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Anti-death immunoglobulin treatment and prophylactic effect in experiment

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Here is studied anti death immunoglobulin treatment and prophylactic effect in conditions of experimental model. The immunoglobulin was taken from discharge endotoxin of dying and dead patients' blood plasma by means of intact mice immunization. It was confirmed that immunoglobulin made by this method effectively protects intact white mice during damage with endotoxin also knowns as "death factor". Here are enlisted opinions about the usage of the immunoglobulin in clinic and perspectives of it.

Key Words. "Factor Death", Immunoglobulin,Polypeptide,Critical condition.

Introduction. The conception of anti death immunoglobulin is based on the discovery of "death factor" in blood plasma of dead and dying patients. The latest was discharged by means of spectrophotometer, immunoadsorption and electrophoresis made on polyacrylamide gel in aids of "becman" apparatus in past 80s. (Z. Kheladze, 1985). The study discovered 13-14cd molecular mass polypeptide (Z. Kheladze,1990-92). When injected it in an organism of intact mice (0,01g/kg) caused immediate death of the animal. Besides, this polypeptide caused suppression of T-lymphocyte function that saves immune memory, blocked reduplication process of DNA in one direction primary and secondary mixed cultures of lymphocytes. (Z. Kheladze, and others, 1990). There was supposed that genes of the polypeptide also known as "death factor" is transferred from organism to organism after birth and is activated directly before death. (Z. Kheladze, Zv. Kheladze, 2012). Also there was created the mean for diagnostics of this endotoxin and was confirmed in blood of critical patients and experimental animals. In addition to that, "background" concentrations of this endotoxin of lethal nature was discovered in blood of healthy person and animal. (Z. Kheladze and others, 1998). There was constructed immunoglobulin and anatoxin against this polypeptide (Z. Kheladze, 2005). This work refers to the study of antilethal immunoglobulin effect in conditions of experimental model.

Materials and Methods. for receiving anti death immunoglobulin, in peritoneal cavity of 15-25g intact mice on 8th, 16th, 24th, 30th, 31th and 31th days 0,004g/ml "death factor" immunosorbent was injected. Also endotoxin was received by the original method (Z. Kheladze, 1985). On 34th day of immunization in peritoneal

cavity Tg-180" cells were injected. After revelation of ascyte liquid that mostly happened on 44th day, from peritoneal cavity 5-25 ml immune ascyte liquid was received supernatant of which was conducted in sephadex "G-200" column. The concentration of received immunoglobulin was carried out by means of "Amicon" firm "P-50" filter. Mollecular mass of this immunoglobulin was 150-160cd, and constanta of sedimentation-7,1S. respiration of animals became frequent, they scratched mugs and after unreasonable running in cage they mice stopped in a one place and then tone and clone types of convulsions begun. Described clinical revelations were typical and lasted 5-30 minutes. When the effectiveness of immunoglobulin was tested, immediately after the first signs of endotoxin poisoning immunoglobulin was injected at different doses. For determination of prophylactic characteristics of immunoglobulin in organism of white mice before 24 hours of anatoxin injection immunoglobulin was injected in advance. In purpose of defining immunoglobulin protecting ability terms in white mice after injection of immunoglobulin prophylactic dose in first 40 days endotoxin lethal dose was also injected-0,01g/kg. Results was discussed according to the number of dead mice. **Results and discussion**. The study was conducted in 6 groups with intact white mice; in each group we had 29 animals. In peritoneum of each animal endotoxin lethal dose was injected 0,01g/kg during 3 minutes after endotoxin injection that was in accordance with the revelation of the first signs of "death factor" poisoning. In the peritoneum of the same animals immunoglobulin was injected. In peritoneum of the first group animals 0,001g/kg immunoglobulin was injected, in second-0,002, in third-0,003, in fourth-0,004, in fifth-0,005, the sixth group was controlled and in place of immunoglobulin, physiological solution that dissolves it was injected in peritoneal cavity. This resulted in a death of all animals in sixth group after injection of endotoxin. Also, 9 of them died in 1th, in 2nd group4 and in 3rd 1. In fourth and fifth groups all of animals survived, but in animals from 4th and 5th groups had signs of endotoxin influence. This indicates that effective dose of prevention of endotoxin lethal dose is immunoglobulin 0,004g/kg dose.

In order to determine immunoglobulin preventive effect animals were divided into 12 groups and each included 10 animals; in peritoneum of them endotoxin lethal dose was injected-0,01g/kg. Among them in the first group-0,001g/kg, in second-0,002g/kg, in third-0,003g/kg, in fourth-0,004g/kg, in fifth-0,005g/kg, in sixth-0,006g/kg, in seventh-0,007g/kg, in eighth-0,008g/kg, in ninth-0,009g/kg,in tenth-0,01g/kg, and in eleventh-0,02g/kg. the final group was controlled and in peritoneum dissolving physiological solution was injected. This resulted in death of animals in twelfth, in addition to that all animals died in the first, second and third groups, in the fourth and fifth groups 9 of them died and in the eighth and

ninth-1 only. In tenth and eleventh groups all animals survived. These data shows that immunoglobulin protecting dose from endotoxin lethal dose is 0,001g/kg and it must be injected before 24 hours of entering endotoxin in an organism.
Also there were determined deadlines of immunoglobulin protection for animals after damage of from "death factor. For this purpose, animals where distributed into ten groups each group contained 10 animals. In peritoneum cavity of all of them 0,004 g/kg immunoglobulin was injected and after this, in their organism lethal dose (0,01g/kg) of endotoxin was injected: in the first group-on 2nd day, in 2- on 3rd day, in 3rd-on 5th day, in 4th-10th days, in 5th-on 15th day, in 6th-on 20th day, in 7th-on 25th day, in 8th-on 30th day, in 9th- on 35th day, and in final group on 40th day. This resulted in death of all of them in 10th, 9th and 8th groups. In 7th group 6 of animals died, in 6th and 5th-4 and 2 animals did not survive. In 4th, 3rd, 2nd and 1st groups all of them overcome toxic effects. This indicates that anti-death immunoglobulin protecting effect lasts during the first fifteen days after the injection of it. It is considerable that in case of the future elaborations the immunoglobulin produced by this way can be used for delaying of death and life prolongation.

Conclusion. Therapeutic doses of anti death immunoglobulin effectively protect intact white mice from lethal doses of "death factor". This immunoglobulin also has preventive peculiarities and protects animals from endotoxin lethal doses; this effect of immunoglobulin is preserved in an organism during the first fifteen days.

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ზ. ხელაძე, ზვ. ხელაძე, სიკვდილის საწინააღმდეგო იმუნოგლობულინის სამკურნალო და პროფილაქტიკური ეფექტის სესწავლა ექსპერიმენტში. კრიტიკული მედიცინის ინსტიტუტი,თბილისი,საქართველო

სიკვდილის საწინააღმდეგო იმუნოგლობულინი მიღებული იქნა თეთრი თაგვების ენდოტოქსინის შემცველი იმუნოსორბენტით იმუნიზაციის მეშვეობით. მიღებული იმუნოგლობულინის მოლეკულური მასა იყო 150-160კდ.ხოლო სედიმენტაციის კონსტანტა - 7,1S..აღნიშნული იმუნოგლობულინის პრევენციული და სამკურნალო ეფექტი შემოწმებული იქნა ინტაქტურ თეთრ თაგვებში ბიოტესტირების მეთოდით.სახელდობრ,სამკურნალო ეფექტი შესწავლისას .თითოეულ ცხიველში შეყვანილი იყო ენდოტოქსინის სასიკვდილო დოზა,.ამ უკანასკნელის შეყვანიდან 1-3 წუთის შემდეგ კი ხდებოდა იმუნოგლობულინის შეყვანა სხვადასხვა დოზით.იმუნოგლობულინის პროფილაქტიკური დოზის დადგენის მიზნით კი თეთრი თაგვების ორგანიზმში წინასწარ შეჰყავდათ სხვადასხვა დოზით იმუნოგლობულინი,ხოლო 24 საათის შემდეგ ლეტალური დოზით შეყვანილი იყო ენდოტოქსინი.იმუნოგლობულინის დამცველობითი უნარის ვადების დადგენის მიზნით კი თეთრი თაგვების ცალკეულ ჯგუფებში იმუნოგლობულინის საპროფილაქტიკო დოზის წინასწარ შეყვანის შემდეგ პირველიდან 40 დღის განმავლობაში შეჰყავდათ ენდოტოქსინის ლეტალური დოზა.შედეგებზე მსჯელობდნენ დახოცილი თაგვების რაოდენობის მიხედვით. დაგენილი იქნა სიკვდილის საწინააღმდეგო იმუნოგლობულინის დადებით სამკურნალო და პროფილაქტიკური ეფექტი ექსპერიმენტში.