. Determined that the most common manifestation leather toxicity chemotherapy regimens FAC, AT, TP, VP is alopecia, which does not require an additional medication.

2. Development of toxic phlebitis and ekstravazatsiy can lead to very serious consequences (ulceration of skin, muscle stricture, amputations), accompanied by severe pain, dysfunction of the affected area, affects the quality of life of patients and requires additional significant financial costs of treatment.

3. Compliance with the rules of prevention and appropriate treatment promptly initiated toxic complications to avoid their development and prevent further deepening degree of phlebitis and ekstravazatsiy toxic chemotherapy.

References

1. Клинические рекомендации. Онкология / под ред. В.И. Чиссова, С.Л. Дарьяловой. – М.: ГЭОТАР-Медиа, 2008. – С. 269-314.

2. Trueb R.M. Chemotherapy-induced alopecia // Semin. Cutan. Med. Surg. – 2009. – Vol. 28(1). – P. 11-14.
3. McGarvey E.L., Baum L.D., Pinkerton R.C. et al. Psychological sequelae and alopecia among women with cancer // Cancer Pract. – 2001. – Vol. 9(6) – P. 283-289.
4. Munstedt K., Manthey N., Sachsse S. et al. Changes in self-concept and body image during alopecia induced cancer chemotherapy // Support Care Cancer. – 1997. – Vol. 5(2). – P. 139-143.
5. Trueb R.M. Chemotherapy-induced anagen effluvium: diffuse or patterned? // Dermatology. – 2007. – Vol. 215(1) – P. 1-2.
6. Vowels M., Chan L.L., Giri N. et al. Factors affecting hair regrowth after bone marrow transplantation // Bone Marrow Transplant. – 1993. – Vol. 12(4). – P. 347-250.
7. Edelstyn G.A., MacDonald M., MacRae K.D. Doxorubicin-induced hair loss and possible modification by scalp cooling // Lancet. – 1997. – Vol. 2(8031). – P. 253-254.
8. Giaccone G., Di Giulio F., Morandini M.P. et al. Scalp hypothermia in the prevention of doxorubicin-induced hair loss // Cancer Nurs. – 1988. – Vol. 11(3). P. 170-173.
9. Kennedy M., Packard R., Grant M. et al. The effects of using Chemocap on occurrence of chemotherapy-induced alopecia // Oncol. Nurs. Forum. – 1983. – Vol. 10(1). – P. 19-24.
10. Macduff C., Mackenzie T., Hutcheon A. et al. The effectiveness of scalp cooling in preventing alopecia for patients receiving epirubicin and docetaxel // Eur. J. Cancer Care (Engl). – 2003. – Vol. 12(2). – P. 154-161
11. Parker R. The effectiveness of scalp hypothermia in preventing cyclophosphamide-induced alopecia // Oncol. Nurs. Forum. – 1987. – Vol. 14(6). – P. 49-53.

12. Ron I.G., Kalmus Y., Kalmus Z. et al. Scalp cooling in the prevention of alopecia in patients receiving depilating chemotherapy // Support Care Cancer. – 1997. – Vol. 5(2). – P. 136-138.
13. Satterwhite B., Zimm S. The use of scalp hypothermia in the prevention of doxorubicin-induced hair loss // Cancer. – 1984. – Vol. 54(1). – P. 34-37.
14. Witman G., Cadman E., Chen M. Misuse of scalp hypothermia // Cancer Treat. Rep. – 1981. – Vol. 65(5-6). – P. 507-508.
15. Forsberg S.A. Scalp cooling therapy and cytotoxic treatment // Lancet. – 2001. – Vol. 357(9262). – P. 1134.
16. Grevelman E.G., Breed W.P. Prevention of chemotherapy-induced hair loss by scalp cooling // Ann. Oncol. – 2005. – Vol. 16(3). – P. 352-358.
17. Wickham R, Engelking C, Sauerland C, Corbi D. Vesicant extravasation part II: Evidence-based management and continuing controversies. Oncol Nurs Forum. 2006 Nov 27;33(6):1143-50. Review.
18. Sauerland C, Engelking C, Wickham R, Corbi D. Vesicant extravasation part I: Mechanisms, pathogenesis, and nursing care to reduce risk. Oncol Nurs Forum. 2006 Nov 27;33(6):1134-41. Review.
19. Kagel EM, Rayan GM. Intravenous catheter complications in the hand and forearm. J Trauma 2004; 56:123-7.
20. Ikeda S, Douchi T, Nagata Y Effective prevention of chemotherapy—induced phlebitis by low-dose heparin: A prospective randomised trial. Ann Oncol, 2004 jun 16(7):942-45.
21. Mader I et al., "Extravasation of cytotoxic agents" Infect Control 2006; 34:308-12.
22. Extravasation guidlines North Trent Cancer Network Approved: 13.11.2008 To be reviewed by: Extravasation Sub-Group from North Trent Haemato-Oncology Nurse Group and the Pharmacist Group.
23. Goolsby TV, Lombardo FA. Extravasation of chemotherapeutic agents: prevention and treatment. Semin Oncol. 2006 Feb;33(1):139-43. Review.

24. Disa Joseph J., Chang Raymond R., Mucci Samuel J. and Nelson H. Goldberg Prevention of Adriamycin-Induced Full-Thickness Skin Loss Using Hyaluronidase Infiltration. New Engl J Med. Vol 15, 2005; 987-993.