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CLINICAL CASE OF SEVERE POISONING WITH PARACETAMOL IN A CHILD

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ABSTRACT. Paracetamol poisoning is an urgent problem in toxicology due to a significant increase in the number of cases worldwide, and the use of paracetamol for suicidal purposes in many countries occupies a leading position in the structure of drug suicides. ***The aim of the work*** is to review a clinical case of paracetamol poisoning. ***Materials and methods:*** paracetamol poisoning in a 17-year-old child at a dose of 600 mg/kg. Intensive care: antidote N-acetylcysteine, hepatoprotection ademetionine, ultrahemodiafiltration, transfusion of fresh frozen plasma. A feature of this case is not only liver damage, but also kidney damage. Intensive care is aimed at cleansing the body of hepatolysis products and uremic toxins. It was possible to avoid hepatocellular damage requiring liver transplantation and renal damage requiring chronic hemodialysis.

KEYWORDS: *paracetamol, poisoning, children*

КЛИНИЧЕСКИЙ СЛУЧАЙ ТЯЖЕЛОГО ОТРАВЛЕНИЯ ПАРАЦЕТАМОЛОМ У РЕБЕНКА

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РЕЗЮМЕ. В настоящее время отравление парацетамолом является актуальной проблемой токсикологии в связи со значительным увеличением числа случаев во всем мире, а применение парацетамола в суицидальных целях во многих странах занимает лидирующие позиции в структуре медикаментозных сиуцидов. ***Цель работы*** – обзор клинического случая отравления парацетамолом. ***Материалы и методы:*** отравление парацетамолом у ребенка 17 лет в дозе 600 мг/кг. Интенсивная терапия: антидот N-ацетилцистеин, гепатопротекция адеметионин, ультрагемодиафильтрация, трансфузия свежезамороженной плазмы. Особенностью данного случая является не только поражение печени, но и почек. Интенсивная терапия направлена на очищение организма от продуктов гепатолиза и уремических токсинов. Удалось избежать необратимого печеночно-клеточного повреждения, требующего трансплантации печени, и необратимого почечного повреждения, требующего проведения хронического гемодиализа.

КЛЮЧЕВЫЕ СЛОВА: *парацетамол, отравление, дети*

INTRODUCTION

Paracetamol is one of the most widely used drugs worldwide for its analgesic and antipyretic properties and is generally safe when taken in the recommended therapeutic dose.

Reports of paracetamol poisoning are frequent and have been studied in many countries. The epidemiological significance of paracetamol poisoning is due to the widespread use and wide availability of the drug. Paracetamol is used as an analgesic and antipyretic. In the Russian Federation (RF) traditionally has the greatest use in children's practice, but in recent years due to the introduction of new dosage forms has become more widely used in adults. For example, the use of paracetamol in oncology is included in the standards of treatment of chronic pain, it is also used in therapy and rheumatology, and in surgical practice, including in combination with opioid analgesics [1].

Paracetamol poisoning is currently an urgent problem of toxicology due to a significant increase in the number of cases worldwide. Paracetamol poisoning in the USA and Australia is the most common cause of severe acute liver injury requiring transplantation [2]. In European countries, this figure averages 20%. In Ireland it is 52%, in Great Britain it is 28%, in France it is 18%, in the Netherlands it is 8%, and in Italy it is 1% [1]. In the Russian Federation, according to the data of 2008, the specific weight of paracetamol poisonings was only 0.67% among all poisonings, but in recent years has increased significantly due to the emergence in the domestic pharmaceutical market a large number of different dosage forms containing paracetamol, including long-acting, under different trade names [3]. At the same time, up to 60% of overdoses were also deliberate self-poisoning.

It should be noted that the use of paracetamol for suicidal purposes in many countries takes the leading position in the structure of medication suicides: in the UK – 44.9%, in New Zealand – 37.6%, in Ireland – 30%, in Canada – 30%, in Australia – 28%, in the USA – 10.9% [3].

The toxic dose of paracetamol is 7.5 g in adults and 150 mg/kg in children [4]. A number of authors point out that hepatotoxic effect is possible already when taking the drug at a dose of 4–5 g in adults or 125 mg/kg in children with concomitant liver diseases, constant intake of drugs, especially those that are inducers of cytochrome P450 (barbiturates, isoniazid, rifampicin, diphenin, etc.), dietary supplements, anorexia, etc. [5].

The toxicity of paracetamol is related to the action of its active metabolite N-acetyl-p-benzoquinonimine (NAPQI) formed by the cytochrome P450 system in the liver. Formed in small amounts, it is detoxified by reduced glutathione (GSH). When a massive dose of paracetamol is taken, GSH is consumed and its regeneration step is limited by cysteine stores. As a result, NAPQI forms covalent bonds with macromolecules of hepatocyte membranes, activating free-radical processes and leading to hepatocyte necrosis [6].

The antidote is N-acetylcysteine, which reduces the toxic effects of NAPQI by restoring cysteine reserves.

AIM

Review of a clinical case of paracetamol poisoning at a dose of 600 mg/kg.

CLINICAL CASE

A 17-year-old child was undergoing treatment in the anesthesiology and resuscitation department of the Children's Republican Clinical Hospital of Ulan-Ude.

The girl was admitted to the hospital for emergency indications. From the anamnesis it is known that she drank 60 tablets of paracetamol 500 mg for suicidal purposes, the next day she was bothered by nausea and vomiting, she sought medical help 37.5 hours after taking the drug. Thus, the taken dose of paracetamol amounted to 30 g (600 mg/kg).

There were complaints of nausea, weakness, lethargy, abdominal pain. Consciousness was clear. Skin was pale pink, clean, warm. Breathing was independent, adequate. Hemodynamics was compensated, with a tendency to hypotension. Heart tones were muffled, rhythmic. Heart rate (HR) was 83 per minute. Blood pressure (BP) was 104/59 mm Hg. The abdomen was of normal shape, soft, not swollen, accessible to deep palpation, moderately painful at palpation in the upper parts, more on the right side. The liver was on the edge of the rib arch. Diuresis was preserved, urine was light yellow.

Laboratory data at the time of admission: Leukocytosis/neutrophilosis (14.9/12.1×10^9/L), elevation of alanine and asparagine transaminases of 1713 U/L and 1039 U/L, respectively, hyperbilirubinemia up to 83.1 μm/L, elevation of lactate dehydrogenase up to 10505 U/L, gamma-glutamyltransferase — 50 U/L, expressed hypocoagulation on coagulogram (activated partial thromboplastin time (APTT) — 30.8 s, fibrinogen — 4.315 g/l, prothrombin time — 27.9 s, thrombin time — 16.1 s, prothrombin index — 19.9%, international normalized ratio (INR) — 2.94).

On admission, toxic liver damage, proceeding by the type of acute hepatitis, liver-cell failure was noted. Potential hepatotoxicity can be assessed by plasma concentration of paracetamol using the Ramek–Mathew 150 nomogram [7]. In our case, the concentration of paracetamol was not determined due to the lack of necessary equipment. The severity of liver damage was assessed by the level of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and INR [7].

Starting intensive therapy.

1. Infusion therapy according to the formula 4:2:1 = 2615.0 ml/day. Polyionic crystalloid solutions and solutions containing meglumine sodium succinate were used.

2. Antidote therapy — Acetylcysteine 150 mg/kg.

3. Enterosorbent Enterosgel per os.

4. Hepatoprotector Ademetionine 400 mg × 2 times daily intravenously.

5. Proton pump inhibitors: Omeprazole 40 mg × × 2 times a day intravenously.

Taking into account the negative dynamics during the first day in the form of increasing hepatic cellular insufficiency, the consilium decided to conduct a session of continuous venous-venous ultrahemodiafiltration with parameters: dialysate flow 2000 ml/h, substrate flow 2000 ml/h, blood flow 100 ml/min,

Table 1. Biochemical blood parameters

Таблица 1. Биохимические показатели крови

Показатель / Parameter	**При поступлении / On admission**	**1-е сутки / day**	**2-е сутки / day**	**3-и сутки / day**	**4-е сутки / day**	**5-е сутки / day**	**6-е сутки / day**
Билирубин, мкмоль/л / Bilirubin, μmol/l	83,1	63	78,3	72,8	54,9	18	18,6
АСТ, ЕД/л / AST, U/l	1039	2154	4900	2076	321	102,6	255
АЛТ, ЕД/л / ALT, U/l	1713	2745	2370	6684	3099	1843	1520
Общий белок, г/л / Total protein, g/l	67,6	57	55,9	51,9	52,2	40	49
Глюкоза, ммоль/л / Glucose, mmol/l	6,9	3,8	10,8	4,5	4,1	4,0	4,89
Лактатдегидрогеназа, ЕД/л / Lactate dehydrogenase, U/l	10505	400	42	1176	–	402	367
Креатинфосфокиназа, ЕД/л / Creatine phosphokinase, U/l	89	125	150	75	–	69	80
Международное нормализованное отношение / International normalized ratio	2,94	5,5	3,72	1,8	1,4	1,19	1,15
Активированное частичное тромбопластиновое время, с / Activated partial thromboplastin time, s	30,8	49,3	36,3	27,6	25,5	25,7	–
Фибриноген, г/л / Fibrinogen, g/l	4,31	1,1	1,14	1,19	1,5	1,8	–
Протромбиновое время, с / Prothrombin time, s	27,9	50,6	34,8	17,6	12	11,6	–
Тромбиновое время, с / Thrombin time, s	16,1	21,3	24,7	23,9	25,8	19	–
Протромбиновый индекс, % / Prothrombin index, %	19,9	9,3	14,8	36,7	68,4	74,4	–

Table 2. Renal function indicators

Таблица 2. Показатели функции почек

Показатель / Parameter	При поступлении / On admission	1-е сутки/ day	2-е сутки/ day	3-и сутки/ day	4-е сутки/ day	5-е сутки/ day	6-е сутки/ day
Диурез, мл/кг/ч / Diuresis, ml/kg/h	сохранен	0,2	0,15	0,3	0,3	1,1	2,6
Мочевина, ммоль/л / Urea, mmol/l	5,4	4,63	3,0	4,2	3,8	9,09	3,55
Креатинин, мкмоль/л / Creatinine, μmol/l	81,4	135	124	100	246	428	84

ultrafiltration 30 ml/h. The levels of alanine and asparagine transaminases increased 2745 U/L and 2154 U/L, respectively.

During the first 24 hours there was an increase in renal failure, decrease in diuresis to 0.2 ml/kg per hour with urea and creatinine levels remaining in the area of normal values. A session of continuous veno-venous ultrahemodiafiltration was continued. Taking into account oliguria, renal ultrasound data (decreased blood flow rate in the right kidney), the ultrafiltration rate was stepwise increased from 70.0 to 200.0 ml/kg per hour. Furosemide was prescribed.

Table 1 shows the dynamics of blood biochemical parameters during the first six days of treatment in the intensive care unit (ICU).

Antidote therapy with acetylcysteine (ACC) was performed according to the Clinical Recommendations (protocol) for emergency medical care in acute poisoning in children according to a 21-hour scheme in three stages: Stage 1 — saturating dose of ACC in the first 60 minutes (150 mg/kg); Stage 2 — maintenance dose of 50 mg/kg for 4 hours; Stage 3 — 100 mg/kg for 16 hours. When blood levels of ALT and AST were found to be elevated more than 2-fold again, intravenous administration of ACC was continued according to the 21-hour protocol [8]. The risk of liver failure increases when acetylcysteine therapy is started later than 10 hours from the toxic dose, and administration of acetylcysteine later than 24 hours from the time of poisoning is unable to prevent liver damage, but implemented from the 36th hour from poisoning can limit the severity of toxic hepatitis [9]. It should also be noted that the use of acetylcysteine is appropriate even in late stages in all poisonings characterized by liver damage [10].

By the end of the first day after admission to the hospital, oliguria was noted in the child. Table 2 shows renal function parameters during the first six days of treatment in ICU.

At renal ultrasound, blood flow velocity indices in the renal artery trunk, interlobular and arch arteries were within normal limits (to the lower limit of normal) on both sides. Moderate decrease in blood flow in segmental arteries on both sides with increased peripheral resistance index on the right side.

Ultrahemodiafiltration was canceled on the fifth day, diuresis was restored, urea and creatinine levels normalized on the sixth day.

Despite the absence of clinically pronounced hemorrhagic syndrome, three transfusions of quarantined fresh frozen plasma were performed in the first three days on the basis of laboratory confirmation of hemostasis disorders (Table 1).

Partial enteral nutrition was started from the second day of treatment in the ICU with gradual expansion to the full volume by the fourth day (table No. 5).

In the hospital the child underwent the following instrumental examinations: ultrasound of the abdominal cavity and urinary system (separately with Doppler study of the renal vessels), electrocardiography, magnetic resonance imaging of the abdomen, echocardiography with color mapping, radiography to visualize the venous catheter.

On the seventh day the child was transferred to the pediatric department. Later, with positive dynamics, he was discharged with recommendations for dispensary registration of a psychologist, nephrologist, and gastroenterologist at the district polyclinic.

CONCLUSION

This clinical observation presents the multifaceted nature of damage in paracetamol poisoning. The peculiarity of this case is not only liver but also kidney

damage. Aggravating factors are the high dose (600 mg/kg) and late medical attention — more than 36 hours after taking the drug. Intensive therapy is aimed at cleansing the body of hepatolysis products and uremic toxins. Irreversible hepatic cellular damage requiring liver transplantation and irreversible renal damage requiring chronic hemodialysis were avoided. The absence of severe hypocoagulation with hemorrhagic syndrome allowed invasive procedures to be performed without complications. The use of antidote therapy with N-acetylcysteine in children is regulated in the 2015 clinical guidelines.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

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REFERENCES

1. Kogoniya L.M., Novikov G.A., Orlova R.V., Sidorov A.V. Practical recommendations for the treatment of chronic pain syndrome in cancer patients. Zlokachestvennyye opukholi. 2020;10(3s2-2):148–167. DOI: 10.18027/2224-5057-2020-10-3s2-49. (In Russian).
2. Wong A., Graudins A. Risk prediction of hepatotoxicity in paracetamol poisoning. Clinical Toxicology. 2017;55(8): 879–892. DOI: 10.1080/15563650.2017.1317349. (In Russian).
3. Zotov P.B., Lyubov Ye.B., Abuzarova G.R., Skryabin Ye.G., Klyashev S.M., Petrov V.G. Paracetamol as a means of suicidal actions in Russia and abroad. Suitsidologiya. 2019;10,4(37):99–119. DOI: 10.32878/suiciderus.19-10-04(37)-99-119. (In Russian).
4. Khoffman R., Nel'son L., Khauland M-E., L'yuin N., Flomenbaum N., Goldfrank L. Pod redaktsiyey Kotenko K.V. Emergency medical care for poisoning. Moscow: Praktika; 2010. (In Russian).
5. Chiew A.L., Isbister G.K., Kirby K.A., Page C.B., Chan B.S.H., Buckley N.A. Massive paracetamol overdose: an observational study of the effect of activated charcoal and increased acetylcysteine dose (ATOM-2). Clinical Toxicology. 2017;55(10):1055–1065. DOI: 10.1080/15563650.2017.1334915.
6. Sav'yuk F., Danel' V., Zobnin Yu.V. Acute paracetamol poisoning: emergency care. Baykal'skiy meditsinskiy zhurnal. 2008;6:107–112. (In Russian).
7. Simonova A.Yu., Belova M.V., Il'yashenko K.K., Kulabukhov V.V., Potskhveriya M.M., Stolbova N.Ye. i dr. Treatment of acute poisoning with paracetamol. Zhurnal im. N.V. Sklifosovskogo. Neotlozhnaya meditsinskaya pomoshch'. 2022;11(2):249–257. DOI: 10.23934/2223-9022-2022-11-2-249-257. (In Russian).
8. Aleksandrovich Yu.S., Pshenisnov K.V., Alekseyeva Ye.A., Selimzyanova L.R. Clinical recommendations (protocol) for providing emergency medical care for acute poisoning in children. Rossiyskoye obshchestvo skoroy meditsinskoy pomoshchi. 2015. (In Russian).
9. Casey D., Geulayov G., Bale E., Brand F., Clements C., Kapur N., Ness J., Patel A., Waters K., Hawton K. Paracetamol self-poisoning: Epidemiological study of trends and patient characteristics from the multicentre study of self-harm in England. Journal of Affective Disorders. 2020;1(276):699–706. DOI: 10.1016/j.jad.2020.07.091.

10. Aleksandrovich Yu.S., Pshenisnov K.V., Kaziakhmedov V.A., Lodyagin A.N., Udaltcov M.A., Kozubov M.Y., Storozhuk O.D. Acetaminophen Poisoning: A Cause of Acute Liver Failure in Pediatrics (Clinical Case). Journal of Emergency Medicine Trauma & Surgical Care. 2020;7:039. DOI: 10.24966/ETS-8798/100039.

ЛИТЕРАТУРА

1. Когония Л.М., Новиков Г.А., Орлова Р.В., Сидоров А.В. Практические рекомендации по лечению хронического болевого синдрома у онкологических больных. Злокачественные опухоли. 2020;10(3s2-2):148–167. DOI: 10.18027/2224-5057-2020-10-3s2-49.
2. Wong A., Graudins A. Risk prediction of hepatotoxicity in paracetamol poisoning. Clinical Toxicology. 2017;55(8): 879–892. DOI: 10.1080/15563650.2017.1317349.
3. Зотов П.Б., Любов Е.Б., Абузарова Г.Р., Скрябин Е.Г., Кляшев С.М., Петров В.Г. Парацетамол как средство суицидальных действий в России и за рубежом. Суицидология. 2019;10,4(37):99–119. DOI: 10.32878/suiciderus.19-10-04(37)-99-119.
4. Хоффман Р., Нельсон Л., Хауланд М-Э., Льюин Н., Фломенбаум Н., Голдфранк Л. Под редакцией Котенко К.В. Экстренная медицинская помощь при отравлениях. М.: Практика; 2010.
5. Chiew A.L., Isbister G.K., Kirby K.A., Page C.B., Chan BSH., Buckley N.A. Massive paracetamol overdose: an observational study of the effect of activated charcoal and increased acetylcysteine dose (ATOM-2). Clinical Toxicology. 2017;55(10):1055–1065. DOI: 10.1080/15563650.2017.1334915.
6. Савьюк Ф., Данель В., Зобнин Ю.В. Острое отравление парацетамолом: неотложная помощь. Байкальский медицинский журнал. 2008;6:107–112.
7. Симонова А.Ю., Белова М.В., Ильяшенко К.К., Кулабухов В.В., Поцхверия М.М., Столбова Н.Е. и др. Лечение острых отравлений парацетамолом. Журнал им. Н.В. Склифосовского. Неотложная медицинская помощь. 2022;11(2):249–257. DOI: 10.23934/2223-9022-2022-11-2-249-257.
8. Александрович Ю.С., Пшениснов К.В., Алексеева Е.А., Селимзянова Л.Р. Клинические рекомендации (протокол) по оказанию скорой медицинской помощи при острых отравлениях у детей. Российское общество скорой медицинской помощи. 2015.
9. Casey D., Geulayov G., Bale E., Brand F., Clements C., Kapur N., Ness J., Patel A., Waters K., Hawton K. Paracetamol self-poisoning: Epidemiological study of trends and patient characteristics from the multicentre study of self-harm in England. Journal of Affective Disorders. 2020;1(276):699–706. DOI: 10.1016/j.jad.2020.07.091.
10. Aleksandrovich Yu.S., Pshenisnov K.V., Kaziakhmedov V.A., Lodyagin A.N., Udaltcov M.A., Kozubov M.Y., Storozhuk O.D. Acetaminophen Poisoning: A Cause of Acute Liver Failure in Pediatrics (Clinical Case). Journal of Emergency Medicine Trauma & Surgical Care. 2020;7:039. DOI: 10.24966/ETS-8798/100039.