Проект:

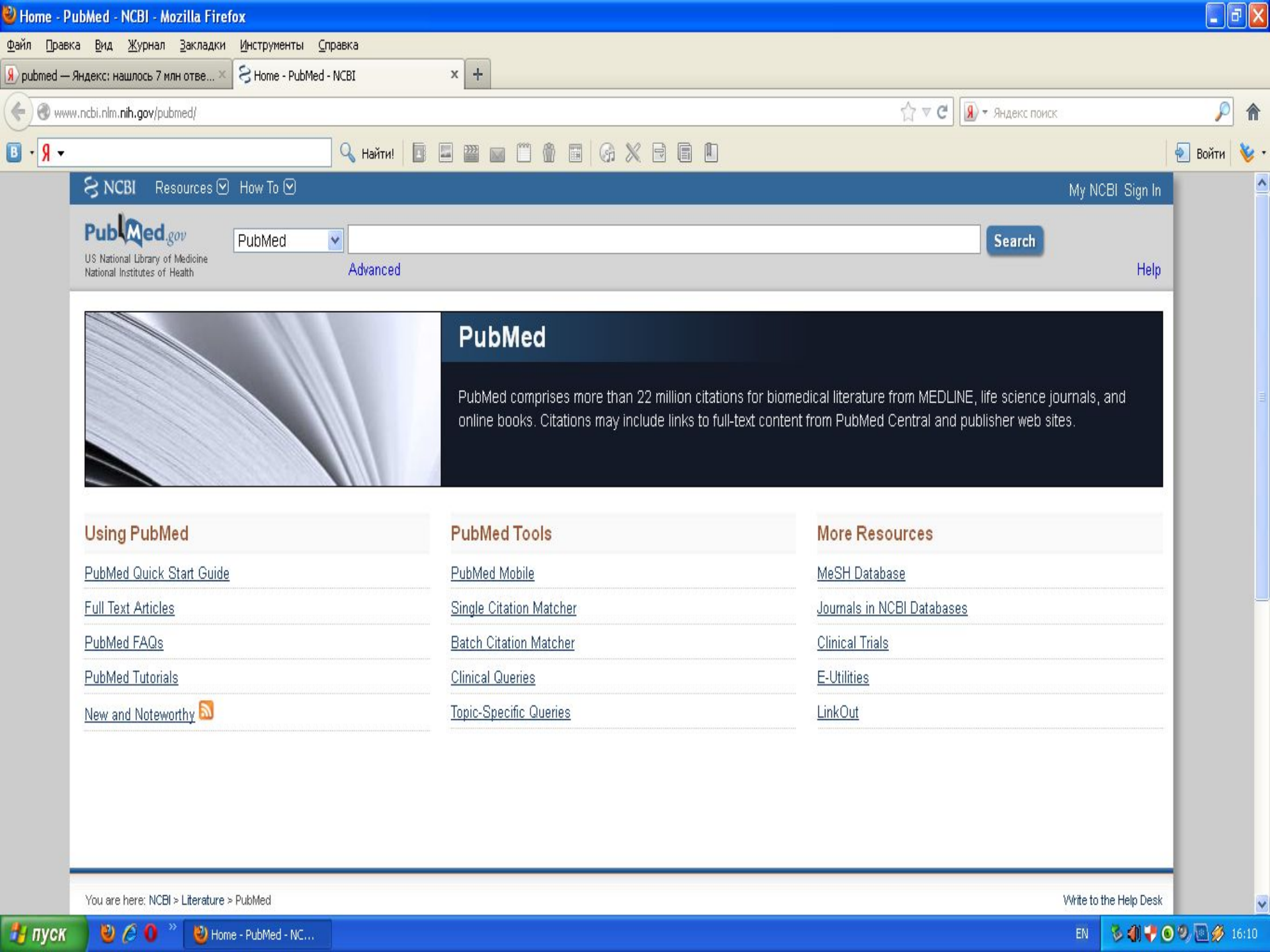
Тақырыбы: Балалардағы лимфобласттық лейкемияны емдеу жолы.

Мәселе:

- 7 жасар ұл балада лимфобласттық лейкемия екені анықталды.Оның жүрек-қантамыр жүйесінде ешқандай ақау жоқ. Лимфобласттық лейкемияны емдеуде антрациклинді қолдану дұрыс па? Антрациклинді қолданғаннан кейін 1-10 жыл аралығында жүрек жетіспеушілігі байқалатыны туралы мәлімет бар.

PICO:

- **Patient:** лимфобласттық лейкемиямен ауыратын 7 жасар ұл бала
- **Intervention:** anthracyclines
- **Comparison:** антрациклинді қолданып және қолданбай емдеген зерттеулерді салыстыру
- **Outcome:** Лабороториялық зерттеу нәтижелерінің жақсаруы,емделу, жүрек қантамыр жүйесіне жанама әсерлерінің жоқ болуы.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1. Comparative Analysis of Different Approaches to Measure **Treatment** Response in Acute Myeloid **Leukemia**.

Inaba H, Coustan-Smith E, Cao X, Pounds SB, Shurtleff SA, Wang KY, Raimondi SC, Onciu M, Jacobsen J, Ribeiro RC, Dahl GV, Bowman WP, Taub JW, Degar B, Leung W, Downing JR, Pui CH, Rubnitz JE, Campana D.
J Clin Oncol. 2012 Sep 10. [Epub ahead of print]

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1. Doxorubicin or daunorubicin given upfront in a therapeutic window are equally effective in children with newly diagnosed acute **lymphoblastic leukemia**. A randomized comparison in trial CoALL 07-03.

Escherich G, Zimmermann M, Janka-Schaub G; on behalf of the CoALL study group.
Pediatr Blood Cancer. 2012 Sep 4. doi: 10.1002/pbc.24273. [Epub ahead of print]

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High VLA-4 expression is associated **with** adverse outcc [Haematologica. 2011]

Recent advances **in** the diagnosis **and**

J Clin Oncol. 2012 Jul 1;30(19):2384-92. Epub 2012 May 21.

PMID: 22614971 [PubMed - in process]

Related citations

5. Cardiac failure 30 years after **treatment** containing **anthracycline** for **childhood** acute **lymphoblastic leukemia**.

Goldberg JM, Scully RE, Sallan SE, Lipshultz SE.

J Pediatr Hematol Oncol. 2012 Jul;34(5):395-7.

PMID: 22584777 [PubMed - indexed for MEDLINE]

Related citations

6. RALLE pilot: response-guided **therapy** for marrow relapse in acute **lymphoblastic leukemia** in children.

Saarinen-Pihkala UM, Parto K, Riikonen P, Lähteenmäki PM, Békàssy AN, Glomstein A, Möttönen M.

J Pediatr Hematol Oncol. 2012 May;34(4):263-70.

PMID: 22246158 [PubMed - indexed for MEDLINE]

Related citations

J Pediatr Hematol Oncol. 2012 Jul;34(5):395-7.

Cardiac failure 30 years after treatment containing anthracycline for childhood acute lymphoblastic leukemia.

Goldberg JM, Scully RE, Sallan SE, Lipshultz SE.

Department of Pediatrics, University of Miami Leonard M Miller School of Medicine, Miami, FL 33101, USA.

Abstract

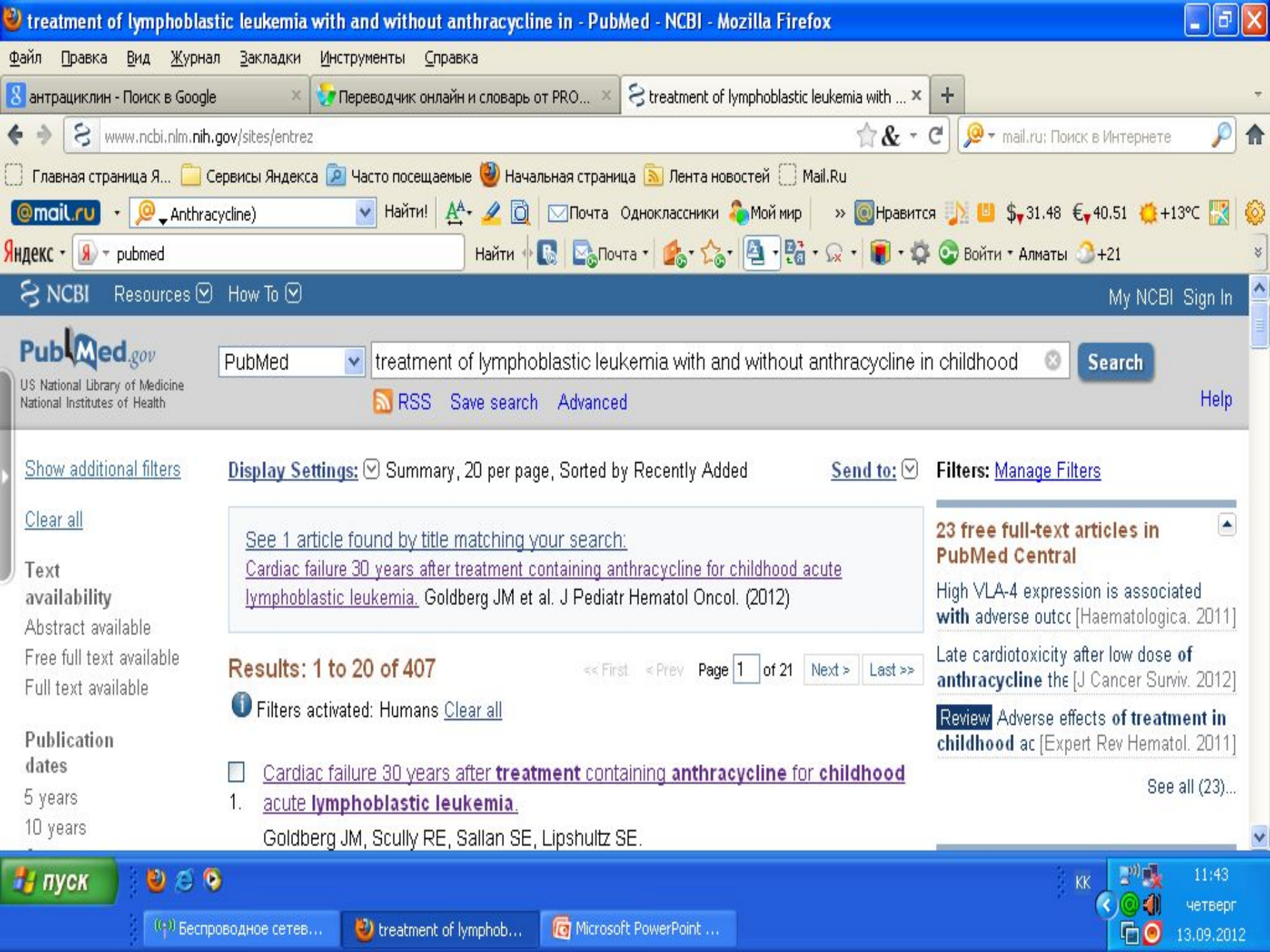
In 1977, a 5-year-old girl diagnosed with acute lymphoblastic leukemia was treated on Dana-Farber Cancer Institute Childhood Acute Lymphoblastic Leukemia Protocol 77-01, receiving a cumulative doxorubicin dose of 465 mg/m(2), cranial radiation, and other drugs. After being in continuous complete remission for 34 months, she developed heart failure and was treated with digoxin and furosemide. At 16 years of age, she was diagnosed and treated for dilated cardiomyopathy. Over the years, she continued to have bouts of heart failure, which became less responsive to treatment. At 36 years of age, she received a heart transplant. Six months later, she stopped taking her medications and suffered a sudden cardiac death.

PMID: 22584777 [PubMed - indexed for MEDLINE] PMCID: PMC3380184 [Available on 2013/7/1]

Publication Types, MeSH Terms, Substances, Grant Support

- Резюме

- В 1977 5-летнюю девочку, диагностированную с острой лимфообластной лейкемией, рассматривали на Детстве Онкологического института Даны-Фарбера Острый Лимфообластный Протокол 77-01 Лейкемии, получая совокупную doxorubicin дозу 465 мг/м (2), черепная радиация и другие наркотики. Будучи в непрерывной полной ремиссии в течение 34 месяцев, она развила остановку сердца и рассматривалась с дигоксином и фуросемидом. В 16 лет возраста ее диагностировали и лечили от расширенной кардиомиопатии. За эти годы она продолжала иметь приступы остановки сердца, которая стала менее отзывчивой к лечению. В 36 лет возраста она получила пересадку сердца. Шесть месяцев спустя она прекратила принимать свои лекарства и перенесла внезапную сердечную смерть.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   J Pediatr Hematol Oncol. 2012 Jul;34(5):395-7.
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2. RALLE pilot: response-guided **therapy** for marrow relapse in acute **lymphoblastic leukemia** in children.
   Saarinen-Pihkala UM, Parto K, Riikonen P, Lähteenmäki PM, Békàssy AN, Glomstein A, Möttönen M.
   J Pediatr Hematol Oncol. 2012 May;34(4):263-70.
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evaluation of a 7-year-long clinical follow-up.

Oztarhan K, Guler S, Aktas B, Arslan M, Salcioglu Z, Aydogan G.

Pediatr Hematol Oncol. 2011 Aug;28(5):380-94. Epub 2011 Jun 24.

PMID: 21699467 [PubMed - indexed for MEDLINE]

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8. Mitochondrial D-loop polymorphisms and mitochondrial DNA content in **childhood** acute **lymphoblastic leukemia**.

Kwok CS, Quah TC, Ariffin H, Tay SK, Yeoh AE.

J Pediatr Hematol Oncol. 2011 Aug;33(6):e239-44.

PMID: 21646920 [PubMed - indexed for MEDLINE]

Related citations

9. Late cardiotoxicity after low dose of **anthracycline therapy** for acute **lymphobl**...**ood**.

Vandecruy...lf D, Benoit Y, Suys B.

J **Cancer** S...ub 2011 Jun 1.

PMID: 21630046 [...DLINE] **Free PMC Article**

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cardiotoxicity *(англ.)*
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J Cancer Surviv. 2012 Mar;6(1):95-101. Epub 2011 Jun 1.

Late cardiotoxicity after low dose of anthracycline therapy for acute lymphoblastic leukemia in childhood.

Vandecruys E, Mondelaers V, De Wolf D, Benoit Y, Suys B.

Department of Pediatric Hemato-Oncology, Ghent University Hospital, De Pintelaan 185, Ghent, Belgium. els.vandecruys@ugent.be

Abstract

INTRODUCTION: Late cardiotoxicity is a known complication of anthracycline therapy but the long-term effects of low cumulative doses are not well documented. We studied late cardiotoxicity in survivors of childhood acute lymphoblastic leukemia (ALL) treated with low anthracycline doses 10 to 20 years earlier.

METHODS: Seventy-seven ALL survivors who received a cumulative anthracycline dose <250 mg/m² and were at least

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- Vandecruys E, Mondelaers V, De Wolf D, Benoit Y, Suys B.
- **Source**
- Department of Pediatric Hemato-Oncology, Ghent University Hospital, De Pintelaan 185, Ghent, Belgium. els.vandecruys@ugent.be
- **Abstract**
- **INTRODUCTION:**
- Late cardiotoxicity is a known complication of anthracycline therapy but the long-term effects of low cumulative doses are not well documented. We studied late cardiotoxicity in survivors of childhood acute lymphoblastic leukemia (ALL) treated with low anthracycline doses 10 to 20 years earlier.
- **METHODS:**
- Seventy-seven ALL survivors who received a cumulative anthracycline dose <250 mg/m² and were at least 10 years after treatment were evaluated for signs of clinical heart failure. Cardiac function was assessed by echocardiography including tissue Doppler measurements of the septal mitral annulus in 37 ALL survivors 10.6-18.3 years (median 13.3 years) after anthracycline treatment with cumulative doses of 180 (n = 19) or 240 mg/m² (n = 18). The control group consisted of 30 healthy volunteers matched for age, sex, BSA, and BMI.
- **RESULTS:**
- No clinical relevant cardiotoxicity was found. Left ventricular shortening fraction (SF) was significantly reduced in male ALL survivors. Three of the 19 male ALL survivors had an SF below 30%. Male ALL survivors showed a significantly lower early filling velocity to atrial contraction velocity ratio but myocardial velocity during early filling was comparable between patients and controls. ALL survivors had a significantly longer isovolumetric relaxation time (IVRT). Thirty percent of the ALL survivors have an abnormal IVRT compared to the normal range of the controls. CONCLUSION AND IMPLICATIONS FOR CANCER SURVIVORS: At a median of 13.3 years after exposure to cumulative doses of anthracyclines of 180 or 240 mg/m², no clinical relevant cardiotoxicity was found but subclinical cardiac abnormalities were present in 30% of the patients.

- Последний cardiotoxicity после низкой дозы anthracycline терапии для острой лимфообластной лейкемии в детстве.
- Vandecruys E, Mondelaers V, Де Уолф Д, Бенуа И, Suys B.
- Источник
- Отдел педиатрической Hemato-онкологии, Гентский университет больница, Де Пентелан 185, Гент, Бельгия. els.vandecruys@ugent.be
- Резюме
- ВВЕДЕНИЕ:
- Последний cardiotoxicity - известное осложнение anthracycline терапии, но долгосрочные эффекты низких совокупных доз не хорошо зарегистрированы. Мы учились, последний cardiotoxicity в оставшихся в живых острой лимфообластной лейкемии (ALL) детства отнесся с низкими anthracycline дозами 10 - 20 годами ранее.
- МЕТОДЫ:
- Семьдесят семь BCEX оставшихся в живых, которые получили совокупную anthracycline дозу <250 мг/м ² и были по крайней мере 10 годами после лечения, были оценены для признаков клинической остановки сердца. Сердечная функция была оценена эхокардиографией включая ткань измерения Doppler относящегося к перегородке напоминающего по форме митру кольца в 37 BCEX оставшихся в живых 10.6-18.3 лет (средние 13.3 лет) после anthracycline лечение с совокупными дозами 180 (n = 19) или 240 мг/м ² (n = 18). Контрольная группа состояла из 30 здоровых добровольцев, подобранных для возраста, пола, BSA и BMI.
- <!--250-->РЕЗУЛЬТАТЫ:
- Никакой клинический соответствующий cardiotoxicity не был найден. Оставленное желудочковое сокращение части (SF) было значительно уменьшено в мужчине BCE оставшиеся в живых. У трех из 19 мужчин BCE оставшиеся в живых был SF ниже 30%. Мужчина, которого BCE оставшиеся в живых показали значительно более низкой ранней скорости заполнения относящемуся к предсердию скоростному отношению сокращения, но миокардиальная скорость во время раннего заполнения была сопоставима между пациентами и средствами управления. У BCEX оставшихся в живых было значительно более длительное isovolumetric время расслабления (IVRT). У тридцати процентов BCEX оставшихся в живых есть неправильный IVRT по сравнению с нормальным диапазоном средств управления. ЗАКЛЮЧЕНИЕ И ЗНАЧЕНИЯ ДЛЯ ОСТАВШИХСЯ В ЖИВЫХ РАКА: В медиане 13.3 лет после воздействия совокупных доз anthracyclines 180 или 240 мг/м ², не был найден никакой клинический соответствующий cardiotoxicity, но подклинические сердечные отклонения присутствовали в 30% пациентов.

Pediatr Blood **Cancer**. 2011 Sep;57(3):461-6. doi: 10.1002/pbc.23012. Epub 2011 Feb 4.
PMID: 21298773 [PubMed - indexed for MEDLINE]
Related citations

17. Long-term results of AIEOP-8805 protocol for acute B-**cell lymphoblastic leukemia** of **childhood**.

Pillon M, Aricò M, Basso G, Locatelli F, Citterio M, Micalizzi C, Testi AM, Barisone E, Nardi M, Lombardi A, Rondelli R, Rosolen A; NHL-Committee of the Italian Association of Pediatric Hematology, Oncology.
Pediatr Blood **Cancer**. 2011 Apr;56(4):544-50. doi: 10.1002/pbc.22787. Epub 2010 Dec 15.
PMID: 21298738 [PubMed - indexed for MEDLINE]
Related citations

18. **Treatment** including **anthracyclines** versus **treatment** not including **anthracyclines** for **childhood cancer**.

van Dalen EC, Raphaël MF, Caron HN, Kremer LC.
Cochrane Database Syst Rev. 2011 Jan 19;(1):CD006647. Review.
PMID: 21249679 [PubMed - indexed for MEDLINE]
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Cochrane Database Syst Rev. 2011 Jan 19;(1):CD006647.

Treatment including anthracyclines versus treatment not including anthracyclines for childhood cancer.

van Dalen EC, Raphaël MF, Caron HN, Kremer LC.

Paediatric Oncology, Emma Children's Hospital / Academic Medical Center, PO Box 22660 (room A3-273), Amsterdam, Netherlands, 1100 DD.

Abstract

BACKGROUND: One of the most important adverse effects of anthracyclines is cardiotoxicity. A well-informed decision on the use of anthracyclines in the treatment of childhood cancers should be based on evidence regarding both antitumour efficacy and cardiotoxicity.

OBJECTIVES: To compare antitumour efficacy of treatment including or not including anthracyclines in children with childhood

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OBJECTIVES: To compare antitumour efficacy of treatment including or not including anthracyclines in children with childhood cancer.

SEARCH STRATEGY: We searched the Cochrane Central Register of Controlled Trials (The Cochrane Library 2010, Issue 2), MEDLINE (1966 to March 2010) and EMBASE (1980 to March 2010). In addition, we searched reference lists of relevant articles, conference proceedings and ongoing trials databases.

SELECTION CRITERIA: Randomised controlled trials (RCTs) comparing treatment of any type of childhood cancer with and without anthracyclines and reporting outcomes concerning antitumour efficacy.

DATA COLLECTION AND ANALYSIS: Two reviewers independently performed the study selection, risk of bias assessment and data extraction.

MAIN RESULTS: We identified RCTs for six types of tumour: acute lymphoblastic leukaemia (ALL) (three trials; 912 children), Wilms' tumour (one trial; 316 children), rhabdomyosarcoma/undifferentiated sarcoma (one trial; 413 children), Ewing's sarcoma

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Review Beneficial and harmful effects of anthracyclines in th [Br J Haematol. 2009]

Review Cardioprotection against the toxic effect [Health Technol Assess. 2007]

Prospective longitudinal assessment of late anthracycline cardiotoxi [Heart. 2004]

Late cardiotoxicity after low dose of anthracycline ther [J Cancer Surviv. 2012]

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- **Treatment including anthracyclines versus treatment not including anthracyclines for childhood cancer.**
- van Dalen EC, Raphaël MF, Caron HN, Kremer LC.
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- **AUTHORS' CONCLUSIONS:**
- At the moment no evidence from RCTs is available which underscores the use of anthracyclines in ALL. However, "no evidence of effect", as identified in this review, is not the same as "evidence of no effect". For Wilms' tumour, rhabdomyosarcoma/undifferentiated sarcoma, Ewing's sarcoma, non-Hodgkin lymphoma and hepatoblastoma only one RCT was available and, therefore, no definitive conclusions can be made about the antitumour efficacy of treatment with or without anthracyclines in these tumours. For other childhood cancers no RCTs were identified and therefore, no conclusions can be made about the antitumour efficacy of treatment with or without anthracyclines in these tumours.

Балалар ісігін антрациклинді қолданып және қолданбай емдеу

ЗЕРТТЕУШІЛЕР: van Dalen EC, Raphaël MF, Caron HN, Kremer LC.

ОРНЫ: Paediatric Oncology, Emma Children's Hospital / Academic Medical Center, PO Box 22660 (room A3-273), Amsterdam, Netherlands, 1100 DD.

- Антрациклиннің ең негізгі жағымсыз әсері - cardiotoxicity. Оның ісікке қарсы және кардиотоксикалық әсерлерінің арасындағы тепе теңдікті зерттеу
- **МАҚСАТЫ:**
- Антрациклиннің ісікке қарсы әсерін балалар рагында оны қолданып және қолданбай емдеу арқылы емдеу және нәтижелерін салыстыру
- **ТАҢДАУ КРИТЕРИЛЕРІ:**
- Антрациклиннің ісікке қарсы әсерін кез келген балалар рагында оны қолданып және қолданбай емдеу арқылы емдеген РБСларды анализдеу
- Берілгендерді жинау және анализ:
- Екі рецензент тәуелсіз түрде берілгендерді жинау және бағалаудан ауытқу қаупін орындады

- **НЕГІЗГІ НӘТИЖЕЛЕР:**
- Біз РБС-ны ісіктің 6 типі үшін идентифицирледік: жедел лимфобластты лейкемия (ALL) (3 сынақ, 912 бала), Вилмс ісігі (бір сынақ ; 316 бала), rhabdomyosarcoma/ дифференцирленбеген саркома (бір зерттеу; 413 бала), Юинг саркомасы (бір сынақ ; 94 бала), ходжкиндік емес лимфома (бір сынақ ; 284 бала) , hepatoblastoma (бір сынақ ; 255 бала). Клиникалық cardiotoxicity 3 РБС да бағаланды: барлық бақылау топтарында айтарлықтай айырмашылық байқалмады, бірақ барлық жеке зерттеулерде антрациклинді қолданбай емделген топта кардиотоксикалығы неғұрлым төмен болғаны анықталды. Жүрек дисфункциясының симптомсыз өткен жағдайлары болмады.

- **ЛЕЧЕНИЕ ВКЛЮЧАЯ ANTHRACYCLINES ПРОТИВ ЛЕЧЕНИЯ НЕ ВКЛЮЧАЯ ANTHRACYCLINES ДЛЯ ДЕТСКОГО РАКА.**
- ван Дэлен ЭК, MF Raphaël, Caron HN, Kremer LC.
- Источник
- Педиатрическая Онкология, Эмма Детская Больница / Академический Медицинский центр, Почтовый ящик 22660 (комната A3-273), Амстердам, Нидерланды, 1100 DD.
- Резюме
- ФОН:
- Одно из самых важных отрицательных воздействий anthracyclines - cardiotoxicity. Хорошо осведомленное решение об использовании anthracyclines в лечении детского рака должно быть основано на доказательствах и относительно эффективности антиопухоли и относительно cardiotoxicity.
- ЦЕЛИ:
- Сравнить эффективность антиопухоли лечения включая или не включая anthracyclines в детях с детским раком.
- СТРАТЕГИЯ ПОИСКА:
- Мы искали Кокрейна Центральный Регистр Контролируемых исследований (Библиотека Кокрейна 2010, Выпуск 2), MEDLINE (1966 до марта 2010) и EMBASE (1980 до марта 2010). Кроме того, мы искали справочные списки соответствующих статей, слушаний конференции и продолжающихся баз данных испытаний.
- КРИТЕРИИ ОТБОРА:
- Рандомизированные контролируемые исследования (RCTs) сравнение обработки любого типа детского рака с и без anthracyclines и сообщения о результатах относительно эффективности антиопухоли.

- СБОР ДАННЫХ И АНАЛИЗ:
- Два рецензента независимо выполнили выбор исследования, риск оценки уклона и извлечения данных.
- ГЛАВНЫЕ РЕЗУЛЬТАТЫ:
- Мы идентифицировали RCTs для шести типов опухоли: острая лимфообластная лейкемия (ALL) (три испытания; 912 детей), опухоль Вилмса (одно испытание; 316 детей), rhabdomyosarcoma/undifferentiated саркома (одно испытание; 413 детей), саркома Юинга (одно испытание; 94 ребенка), неходжкинская лимфома (одно испытание; 284 ребенка) и hepatoblastoma (одно испытание; 255 детей). У всех исследований были методологические ограничения. Поскольку ВСЕ никакие доказательства значительной разницы в эффективности антиопухоли не были идентифицированы в метаисследованиях, но в большинстве отдельных исследований было предложение лучшей эффективности антиопухоли в пациентах, отнесся с anthracyclines. И для опухоли Вилмса и для саркомы Юинга была идентифицирована значительная разница в и полном выживании без случаев в пользу лечения с anthracyclines, хотя для опухоли Вилмса значительная разница в полном выживании исчезает с долгосрочным продолжением. Для rhabdomyosarcoma/undifferentiated саркомы неходжкинской лимфомы и hepatoblastoma не было идентифицировано никакое различие в эффективности антиопухоли между контрольными группами. Клинический cardiotoxicity был оценен в трех RCTs: никакая значительная разница между обеими контрольными группами не была идентифицирована, но во всех отдельных исследованиях было предложение более низкого уровня клинического cardiotoxicity в пациентах, которые не получали anthracyclines. Ни одно из исследований не оценило бессимптомную сердечную дисфункцию. Для другого детского рака не были идентифицированы никакие RCTs.
- ЗАКЛЮЧЕНИЯ АВТОРОВ:
- В настоящее время никакие доказательства от RCTs не доступны, который подчеркивает использование anthracyclines ВСЕГО. Однако, "никакие доказательства эффекта", как идентифицировано в этом обзоре нет

Қорытынды:

- Бұл мақаланы зерттей отырып оны бірнеше РБС деп айта аламыз. Бұл зерттеуге 300-900 бала қатысқан және бірнеше сынақтар жүргізілген. Соған байланысты бұл зерттеу нәтижелеріне сенуге болады. Оның нәтижелеріне сүйенсек антрациклиннің айқын емес кардиотоксикалық әсері бар. Сондықтан мүмкіндігінше басқа препараттарды қолдануға тырысамыз.