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Observational studies on prophylaxis of hepatitis B virus reactivation with long or short course oralAgents among patients with acute myeloidleukemia

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Abstract: Background and purpose:hepatitis B virus (HBV) reactivation is one of serious complications among patients with acute myeloid LeukeMia (AML) following cytotoxic induction and consolidation chemotherapy.Nucleoside analogs including lamivudine and entecavir have been widely used as prophylactic or preemptive treatment for HBV reactivation.This study is to investigate clinical efficacy and safety of a long or short course oral ANTI-HBV for agents HBV reactivation in AML patients with HBV infection during chemotherapy.Methods:themedical records AML patients with HBV infection receiving aT least 4 courses of chemotherapy were

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Theretrospectively identified and systematically analyzed.These patients were further divided into four groups according to their hepatitis B surface antigen (HBsAg) status prior to initiation of chemotherapy and duration of prophylactic therapy.Reactivation of HBV and toxicity profiles of oral antiviral agents were systematically analyzed and compared among differeNT groups.Results:HBV reactivation and documented hbv-related hepatitis wereSignificantly lower in AML patients under long course antiviral prophylaxis (i.e. continuing oral antiviral therapy for atLeast 6 months after cessation of chemotherapy, LCP group) than in the patients with short course antiviral (i.e. continuing oral antiviral therapy for one month after cessation of chemotherapy, SCP Group), which was 5.56% (1/18) And0%(0/18) compared with 45.45% (5/11) and 36.36% (4/11) (p=0.018 and p=0.014). There was little difference in the incidence of antiviral resistance between LCP and SCP groups [11.11% (2/18) V5 9.09% (1/11), p>0.05].Furthermore, the rates of HBV reactivation and hbv-related hepatitis were significantly lower in AML patients with PositivE-HBsAg (HBsAg ^0.05 iu/ml) under long course antiviral prophylaxis than in HBsAg positive patients who received short couRSE antiviral agents [8.33% (1/12) and0%(0/12) V5 66.67% (4/6) and 66.67% (4/6), p=0.022 and p=0.005].Meanwhile, there was little difference in the rates of antiviral resistance-LCP and SCP between groups HBsAg amonge patients [8.33% (1/12) V5 16.67% (1/6), p>0.05].In addition, the rates of HBV reactivation and hbv-related hepatitis as so as antiviral resistance were shown to have LiTtle difference in AML patients with negative HBsAg (hbsag<0.05 iu/ml) between LCP and SCP groups.Concerning antiviral agent toxicity, no grade 3-4 toxicity occurred in patients from LCP or SCP group.Conclusion:Long course prophylaxis with oral antiviral agent appears to be an effective and tolerated preventative approach for reducing risks of HBV reactivation and associated events in AML pAtients with positive HBsAg during chemotherapy, which serves as a platform for the design of prospective clinical.

Keywords: Acute myeloid leukemia;Hepatitis B virus reactivation;Prophylactic antiviral therapy

Acute myeloid leukemia(Acutemyeloidleukemia,AML)is a class of heterogeneous hematopoietic stem progenitor

cells, malignant cloningSexual disease,to anthracene ring drugs(like erythromycin and methoxy)erythromycin etc)Combined with cytosine-induced chemotherapyand the consolidated chemotherapy of high-dose chemotherapeutic

drugs after remission isAMLThe primary treatment for is.AMLmergeHBVinfected patientsafter chemotherapy hepatitis B virus(hepatitisBvirus,HBV)re-activating can cause different degrees of liver dysfunctionaffect chemotherapy process,even causes fulminant hepatitis and endangersLife.so,actively explore preventionAMLmergeHBVsenseInfected patientsHBVvirus reactivation Effective policy is necessarySex and clinical significance.Recent research Discovery,nucleoside antiHBVdrug(including lamivudine and Grace Entecavir)prophylactic treatmentcan significantly reduceHBVre-activating risk,But these studiesmainly focused on lymphoma patients receiving immunotherapy[1-3],inAMLMergeHBVinfected patients with prophylactic nucleosideclass antiHBVDrug Report still less,also,about anti-HBVAsystematic study of drug use and timing is still missing.Viewon this,The study passes retrospective analysisexampleAMLmergeHBVinfect and accept at least4Pro for patients undergoing chemotherapybed data,explore nucleoside resistanceHBVdrug prevention virus again

Live clinical efficacy and safety and the ideal course of treatment.

1. Data and methods

1.1 patients select

This studyis for peopleYear1Month one2016Yearmonth periodnineth People's Hospital affiliated to Shanghai Jiaotong University Medical School The blood insideExample AML mergeHBVinfected and accepted at least4patients with chemotherapy,among men: Cases,women@Example,Age~year old,median ageyear old.specific personStandard as follows: ① conforms to who(WorldHealth Organization,who)myeloid tumor typing2008versionAMLDiagnostic Criteria; ② before chemotherapyHBV-related antigen,includesHBVsurface antigen(hepatitisBSurfaceantigen,HBsAg),eantigens and antibodies(hepatitisBeantigenthenhepatitis Beantibody,HBeAgandHbeab)and core antibody(hepatitisBCoreantibody,Hbcab)serological detectionresults at least1Positive; ③ Imaging for cirrhosis-free andleukemia liver invasion ④ HBVDNA (hepatitis Bvirusdeoxyribonucleicacid)Quantitative polymerase chain reaction(quantitativepolymerasechainreaction,PCR)Check

The number of copies is less than or equal to$2x^4$/ML; ⑤ liver function QuarantineAlanineaminotransferase(alanineaminotransferase,ALT),aspartic acid aminotransferase(aspartateaminotransferase,AST)and Total bilirubin no more than positiveconstant1.5Times; ⑥ excludes other neoplastic diseases,Immune Disorderssick,Diabetes and obesity.iAll patients accepted at least4A course of induction and consolidation of chemotherapy,where induction chemotherapy is going toaDextran combined with cytidine(idarubicin+cytarabine,IDA+Ara-C"")IAScheme,that is, norepinephrine8~mg/(2. (/(.D),1~3Day,glycoproteinmg/(2. (/(.D),1~7Day,Dis1Cycle;consolidates chemotherapy for large doses of sugar2~3/m^2,everyH1Times,1, 3, 5Day,Dis1Cycle.

1.2 Research Methods

1.2.1 treatments and Groups

induces chemotherapy at the startof,Synchronous Oral entecavirmg/d/,at the same time giving patients support treatment.based on patienttaking anti-HBVdrug duration is divided into two groups: ① Long courseprevent(LongCourseprophylaxis,LCP)GrouporalantiHBVdrugs continue until end of chemotherapy6months above; ② ShortSession Prevention(shortCourseprophylaxis,SCP)Group,Portanti-HBVdrugs continue until chemotherapy ends1monthsless than;at the same time,According to the patientHBsAgserological Detection results are divided into twoGroup: ①HBsAgPositive Group,refers to the patient's serumHBsAgLargeto equal to0.05IU/ML;②HBsAgNegative Group,is the patientPerson SerumHBsAgless than0.05IU/ML.

1.2.2 observe metrics and evaluation criteria

collect people group patients before and after each chemotherapy cycle and chemotherapyHistory of follow-up visits,General physical Check,allblood cell count,coagulation indicator,Serum liver and kidney functionindex,serumHBV-related antigens andHBV-DNASetamount(with fluorescence quantificationPCRMethod,detect lower-bound copies of5.0x2a/mL)Clinical Data,system analysis and evaluation

sufferingpersonHBVreactivation rate,HBVassociated hepatitis Burst rate,HBVTherate of primary drug resistance and the frequency of liver failure.evaluation criteria such asunder:

(1)HBVre activate:SerumHBVDNAlevel baseline elevationtentimes or above,or lack ofHBVDNABaseline The absolute number of copies exceeded2.0xten^{4}//mL,orPerson SerumHBVDNAfrom negative to positive;(2)HBVrelated hepatitis Outbreak:whenALThorizontal rise greater than5double positiveconstant Upper limit;(3)HBVprimary drug resistance:nucleoside(acid)similartoObject TherapyWeek,HBVDNAload descending less than1LogTenIU/ML);(4)liver failure: ①has ascites or otherPortal Hypertension, ②hepatic encephalopathy(Ctype), ③Serumtotal bilirubin greater than51.3wowol/Land albumin less thanG/L,④prothrombin activity is less than or equalto40%.

1.2.3 adverse reaction observation

observe and record adverse reactions:includes type,frequency andseverity.Adverse Reactions Reference US National Cancer Researchadverse reaction rating standard(NationalcancerInstitute CommonterminologyCriteriaforAdverseEvents,NCI-Ctcae) 4.03version,and evaluates itsrelevance tothe drug.where the entecavir most common drug badeventfor creatine kinase(Creatinekinase,CK)elevation.rootunderCKHorizontal4level:1level(3~<5xisin normalvalueLimited;2Level(5~<7)xMaximum normal value;3level(7~<10) xMaximum normal value;4level greater than or equaltenxMaximum normal value.1.3statistical processing

All data takestheSPSS13.0Software Analysis,Count Capitalmaterial with ratio and composition ratio for,with/Validation comparison between groups,Pthe<0.05is statistically significant for the difference.

2. knotFruit

2.1 General clinical data for patients with long and short course of treatment group

LCPandSCPgroup patients areandOneExample,two groupsofmiddle age,gender composition,AMLTyping,Prognosis is dividedintolayer and induction and consolidation of chemotherapy sessions,Analysis Comparison,no significant difference(P>0.05,Table1)).

2.2 patients with long-duration treatment groupHBVToreactivate and itsrelated eventincidence

LCPTheGroup has only1patients at the end of chemotherapy3MonthappearHBVre activate,reactivation rate5.56% (1/18),anddid not occurHBVassociated hepatitis;SCPTheGroup has5Example patient occursHBVre-Activate,where3The example occurs at the end of the chemotherapy3~5Month,1The example appears in the chemotherapy section4Session,another1Example InitialHBV-DNAnegative patients in chemotherapy4A session virusre-Activate,HBVThe total reactivation rate is45.45% (5/11),thisoutsideHBVassociated hepatitis incidence is36.36% (4/11).LCP

Group PatientsHBVThereactivation rate and the associated hepatitis burst rate are allsignificantly lower thanSCPGroup patients(corpse=0.018and Corpse=0.014).sameas whenLCPandSCPgroup patients 'HBVprimary drug resistance rate11.11%$_{c}$(2/18)and9.09%$_{c}$(1/11),There is no statistically significant difference(corpse>0.05).

Further subgroup analysis displays,LCPin the groupHBsAg(+)PatientsHBVthe reactivation rate and the associated hepatitis burst rate are8.33%<1/12and0%<0/12,andSCPin the group1ExampleHBsAg(+)The patient occurs during chemotherapyHBVreactivation and concomitant hepatitis,other3case at end of chemotherapy6appears in the monthHBVre-excitationLive with hepatitis,HBVreactivation rate and associated hepatitisburst rates are66.67% (4/6),significantly higher thanLCPGroupHBsAg(+)patient(Corpse=0.022and the user=0.005;at the same time,LCPandSCPGroupHBsAg(+)PatientsHBVThe primary drug resistance rate is8.33% (1/12)and16.67% (1/6),There is no statistically significant difference(corpse>0.05).another,LCPGroup has1exampleHBsAg(-)Patient sendliveHBVprimary drug resistance,andSCPTheGroup has1ExampleHBsAg(-)Patientson chemotherapy page4session appearsHBVand then activatethe,but not concurrent liverinflammatory,continue taking medicationHBV-DNAdrops again to the measured value with theunder.LCPandSCPGroupHBsAg(-)PatientsHBVreactivation Rate,hepatitis

Incidence and primary resistance rate in theLCPGroup0% (0/6), 0%> (0/6)and16.67%> 1/6);onSCPGroup to20%> (1/5), 0% (0/5)and0% (0/5),There is no statistically significant difference(P>0.05).The specific numeric and statistical analysis of the above subgroup analysis for is shown in the table2.

2.3 adverse drug reactions in patients withlong and short course of treatment group

LCPandSCPGroup Patients1~2levelCKelevated occurrence rate, respectivelyfor22.22%> (4/18)and27.27%> (3/11),Difference No statisticsmeaning(P>0.05).Two groups of patients did not appear3~4levelCKelevationto cause undesirable events to stop drugs.addition,Two group of patients followupThedoes not occur during the medication the Grace Entecavir relatedto3level above hematologyor non-hematological toxicity.No liver failure throughout the follow-upexhaustive((table3).Two groups of patients with adverse reactions during chemotherapy the result of the reaction ofthetreatment drug factor Interference no statistical comparison.

3. To askon

is currently,Blood tumor mergeHBVinfected patients with chemotherapyperiod and follow-up periodHBVre-activating issues getting heavierview[4],especially in ChinaHBVpeople with high infection ratesThe area is more closely watched.clinical studies show,before and after chemotherapy andgeneral monitoring of follow-up periodHBVSerum related antigen and(or)HBVDNAlevel,and give prevention and preemptive treatment can significantlyLower patientHBVReactivate Risk,Toenable the patient to receive a clinicalbenefits[5].recent,Taiwan A large retrospective study shows,AMLmergeHBVvirus reactivation after chemotherapy for infected patientsnot low,recommend giving patients nucleoside resistanceHBVpreventative GovernanceTherapy (4) Other research also finds,AMLPatientsHBVand then activatetheis no less thanA lymphoma patient receiving immune chemotherapy,same needto prevent antiviral treatment[7].however,antiHBVPreventive treatmenthealing time,Selection Of course and antiviral drugs still notClear and pending further study.

This study found that,Long Course drug prevention groupAMLPatients,HBVreactivation rate and associated hepatitis burst rates are significantly loweron short course prevention group patients,promptAMLMergeHBVInfectionpatients with prophylactic antiviral therapy at least until the end of chemo.6Month above,Although sample size is small,But this is reported at home and abroadSimilar to the conclusions of clinical guidelines[8-10].However, you must refer tooutof,still has 1 duringLong course antiHBVmedicationcases appearvirus reactivation,and the original drug resistance to the grace Entecavir,So,on antiHBVThere is still a need to monitor the liver closely during the treatment.features and plasma virus load,Once a virus recovery is found,considerHBVShow drug-resistant problems,detect virus mutations in a timely mannerand adjust antiHBVmedication.also,This study also found,ShortsessionPreventive Medication Group,HBsAg(+)patient'sHBVreactivaterate and associated hepatitis burst rates are significantly higher than long course of preventionGroupHBsAg(+)Patients,promptsHBsAg(+)high-risk groupsto be treated with foot treatmentHBVPreventative treatment;session Insufficientcan causeHBVreactivate and sudden hepatitis,This furthercertificateAMLMergeHBsAg(+)patient prophylactic antiviral treatmentnecessity.andHBsAg(-)Thepatient is treated with a duration of treatmentHBVAfter preventive treatmentHBVand then activatethe,hepatitis Outbreaks and primary drug resistanceincidence no significant difference,description forHBsAg(-)patients areNo need for a foot course antiviral therapy pending further study.otheroutside,has1exampleHBsAg(-)patient with chemotherapy4A session appearsHBVre-Activate,Prompt for induction or consolidation after chemotherapyAMLpatient's bodyHBVprotective antibodies drop and cause virus to be stimulated againlive.so,HBsAg(-)patients are still required to monitor during chemotherapymeasuring plasma virus load[11-12].This study adverse drug reaction examinationtest results show,There is no in the medication group3leveloverCKelevated level or toxic reaction,prompt for a cardWei as prophylactic anti-HBVdrugs with good security andtolerated.of course,This study is based on retrospective study of Nature andsample size still has limitations,There's room for further improvement.

Summary,AMLMergeHBVinfected patients save after chemotherapyon virus reactivation risk.Long course of oral

administration Entecavir isloweringAMLmergeHBsAgpositive infection patients after chemotherapy virusre-activation and virus-related event incidence valid and safesexual Good prevention regimen,Worth further forward-lookingResearch.

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