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PATHOGENETIC FEATURES THE LATE CURRENT MANIFESTATIONS IN AN EXPERIMENT TRAUMATIC DISEASE AND ITS CORRECTION TIOTRYAZOLIN

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Abstract

The late manifestations of traumatic disease (14-28 days) accompanied by a significant breach of the morphofunctional state of liver development phase of exacerbation in 21 days. Application Thiotriazoline during stimulation of endogenous processes injured body (7 to 14 days) accompanied by a significant decrease in the intensity of the liver tissue lipid peroxidation, cytolysis, swelling organ, improve the functioning of microsomal enzyme systems, essentially eliminates the acute phase after 21 days of post-traumatic period, reduces the signs of inflammation after 28 days.

Keywords: experimental polytrauma, traumatic disease, liver, lipid peroxidation, cytolysis, bile formation.

Introduction. Injuries belongs to the current challenges. In its structure prevalent in recent years and combines multiple severe lesions, accompanied by the development of traumatic disease and are characterized by significant mortality [5]. In the pathogenesis of traumatic disease distinguished from acute reactions to trauma (up to 2 days), during the early manifestations (14 days), during late manifestations and rehabilitation period [8]. Today conclusively proven that these periods inherent oscillatory character of the phases of the acute symptoms subsided

and the pathological process [1, 6, 7]. The largest deviations are observed through 1-7 and 21-28 days after causing injury, regardless of its origin, which is accompanied by increased animal deaths. However, there is an assumption that the subsiding of the pathological process in 7 to 14 days indicates the involvement of endogenous mechanisms sanogenesis that targeted us the possibility of preventing deterioration injury desease during its later held by acting on its key mechanisms during this time period.

The writings of V. Yale et al (2011) based on performance evaluation of endogenous intoxication Thiotriazoline shown to be effective during the early manifestations of trauma [4]. This drug is a classic antioxidant, reduces the need for tissue oxygen has a pronounced anabolic capacity capable normalize metabolism and enhance energy supply of tissues [9]. Poly-functional drug makes it a promising means of stimulating mechanisms sanogenesis in polytrauma.

Objective: To find out pathogenic characteristics traumatic disease during its later manifestations and explore possible prevention of organ failure by stimulating endogenous treated mechanisms of thiotriazoline.

Materials and methods. Experiments were performed on 108 nonlinear white male rats weighs 200-220 g animals were divided into 3 groups: control (12 animals) and two experimental (in 448 animals). In the first experimental group multiple trauma modeled and simulated treatment by intraperitoneal administration of saline equivalent to the basic therapeutic drug dose, the second experimental group modeled multiple trauma and perform correction by intraperitoneal administration Thiotriazoline of "Arterium" (Ukraine) as a 2.5 % solution in dose of 9.07 $mg \cdot kg^{-1}$, which corresponded to an average daily dose of 100 mg for adults [10]. Drugs were administered once at the same time in the morning. Course administration was 7 days: 7 to 14 days.

Multiple trauma modeled by applying shock dosed on each thigh specially designed device. Shot Power was established empirically and allowed in a single application to obtain closed fracture of the femur. The procedure is performed

under thiopental sodium anesthesia (40 mg kg). Research key indicators performed after 14, 21 and 28 days after application of multiple trauma, which corresponded to the late manifestations of traumatic disease [6].

The criterion of systemic impact on the internal organs become morpho-functional state of the liver, which is sensitive to any negative environmental effects [2].

In the first series of experiments investigated bile formation liver function [11]. Under thiopental-sodium anesthesia (60 mg per kilogram of body weight) of animals the cateter is put in common bile duct and bile sampling was carried out for 1 hr. As determined by the concentration of total bile, bile acids, total bilirubin and direct its fraction. On the basis of the results expected degree conjugation bilirubin. Then the animals were sacrificed by total bleeding from the heart.

In the second series of experiments, the animals blood, which established the activity of alanine aminotransferase (ALT) standardized method for Biochemical Humalyzer 2000 and liver tissue, which determined the content of malondialdehyde (MDA) [3]. All animals spent weighing and counting of liver mass ratio.

All experiments were performed in compliance with the general rules and regulations of the European Convention for the Protection of Vertebrate Animals used for research and other scientific purposes (Strasbourg, 1986), the general ethical principles of animal experiments (Kyiv, 2001), the Law of Ukraine "About protection of animal Conduct" (2006).

The resulting digital material analysed statistically. Significance differences between experimental and control groups are assessed using the program STATISTICA 10.0 ("StatSoft, Inc.", USA).

Results and discussion. As can be seen from the table.1, after 14 days of content in liver tissue MDA is more than 2 times the control level ($p < 0,001$) and remained at the same level after 21 and 28 days ($p <0.001$). Thus, in the late period of trauma in the liver observed high intensity of lipid peroxidation. A characteristic

feature of its dynamics consistently high content of secondary products from 14 to 28 days.

On the background of Thiotriazoline within 14 days of the contents of MDA in liver tissue was significantly lower than in untreated animals - by 51,2 % ($p<0,001$), but higher than the level of control animals by 21,8 % ($p<0,05$). Later in 21 days and in the background the introduction Thiotriazoline was marked increase of MDA - by 25,6 % ($p<0,001$), but this value was statistically significantly lower than in untreated animals – 42,4 % ($p<0,001$). After 28 days in the treated animals studied parameters decreased lipid peroxidation, but not statistically significantly different from the value recorded in the previous observation period. In these experimental conditions, the level of MDA in the liver tissue was 43,9 % lower than in animals that did not conduct correction ($p<0,001$).

Thus, during treatment Thiotriazoline significantly decreased the intensity of lipid peroxidation in liver tissue in all periods of observation period late manifestations traumatic disease.

Table 1 - Indicators of morpho-functional state of the liver in the dynamics of the late manifestations of trauma and its correction thiotriazoline (M±m)

Index	Conditions of experiment	Control	Multiple trauma		
			14 th day	21 th day	28 th day
MDA, mkmoll·kg^{-1}	Not treated	0,202± 0,016	0,504± 0,016***	0,537± 0,024***	0,508± 0,027***
	Thiotriazoline		0,246± 0,009*	0,309± 0,011***	0,285± 0,010***
p			<0,001	<0,001	<0,001
ALT, od·l^{-1}	Not treated	51,31± 2,34	184,7± 4,2***	199,1± 3,1***	125,6± 13,6***
	Thiotriazoline		61,12± 2,35*	101,8± 5,35***	89,91± 5,56***
p			<0,001	<0,001	<0,001
Total bile acids, g·l^{-1}	Not treated	6,44± 0,24	6,32± 0,15	5,41± 0,17*	5,92± 0,22$^{\#}$
	Thiotriazoline		7,08±	6,23±	6,42±

			0,13*	0,22	0,19
p			<0,05	<0,05	>0,05
Degree of bilirubine conjugated, %	Not treated	66,13± 3,35	58,13± 1,55#	51,45± 2,25**	60,47± 3,80
	Thiotriazoline		61,00± 2,40	60,63± 1,76	65,19± 3,26
p			>0,05	<0,01	>0,05
Index of liver weight, %	Not treated	2,499± 0,024	3,359± 0,046***	3,300± 0,096***	3,097± 0,061***
	Thiotriazoline		3,263± 0,046***	3,175± 0,052***	2,816± 0,049***
p			>0,05	>0,05	<0,01

1. n - number of observations (identical in groups for each indicator)

2. * # - significance of differences in relation to the control group

(* - p<0,05; ** - p<0,01; *** - p<0,001; # - p<0,10);

3. p - significance of differences between treated and untreated by thiotriazoline animals.

After 14 days of post-traumatic period ALT activity in serum was 3,6 times greater than the control level (p<0,001). Further, the value of this indicator grew and is up 7,8 % from the previous observation period (p<0,05) and after 28 days significantly reduced: at 32,0 % with respect to the value of 14 days of observation (p<0,001) and by 36.9% with respect to the same level 21 days of observation (p<0,001). Despite the substantial decline, the value of the indicator in 28 days continued statistically significantly exceed the level of control (2,4 times, p<0,001).

In terms of the dynamics Thiotriazoline deviations of the studied parameters was significantly lower. Within 14 days of serum ALT activity was only 19,1 % greater than the control level (p<0,05), which was 3,6 times lower than for a group of untreated animals (p<0,001). After 21 days the activity of serum ALT increased (by 66,6 % with respect to the previous observation period) and at 28 days - reduced, not reaching the level of 14 days. In these terms the value of the studied

parameters was statistically significantly lower than in untreated animals (by 48,9 and 28,4 %, p<0,001).

Therefore, the use Thiotriazoline accompanied by lower levels of marker enzyme cytolysis of hepatocytes, since the 14 day experiment. Subsequently, after 21 days it increased, decreased after 28 days, while remaining significantly lower than in untreated animals.

In trauma in 14 days total content of bile, bile acids hardly differed from the control level. After 21 days the value of the studied parameters decreased and became lower by 14,4 % on the preliminary observation period (p<0,05) and 16,0 % less than the control level (p<0,05). After 28 days the value of this index increased, but did not differ from the previous period, but intended to lower the value on the control (8,1 %, p<0,10).

Application thiotriazoline helped to preserve the level of total bile acid level control, and in 14 days the value of the studied parameters was 9,9 % greater than the control level (p<0,05). During this period, and in 21 days the content of total bile, bile acid-treated animals was statistically significantly higher, than in untreated (by 12,0 and 15,2 %, p<0,05).

Thus, after 14 days of total content of bile, bile acids were not significantly different from the level of control animals. After 21 days of total bile acids decreases and becomes lower than the control and previous term. After 28 days - moderately increases, I reaching level 14 days. Treatment Thiotriazoline accompanied by an increase in the content of total bile acids, in bile after 14 and 21 days.

Degree conjugative bile bilirubin after 14 days of post-traumatic period in relation to the control group intended to lower values (12,1 %, p<0,10), in 21 days was significantly decreased (21,2 %, p<0,01) and returned to normal after 28 days. Under the influence of the degree of conjugation of bilirubin treatment at all time period of the late period of trauma was at the level of the control group (p<0,05), and after 21 days was statistically significantly higher level of untreated animals

(17,8%, $p<0,01$).

Thus, the use of thiotriazoline contributes severe violations of protection conjugation, indirect bilirubin, which is most pronounced at 21 hours.

After 14 and 21 days after trauma simulation been reported significantly higher liver mass index in relation to the control group - by 34,4 and 32,0 % ($p<0,001$). After 28 days of post-traumatic period, this figure decreased: on the preliminary observation period by 6,2 % ($p<0,05$), but did not reach the level of the control group and remained statistically significantly higher (26,4 %, $p<0,001$).

Application of thiotriazoline not affect the value of the index liver weight after 14 and 21 days of the experiment in relation to the control group and a group of untreated rats. After 28 days, the figure was significantly decreased by 11,3 % from the previous observation period ($p<0,01$), but did not reach the level of control and at 12,7 % was higher ($p<0,001$). At the time of observation it became 9,1 % less than in the untreated rats was statistically significant ($p<0,01$).

Thus, in the later period of trauma observed mass index increased liver of experimental animals, which reduced only by tiotryazoline after 28 days.

Our results indicate that the period of late manifestation traumatic disease accompanied by a significant breach of the morphofunctional state of liver shows increased levels of lipid peroxidation, events cytolysis, decreased activity of hepatic microsomes, where the common bile acids are synthesized and is conjugative bilirubin, and elevated liver mass ratio, indicating that the inflammation and swelling of the body. After 21 days comes exacerbation of the pathological process observed by several authors after playing traumatic disease using other models [1, 6, 7]. This points to the universality of the detected phase flow traumatic disease.

Application of thiotriazoline accompanied by a pronounced positive effect on almost all studied parameters, essentially eliminates the acute phase after 21 days of post-traumatic period, reduces signs of inflammation after 28 days.

So use of thiotriazoline a phase activation of endogenous mechanisms

against sanogenesis traumatic disease is a promising field for the prevention of organ failure and stimulation of restorative processes in the body injured, requiring further in-depth research.

Conclusions. 1. Period late manifestations traumatic disease (14-28 days) accompanied by a significant breach of the morphofunctional state of the liver, manifested elevated levels of lipid peroxidation, events cytolysis, decreased activity of hepatic microsomes, and increased liver mass ratio and the development of acute phase in 21 days.

2. Application of thiotriazoline during stimulation of endogenous processes injured body (7 to 14 days) accompanied by a significant decrease in the intensity of the liver tissue lipid peroxidation, cytolysis, swelling organ, improve the functioning of microsomal enzyme systems, essentially eliminates the acute phase after 21 days of post-traumatic period, reduces the signs of inflammation after 28 days.

References

1. Борис Р. М. Динаміка показників пероксидного окиснення ліпідів у період ранніх і пізніх проявів травматичної хвороби за умов експериментальної краніо-скелетної травми та її корекції клітинною терапією / Р. М. Борис, А. І. Гоженко, А. А. Гудима // Клінічна та експериментальна патологія. – 2013. – Т. XII, № 2 (44). – С. 31–34.

2. Гудима А.А., Сван О.Б., Дацко Т.В. Структурний стан печінки після механічної травми шкірних покривів і його корекція ліофілізованими ксеродермо-трансплантатами // Зб. матер конф.: “Досвід і проблеми застосування сучасних морфологічних методів досліджень органів і тканин у нормі та при діагностиці патологічних процесів”. – Тернопіль: Укрмедкнига, 2007. – С. 32-34.

3. Доклінічні дослідження лікарських засобів : методичні рекомендації; за ред. чл.-кор. АМН України О. В. Стефанова. – К. : Авіценна, 2001. – 528 с.

4. Ельский В. Н. Использование тиотриазолина в раннем периоде травматической болезни / В. Н. Ельский, С. В. Пищулина, М. С. Кишеня и др. // Питання експериментальної та клінічної медицини. – 2011. – Вип. 15, Т. 1. – С. 110-112.

5. Заруцький Я. Л. Об’єктивізація оцінки тяжкості та хірургічної тактики при поєднаних пошкодженнях / Я. Л. Заруцький, Л. М. Анкін, В. М. Денисенко [та ін.] // Проблеми військової охорони здоров’я : збірник наукових праць. — 2006. — Вип. 17. — С. 127–135.

6. Козак Д. В. Особливості показників пероксидного окиснення ліпідів в динаміці раннього і пізнього періоду політравми / Д. В. Козак // Актуальні проблеми транспортної медицини. – 2012. – № 3. – С. 103-106.

7. Козак Д. В. Вплив політравми на динаміку раннього апоптозу тканинних лімфоцитів / Д. В. Козак, А. А. Гудима // Медична хімія. – 2012. – Т. 14, № 3. – С. 86-88.

8. Куршакова И. В. Типовые патологические процессы, как патогенетическая основа формирования неврологических ослонений травматической болезни / И. В. Куршакова // Актуальные вопросы сочетанной шокогенной травмы и скорой помощи: Сб. науч. тр., посвят. 70-летию НИИ скорой помощи им. И. И. Джанелидзе и 20-ти летию отдела (клиник) сочетанной травмы /Санкт-Петербург. НИИ скорой помощи им. И. И. Джанелидзе. – Спб, 2002. – С. 181-185.

9. Мазур И. А. Тиотриазолин: фармакологические аспекты и клиническое применение / И. А. Мазур, Н. А. Волошин, И. С. Чекман и др.— Запорожье, Львов: НАУТІЛУС, 2005.— 156 с

10. Мазур И. А. Клиническое применение тиотриазолина в терапии / И. А. Мазур, Н. А. Волошин, И. С. Чекман и др. // Сучасна гастроентерологія. – 2006. – № 1. – С. 71–74.

11. Методические рекомендации по экспериментальному изучению желчегонной, холеспазмолитической, холелитиазной и гнепатопротекторной активности новых лекарственных веществ / С.М. Дроговоз, С.И. Сальникова, Н.П. Скакун, В.В. Слышков. – К. :ФКМЗ Украины, 1994. – 46 с.

1. Boris R.M. Dynamics of lipid peroxidation during early and late manifestations of traumatic disease in experimental cranio-skeletal injuries and correction of cellular therapy / R.N. Boris, A.I. Gozhenko, A.A. Hudyma // The clinical and exneexperimental pathology. - 2013. - T. XII, № 2 (44). - P. 31-34.

2. Hudyma A.A. The structural condition of the liver after mechanical injury of the skin and its correction lyophilized xerodermo-transplants / A.A. Hudyma, A.B. Swan, T.V. Dacko // Coll. Mater Conf. "Experience and Problems of the application of modern methods of morphological studies of organs and tissues in normal and pathological processes in the diagnosis." - Kiev: Ukrmedknyha, 2007. - P. 32-34.

3. Preclinical studies of drugs: guidance, ed. Corr. AMS of Ukraine A. Stefanova. - K.: Avicenna, 2001. - 528 p.

4. Yelskiy V.N. Using tyotryazoline in the early period traumatic disease / V.N. Yelskiy, S.V. Pyschulyna, M.S. Kishenya et al // Problems of experimental and clinical medicine. - 2011. - Issue. 15, T. 1. - P. 110-112.

5. Zarutsky Y.L. Evaluation and assessment of severity of surgical tactics in combined damage / Y.L. Zarutsky, L.M. Anqing, V.M. Denysenko [et al.] // Problems of Military Health Care: Collected works. - 2006. - Issue. 17. - P. 127-135.

6. Kozak D. Features of indicators first oxide oxidation of lipids in the dynamics of early and late period of trauma / D.V. Kozak // Actual problems of transport medicine. - 2012. - № 3. - P. 103-106.

7. Kozak D. Effect of multiplay trauma on the dynamics of early apoptotic lymphocytes fabric / D. Kozak, A. Hudyma // Medicinal chemistry. - 2012. - T. 14, № 3. - P. 86-88.

8. Kurshakova I.V. Typical pathological processes, such as the pathogenetic basis for the formation of traumatic neurological disease / I.V. Kurshakova // Topical issues of trauma shock genicity and ambulance: Sat. scientific. tr., initiations. 70th anniversary NII ambulance by I. Janelidze and 20 year anniversary Division (Clinical) trauma / Saint Petersburg. NII ambulance by I. Janelidze. - St. Petersburg, 2002. - P. 181-185.

9. Mazur I.A. Tyotryazolyn: pharmacological aspects and clinical application / I.A. Mazur, N.A. Voloshin, I.S. Chekman etc. - Zaporozhye, Lvov: NAUTILUS, 2005. - 156 p.

10. Mazur I.A. Clinical application of tyotryazolin in therapy / I.A. Mazur, N.A. Voloshin, I.S. Chekman et al / / Current Gastroenterology. - 2006. - № 1. - P. 71-74.

11. Guidelines on the experimental study choleretic, holespazmoliticheskoy, holelitiaznoy and gnepatoprotektornoy activity of new drugs / S.M. Drogovoz, S.I. Salnikova, N.P. Skakun, V. Slushkov. - K. FKMZ Ukraine, 1994. - 46 p.