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HYPOVOLEMIA TREATMENT IN SURGICAL PATIENTS USING COMBINED SOLUTION GECOTON® IN INFUSION THERAPY

Summary. *The paper deals with a problem of optimizing infusion therapy including combined polyelectrolyte, colloid osmotic solution of a new generation (Gecoton®) for hypovolemia treatment in the dehydrated patients after surgery. The study demonstrated that Gecoton® used at a dose of 400 ml for 3 days combined with crystalloid solutions in surgical patients with grade 2 dehydration allowed to treat hypovolemia, normalize hemodynamic parameters and reduce dehydration symptoms on the 2nd day.*
Key words: *hypovolemia, dehydration, infusion therapy, Gecoton®.*

The infusion-transfusion therapy with crystalloid and colloid solutions is commonly used in the emergency medicine. Many authors note the positive properties of colloids, for example, hydroxyethyl-starch solution (HES) 130/0.42 reduces the capillary leakage [1]. The use of HES in severe injuries was associated with an increase in intravascular volume more than with the use of crystalloids [2]. At the same time, T.P. Simon et al. consider that HES solutions are more effective in maintaining the volume of circulating plasma (VCP), mean blood pressure, systemic and tissue oxygenation, as compared to colloids. HES infusion results in specific coagulation disorders involving changes in blood viscosity and rheological properties, as well as in activating the fibrinolysis. HES inhibit the damaging effect of activated neutrophils depending on the degree of inflammatory response [3]. In this case, HES 130/0.42 had a sure lesser effect on coagulation than HES 200/0.5, especially on APTT and von Willebrand factor [4]. There is information that balanced saline solutions are preferable for volumetric replenishment of VCP. At the same time, however, there is insufficient evidence of their compared effectiveness and safety [5].

Recently, however, adverse results of the use of HES, particularly, in septic shock patients were reported [6]. death, acute kidney injury and the need for renal

The use of a 6% HES solution (130/0.42) compared to Ringer's acetate is associated with increased mortality within 90 days (p = 0.03) and a 35% increase in the need for renal replacement therapy [10]. However, there is no evidence of adverse effects on the kidneys and increased mortality (p = 0.079) with the post-operative use of tetrastarch [11]. In addition, and there is no sufficient data on such adverse effects for surgical patients and hypovolemic patients. The CRISTAL study showed that colloid treatment of patients with hypovolemia ensures a reduction of 90-day lethality compared with the use of crystalloids. Colloids are traditionally used to increase the intravascular volume, but now there is a need for proof of their clinical relevance [12]. Therefore, the Pharmacological Risk Assessment Committee (PRAC) of the European Medical Agency (EMA), taking into account the opinion of Jean-Louis Vincent and Daniel de Backer, in 2013 recommended the use of HES solutions for the treatment of hypovolemia secondary to acute blood loss. The established advantage of colloids in respect of viability needs further research. At the same time, the advantages of crystalloids as compared to colloids cannot be clearly asserted. It is obvious that there is a need for further research to show the positive

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features of hyperosmolar solutions and HES solutions. The advantages of replenishment of extravascular fluid deficiency with crystalloids are known, as well as their insufficient effect to correct the intravascular deficiency [14]. Therefore, the infusion therapy (volemic resuscitation) includes a combined, polyelectrolyte, colloid hyper-osmotic solution of a new generation (Gecoton®); active ingredients: 100 ml of the solution contains 5000 mg of hydroxyethylstarch 130/0.4, 5000 mg of xylitol, 1500 mg of sodium lactate, 800 mg of sodium chloride, 30 mg of potassium chloride, 20 mg of calcium chloride, 10 mg of magnesium chloride; excipients: water for injection.

Objective of the study: Optimization of infusion therapy including combined, poly-electrolyte, colloid-hyperosmotic solution of a new generation Gecoton®, manufactured by Yuria-Pharm LLC, for the treatment of hypovolemia in the dehydrated patients after surgery.

Criteria for inclusion: treatment of hypovolemia in surgical patients; male and female aged 35-60 years; patient's consent to participate in the study.

Exclusion criteria: hypersensitivity to active ingredients; overhydration, hypervolemia; renal failure (creatinine > 177 μmol/l); hypocoagulation, hypofibrinogenemia, thrombocytopenia; oedema, degree III hypertensive disease; cardiovascular decompensation, chronic liver disease.

Materials and methods

37 patients were examined and treated.

Clinical examination of the patients included a systemic haemodynamics assessment: heart rate (HR, min-1), mean blood pressure (MBP, mm Hg), central venous pressure (CVP, mm Hg). The degree of dehydration was assessed by P.I. Shelestiuk tissue hydration test (STHT, min) [13]. Hemostasis was assessed using the following parameters: prothrombin index (PTI, %), platelet count (x109/l), fibrinogen (g/l), international normalised ratio (INR, units), activated partial thromboplastin time (APTT, sec). Renal function was assessed by daily diuresis and blood creatinine (μmol/l). Total protein (g/l), amilase (un.), hemoglobin (g/l), hematocrit (l/l) values were assessed. The dynamics of the parameters is reflected in stages: 1st stage — baseline values and the first administration of Gecoton® solution in the composition of the infusion therapy; 2nd stage — after 24 hours, second administration of Gecoton® solution; 3rd stage — 48 hours, third use of Gecoton® solution; 4th stage — 72 hours; 5th stage — 96 hours from the beginning of the study. Statistical processing has been done by analysis of variance using Student t-test and Statistica 6.1 software.

Results and Discussion

In table 1, haemodynamic parameters are presented at various stages of the study. The patients were dehydrated and showed signs of hypovolemia on admission: thirst, dryness of mucosa and skin cover, reduction of subcutaneous tissue tone and daily diuresis (743.5 ± 61.0 ml). MBP was recorded within the reference values of 91.9 ± 13.2 mm Hg; tachycardia — HR 91.7 ± 20.1 per minute, average CVP was 0.92 ± 1.08 mm Hg.

Laboratory parameters are presented in table 2. A decrease in hematocrit to 31.9 ± 7.6 l/l is observed, which is not characteristic of dehydration and is associated with post-hemorrhagic anaemia in patients — hemoglobin was 104.7 ± 10.9 g/l; therefore, the use of hematocrit to esti-mate the extent of dehydration in the study is not appropriate. For this purpose, P.I. Shelestiuk tissue hydration test was used in which the time-frame was shortened to 22.4 ± 11.7 minutes, corresponding to the 2nd degree of dehydra-tion (estimated volume of crystalloid infusion by P.I. Shelestiuk to eliminate dehydration is 5.6 — 8.4 liters per day).

Prior to the administration of the osmotic solution, the patients were infused 400 ml of Ringer's solution. Afterwards, Gecoton® was administered daily for 3 days at a recommended daily dose of 400 ml at the rate of 200 ml/h followed by crystalloid infusion within 24 h. By the end of Day 1, an average of 2433.33 ± 238.80 ml of crystalloids were administered. In this case, MBP was within the reference values of 93.9 ± 9.9 mm Hg, HR dropped to 84.9 ± 12.9 bpm, CVP increased to 3.99 ± 2.60 mm Hg ($p < 0.05$), daily diuresis increased and reached an average of 2051.6 ± 108.0 ml, which indicated the elimination of hypovolemia manifestations. STHT time increased to 30.6 ± 18.6 minutes, which corresponds to the 1st degree of dehydration.

Table 1. Hemodynamic parameters of patients per stage

Parameter \ Stages	1st	2nd	3rd	4th	5th
HR, min^{-1}	91,7 ± 20,1	84,9 ± 12,9	84,6 ± 19,5*	80,8 ± 10,2*	75,8 ± 9,7*
MBP, mm Hg	91,9 ± 13,2	93,9 ± 9,9	94,6 ± 8,2	97,9 ± 8,5	97,8 ± 8,1
CVP, mm Hg	0,92 ± 1,08	3,99 ± 2,16*	5,11 ± 2,79*	4,40 ± 3,14*	7,16 ± 2,88*

Note: hereinafter: * – p < 0.05, significant differences compared to the baseline.

Table 2. Clinical laboratory parameters of patients per stage

Parameter \ Stages	1st	2nd	3rd	4th	5th
Hemoglobin, g/l	104,7 ± 10,9	94,5 ± 7,5	92,8 ± 7,7	92,9 ± 4,9	93,4 ± 6,5
Hematocrit, l/l	31,9 ± 7,6	28,9 ± 7,6	28,9 ± 6,9	27,1 ± 5,1	28,2 ± 5,2
Total protein, g/l	56,6 ± 10,8	55,1 ± 10,4	52,2 ± 5,8	55,1 ± 6,2	56,2 ± 6,6
Urea, μmol/l	4,3 ± 1,9	4,60 ± 2,19	4,6 ± 3,1	4,2 ± 2,6	4,4 ± 2,3
Creatinine, μmol/l	110,3 ± 46,1	116,2 ± 47,6	115,4 ± 39,9	117,2 ± 32,1	117,3 ± 32,2
Diuresis, ml	743,5 ± 61,0	2051,6 ± 108,0	2089,6 ± 83,0	2246,6 ± 93,0	2154,7 ± 97,0
Amilase, Un.	19,1 ± 6,9	20,1 ± 8,4	22,7 ± 12,5	18,1 ± 7,5	21,2 ± 8,1
STHT, min	22,4 ± 11,7	30,6 ± 18,6	38,3 ± 17,0	43,9 ± 27,5*	48,6 ± 23,6*

Table 3. Hemostasis parameters of patients per stage

Parameter \ Stages	1st	2nd	3rd	4th	5th
Platelets, × 109/l	234,4 ± 135,0	294,4 ± 115,3	229,9 ± 127,4	260,1 ± 118,4	253,1 ± 119,1
INR	1,09 ± 0,34	1,22 ± 0,37	1,12 ± 0,48	1,23 ± 0,29	1,20 ± 0,32
PTI, %	88,5 ± 9,3	83,5 ± 12,4	93,6 ± 22,1	87,7 ± 20,5	90,1 ± 21,4
APTT, sec	39,6 ± 6,4	37,6 ± 7,7	35,3 ± 2,8	31,3 ± 1,8	34,8 ± 3,6
Fibrinogen, g/l	3,8 ± 1,3	3,9 ± 1,2	4,2 ± 1,0	4,5 ± 1,4	4,3 ± 1,6

On Day 2, an average of 2014.29 ± 114.20 ml of crystalloids were administered. MBP was 94.6 ± 8.2 mm Hg, HR did not change (84.6 ± 19.5 per minute) compared to the previous step, CVP increased to an average of 5.11 ± 2.79 mm Hg ($p < 0.05$), the daily diuresis did not decrease — 2089.6 ± 83.0 ml, and the STHT time increased to an average of 38.3 ± 17.0 minutes ($p < 0.05$), which indicated the elimination of dehydration manifestations.

On Day 3, the volume of crystalloids was reduced to 1455.0 ± 155.6 ml due to the possibility of enteral replenishment of the liquid by patients. In this case, MBP was 97.9 ± 8.5 mm Hg, HR reduced to 80.8 ± 10.2 per minute ($p < 0.05$), the average CVP was 4.40 ± 3.14 mm Hg ($p < 0.05$), daily diuresis was sufficient (2246.6 ± 93.0 ml), the STHT time increased to 43.9 ± 27.5 minutes ($p < 0.05$).

On the 4th day, the examined parameters were within the reference range: MBP — 97.8 ± 8.1 mm Hg, HR — 75.8 ± 9.7 per minute ($p < 0.05$), CVP — 7.16 ± 2.88 mm Hg ($p < 0.05$), daily diuresis — 2154.7 ± 97.0 ml and STHT time — 48.6 ± 23.6 min ($p < 0.05$).

Changes in the concentrations of creatinine and amylase at the study stages are not significant, indicating that the kidney and pancreas function were not impaired. No substitutive renal therapy was required. In table 3, certain parameters characterizing homeostasis are presented at various stages of the study. At the 1st stage, no changes were detected in the laboratory parameters of hemostasis, which were within the reference values except fibrinogen, which was 3.8 ± 1.3 g/l. At the 5th stage, the number of platelets was (253.1 ± 119.1) • 109/l, INR — 1.20 ± 0.32, PTI — 90.1 ± 21.4%, fibrinogen — 4.3 ± 1.6 g/l, but these differences were not significant. There also was an insignificant decrease in APTT (34.8 ± 13.6 s).

Conclusions

1. The use of Gecoton® solution at a dose of 400 ml for 3 days in combination with crystalloids in surgical patients with degree 2 dehydration allowed to treat hypovolemia, to stabilize the hemodynamic values and eliminate the symptoms of dehydration on the second day.

2. No changes in the hemostasis, as well as renal function were established, which indicates the safety of Gecoton® solution.

3. Thus, the above data show that the use of combined infusion solution Gecoton® is suitable for the perioperative infusion therapy of surgical patients.

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КОРЕКЦІЯ ГІПОВОЛЕМІЇ У ХІРУРГІЧНИХ ХВОРИХ ІЗ ВИКОРИСТАННЯМ КОМБІНОВАНОГО РОЗЧИНУ В КОМПЛЕКСІ ІНФУЗІЙНОЇ ТЕРАПІЇ

Резюме. У статті розглядається питання оптимізації інфузійної терапії з включенням комбінованого, поліелектролітного, колоїдно-гіперосмолярного розчину нового покоління (Гекотон®) для корекції гіповолемії при зневодненні в хірургічних хворих. Проведене дослідження показало, що використання розчину Гекотон® в дозі 400 мл упродовж 3 діб у комбінації з кристалоїдами в хірургічних хворих з 2-м ступенем дегідратації дозволило коригувати гіповолемію, стабілізувати гемодинамічні показники й усунути ознаки зневоднення на другу добу.

Ключові слова: гіповолемія, зневоднення, інфузійна терапія, Гекотон®.

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HYPOVOLEMIA TREATMENT IN SURGICAL PATIENTS USING COMBINED SOLUTION IN INFUSION THERAPY

Summary. The paper deals with a problem of optimizing of infusion therapy included combined multiple electrolyte, colloid osmotic solution of a new generation (Gecoton®) for hypovolemia treatment the dehydrated patients after surgery. The study demonstrated that Gecoton® used 400 ml during 3 days combined with crystalloid solutions in surgical patients with 2 grade dehydration allowed treat hypovolemia, normalize hemodynamic parameters and reduce dehydration symptoms on the 2nd day.

Key words: hypovolemia, dehydration, infusion therapy, Gecoton.