氏名	張（ジャン） 祁雁（チ ヤン）
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学位論文名	Evaluation of the Observed Cisplatin Nephrotoxicity in Adult Cancer Inpatients : A Historical Cohort Study by Using Clinical Data Warehouse （シスプラチンによる成人入院癌患者の腎毒性の評価：データウェアハウスを用いた臨床研究）
論文審査委員	（主査） 教授 武田 裕 （副査） 教授 磯 博康　教授 黒川 信夫

論文内容の要旨

〔目　的〕

Cisplatin (CDDP) nephrotoxicity have been well investigated in animal data. However, studies on human data are still limited. In the present study, we have conducted a historical cohort study to evaluate the observed cisplatin nephrotoxicity in adult cancer inpatients treated at a national university hospital in Japan by using data warehouse.

〔方法ならびに成績〕

Methods : The order entry system and the electronic patient record system have been implemented in Osaka University Hospital. The prescription data, laboratory test results and hospital recoreds etc. are stored in the databases of the hospital information system. All patient data have been transferred to the clinical data warehouse (CDW), which is a database specified for data analyses. In this study adult cancer inpatients from January 1st, 2000 to December 31st, 2004 were selected and patients' admission history ; oral and injection prescription ; medication master and laboratory test results were downloaded from the CDW. The patients whose sCr level on admission was <1.2 mg/dl were divided into three groups based on the exposure of CDDP, non-exposure of CDDP but with other anticancer agents (Non-CDDP Group) and non-exposure of any anticancer agents (Control Group). In order to match patients' characteristics among three groups, we categorized the patients based on gender, age, sCr levels on admission and LOS. Then we compared the number of patients in each category and randomly selected patients from groups with a larger number to equalize the number of patients among them. Patients whose sCr$\geqq 1.2$ mg/dl at least once during hospitalization were considered as those having the occurrence of the nephrotoxicity and their sCr<1.2 mg/dl on discharge as having recovered from the nephrotoxicity. The rates of nephrotoxicity and the rates of recovery among the three groups were compared (Chi-square test). Logistic regression was performed to evaluate associations between the

dichotomized outcomes (observed nephrotoxicity) and the CDDP dose or CDDP total accumulated doses.

Results : Totals of 521 patients in the CDDP group, 1993 patients in the Non-CDDP group and 6157 patients in the Control group were identified in this study. However, significant differences were found on gender, age, sCr level on admission and LOS among the three groups. Through the processes of stratification and randomly selecting patients, 454 patients in each group were identified. The diversities of characteristics among them were eliminated.

The rate of observed nephrotoxicity was 28.0%, (127/454) in the CDDP group, 19.6% (89/454) in the Non-CDDP group and 19.4% (88/454) in the Control group, respectively. The rate in the CDDP group was significantly higher than both of that in the Non-CDDP group (P=0.0031) and that in the Control group (P=0.0023). The rate in the Non-CDDP gourp was not significantly different from that in the Control group (P=0.9332). The Risk Ratio (RR) was 1.43 (95% CI : 1.13-1.81) between the CDDP vs the Non-CDDP group, 1.44 (95% CI : 1.14-1.83) between the CDDP vs the Control group and 1.01 (95% CI : 0.78-1.41) between the Non-CDDP vs the Control group. The recovery rate was 69.3% (88/127), 61.8% (55/89) and 69.3% (61/88) in the three groups, respectively (P=0.903). The observed CDDP nephrotoxicity was dose associated (P=0.037) but not total accumulated doses associated (P=0.144).

Historical cohort study has not been widely used in the past due to it generally required large-scale medical databases. The lack of other alternative exposures has also been argued as a common problem of this kind of study design. In this study, as we have massive clinical data pooled in the CDW, we were able to solve this problem by forming the Non-CDDP group as an alternative exposure for enhancing the analyses.

〔 総　　括 〕

We have estimated the observed cisplatin nephrotoxicity in our hospitalized adult cancer inpatients by using CDW. It occurred in about 28.0% of patients. The observed nephrotoxicity was associated with CDDP dose but not associated with CDDP total accumulated doses, and is considered to be reversible at the end point of therapy (discharge). The method of applying historical cohort design by using CDW is useful for evaluating medication adverse effects.

論文審査の結果の要旨

病院情報システムの薬剤処方データ、血液検査データなどを診療情報データウェアハウスに格納し、新しい臨床研究の方法論を医療情報学的に確立しつつある。本研究は、成人入院患者（2000年1月から2004年12月31日）を対象に、Cisplatin投与群、非投与群、コントロール群を抽出し、薬剤と腎毒性の関係を解析した。方法は、総数8671件から性、年齢、在院日数を三群に有意差がないように調整し、各群454名のデータベースを作成した。クレアチニン値を目的変数、Cisplatin 一日量、総投与量などを説明変数にロジスティック回帰分析などを行った結果、腎毒性の発症率、薬剤投与中止後の回復率など新しい知見を得ることができ、診療情報データウェアハウスの臨床疫学研究への有用性を明らかにすることができた。よって本研究は学位の授与に値すると考えられる。