Drug-food Interaction of Ceftriaxone Used in Treatment of Different Diseases with Food containing - Calcium Products for In-patients of the Didactic Parturition Hospital of Al-Zahraa'

Saad Saleem Raheem

Department of Community Health ,College of Health and Medical Technology,kufa, Foundation of Technical Education, University of Al- Furat al- Awsat techniques
pharmasaad@yahoo.com

Abstract

The study was carried on 402 clinical cases of in-patients pediatric patients of the Dedacticparturition Hospital of Al-Zahraa'. They were treated with different medications [(244 clinical cases of male in-patients and 158 clinical cases of female in-patients, table 1) against different diseases infection, table 1 (Meningitis, Pneumonia, Enteritis and Bronchitis)]. The data partook of the drug-food interaction between a drug (Ceftriaxone) with calcium containing - food (milk, which are including artificial and normal lactation) (table 1) (figure 1). The results showed that the four factors (normal lactation, artificial lactation, treatment by Ceftriaxone and non treatment by Ceftriaxone groups) had the same average effect on the gender (male and female) of peadiatric in-patients of the Dedactic Parturition Hospital of al-Zahraa'. Superiority was of (treated by Ceftriaxone) group according to (non treated by Ceftriaxone)] group on each the gender (male and female) (p<0.05), In other hand there were no significant differences (p<0.05) between (normal and artificial lactation) on the in-patients (male and female) and both of them had the same average effect on the in-patients peadiatric in the Dedicated Hospital of Al-Zahraa'. These results were calculated by two way analysis (ANOVA and F-test analyze).

Objectives

Studying the drug - food interactions between the antibiotic (Ceftriaxone) that it is used in treatment of different diseases and calcium containing-products (milk), and their effect of both of them on the gender (male and female) that they have artificial and normal lactation for in-patients of Dedactic Parturition Hospital of al-Zahraa'.

Materials and Methods

The data were taken randomly from the peadiatric in-patients' files of the Statistics Department of the Didactic Parturition Hospital of al-Zahraa'. These data included 402 clinical cases of in-patients [(244 clinical cases of male pediatric in-patients and 158 clinical cases of female pediatric in-patients, table1). They were treated with different medications against different diseases (four disease states)]. These data were analyzed statically with SPSS 8.0 statistical package (ANOVA- analysis of variance - two way analysis), also the values between groups were compared by independent sample (F- test). (P) values less than or equal to 0.05 has been evaluated as statistical significant [**Wayne, 2010**].

Conclusions

Ceftriaxone and non treatment by Ceftriaxone groups of pediatric in-patients have the same average effect on the gender (male and female) of peadiatric in-patients of the Didactic Parturition Hospital of al-Zahraa' .Superiorities of groups of the pediatric in-patients that treated with antibiotic (Ceftiaxone) according to the another groups on the gender (male and female).

Keywords*: Drug-food interaction, Food containing - Calcium Products, Ceftriaxone .*

الخلاصة

نفذت هذه الدراسة على 402 حالة سريريه للمرضى الأطفال الراقدين في مستشفى الزهراء التعليمي للولادة والذين عولجوا بمختلف العلاجات [(244 حالة سريريه للمرضى الذكور و 158 للمرض الإناث , جدول 1) ضد مختلف الأمراض,جدول 1 (التهاب السجايا, التهاب الرئة, التهاب الأمعاء و التهاب القصبات)]. تناولت البيانات التداخل الدوائي – الغذائي بين للسفترياكسون مع الغذاء المحتوي على الكالسيوم (الحليب, والمتضمنة الرضاعة الطبيعية والرضاعة الاصطناعية), جدول1. بينت النتائج بأن العوامل المؤثرة الأربعة (الرضاعة الطبيعية والاصطناعية والمجاميع المعالجة بالسفترياكسون والغير معالجة به) تمتلك نفس التأثير على جنس المرض الراقدين في المستشفى (الذكور والإناث) والذين يعانون مختلف الأمراض. تفوق المجموعة المعالجة بالسفترياكسون بالمقارنة بالغير معالجة بنفس الدواء على الجنس من الذكور والإناث تحت مستوى المعنوية (p<0.05), من ناحية أخرى ليست هناك فروقات معنوية (p<0.05) للمجاميع

(الرضاعة الطبيعية والاصطناعية) أي أنه ليست هناك تأثير لهم على الذكور والإناث للمرضى الراقدين الأطفال في مستشفى الزهراء التعليمي للولادة, حسبت هذه النتائج بواسطة اختبار way (F-test ,analysis) .

الأهداف : دراسة التداخل الدوائي – الغذائي بين المضاد الحياتي (السفترياكسون) والمستخدم في علاج العديد من الأمراض المختلفة مع الغذاء المحتوي على الكالسيوم (الحليب) وتأثير كل منهم على الجنس (الذكور والإناث) من المرضى الأطفال الراقدين في مستشفى الزهراء التعليمي للولادة.

المواد وطرائق العمل : أخذت هذه البيانات من ملفات المرضى الأطفال الراقدين في مستشفى الزهراء التعليمي للولادة, وقد تضمنت هذه البيانات (402 حالة سريريه للمرضى الأطفال الراقدين [(244 حالة سريريه للمرضى الأطفال الذكور الراقدين و158 للمرضى الأطفال الإناث, جدول 1) والذين عولجوا بالعلاجات المختلفة ضد العديد من الأمراض المختلفة (أربعة حالات مرضية). خَللت هذه البيانات إحصائياً الرزمة الإحصائية (SPSS 8.0– ANOVA– analysis of variance – two way analysis), وكذلك تم مقارنة القيم بواسطة العينة المستقلة (test –F). إن القيم كانت اصغر أو تساوي 0.05 والتي قيمت على أساس الفروقات الإحصائية [Wayne, 2010] .

الاستنتاجات : المجاميع من المرضى المعالجين بالسفترياكسون والغير المعالجين به لها نفس معدل التأثير على جنس المرضى (الذكور والإناث) من المرضى الأطفال الراقدين في المستشفى. تفوق المجاميع من المرضى الأطفال المعالجين بالمضاد الحيوي (السترياكسون) على المجاميع الأخرى وذلك بتأثيرها كلا الجنسين من المرضى الراقدين في مستشفى الزهراء التعليمي للولادة.

الكلمات الدالة : التداخل الدوائي–الغذائي, الغذاء المحتوي على الكالسيوم, سفترياكسون .

Introduction

Many medicines have powerful ingredients that interact with the human body in different ways. Diet and lifestyle can sometimes have a significant impact on drugs. A drug interaction is a situation in which a substance affects the activity of a drug, i.e. the effects are increased or decreased, or they produce a new effect that neither produces on its own. Typically, interactions between drugs come to mind (drug-drug interaction). However, interactions may also exist between drugs and foods (drug-food interactions), as well as drugs and herbs (drug-herb interactions) **(Frankel ,2003).** The most important interactions are those associated with a high risk of treatment failure arising from a significantly reduced bioavailability in the fed state. Such interactions are frequently caused by chelation with components in food. In addition, the physiological response to food intake, in particular, gastric acid secretion, may reduce or increase the bioavailability of certain drugs **(Nekvindová , and Anzenbacher, 2007; Schmidt *et al.,* 2002).** Drug interactions can alter the pharmacokinetics and/or pharmacodynamics of a drug. The pharmacodynamic interaction may be additive, synergistic, or antagonistic effects of a drug. Drug interactions (DIs) represent an important and widely under recognized source of medication errors **(Hansten, 2004). Frankel (2003) and Ayo *et al.,*(2005)** have confirmed that The gastrointestinal absorption of drugs may be affected by the concurrent use of other agents that have a large surface area upon which the drug can be absorbed bind or chelate, alter gastric pH **(Schmidt *et al.,* 2002; Nekvindová , and Anzenbacher, 2007),** alter gastrointestinal motility, or affect transport proteins such as P-glycoprotein. A reduction only in absorption rate of a drug is seldom clinically important, whereas a reduction in the extent of absorption will be clinically important if it results in sub therapeutic serum levels **(Hansten, 2004).** The interaction of natural products and drugs is a common hidden problem encountered in clinical practice. The interactions between natural products and drugs are based on the same pharmacokinetic and pharmacodynamic principles as drug-drug interactions. Several fruits and berries have recently been shown to contain agents that affect drug-metabolizing enzymes **(Molden and Spigset, 2007).** Grapefruit is the most well-known example, but also sevillian orange, pomelo and star fruit contain agents that inhibit cytochrome P450 3A4 (CYP3A4), which is the most important enzyme in drug metabolism **(Kirby and Unadkat 2007).**

The study of drug-drug, food-drug, and herb-drug interactions and of genetic factors affecting pharmacokinetics and pharmacodynamics is expected to improve drug safety and will enable individualized drug therapy. Drugs can show their efficacy only if administered in appropriate quantity with appropriate combination of drugs and foods and at appropriate time **(Itagaki *et al.,* 2008).** In contrast to the easy access to information on drug-drug interactions, the information about food-drug interaction is not always available conveniently. It is a difficult and complex problem to accurately determine the effects of food and nutrients on a particular drug **(Joshi and Medhi, 2008).**

Objectives

Studying the drug – food interactions between of the antibiotic (Ceftriaxone) that it was using in treatment of different diseases and calcium containing-products (milk), and effect of them on the gender (male and female) that they have artificial and normal lactation for in-patients of Didactic Parturition Hospital of al-Zahraa'. This article aims to help the healthcare professionals specially physicians and pharmacists and patients to become more knowledgeable about drug and food interactions .

Materials and Methods

The data have been taken randomly from the peadiatric in-patients' files of the Statistics department in the Didactic Parturition Hospital of al-Zahraa'. These data included 402 clinical cases of in-patients [(244 clinical cases of male in-patients and 158 clinical cases of female in-patients , table 1). They were treated with different medications against different diseases (four disease states)]. The data were analyzed statically with SPSS 8.0 statistical package (ANOVA- analysis of variance - two way analysis), also the values between groups were compared by independent sample (F-test). (P) values less than or equal to 0.05 were evaluated as statistical significant [**Wayne, 2010**].

Results

The results show the four factors (normal lactation, artificial lactation, treatment by Ceftriaxone and non treatment by Ceftriaxone groups) have the same average effect on the gender (male and female) of peadiatric in-patients of the Didactic Parturition Hospital of al-Zahraa' that they are suffer from the different diseases (Meningitis, pneumonia, Enteritis and Bronchitis) ($F_{calculated}$ (6.45) is less than $F_{tabulated}$ (15.44)-ANOVA – two way analyze), so that there are no significant differences ($p<0.05$) among four groups factors with the gender (male and female) of in-patients of the Didactic Parturition Hospital of al-Zahraa' (table 1) (figure 1) [**Wayne, 2010**]. There are significant difference ($p<0.05$) between groups of (treatment and non treatment by Ceftriaxone) and this result means superiority of (treated by Ceftriaxone) factor is more than (non treated by Ceftriaxone) factor on each of the gender of pediatric in-patients. These results are calculated by F-test analysis), in other hand there are no significant differences ($p<0.05$) between (normal and artificial lactation) that have the same average effect on the peadiatric in-patients (male and female) according to Statistic model (F-test analysis) (table 1) [**Wayne, 2010**].

Table 1, shows data of drug-food interaction of Ceftriaxone with calcium containing products of pediatric in-patients that have normal and artificial lactation, according to the gender (male and female).

Disease	Gender		Normal Lactation		Artificial Lactation		Treatment by Ceftriaxone		Non Treatment by Ceftriaxone	
	male	female	male	Female	male	female	male	Female	male	female
Meningitis	87	52	17	20	11	5	55	15	4	12
Pneumonia	50	15	11	14	12	2	15	20	12	14
Enteritis	58	17	10	9	15	4	25	2	8	2
Bronchitis	49	21	14	7	3	2	20	36	12	4
Total	**244**	**158**	**52**	**40**	**41**	**13**	**115**	**73**	**36**	**32**
Total	**402**		**92**		**54**		**188**		**68**	

Analyzed by ANOVA-two way analysis, and independent sample (F-test analysis), the significant differences ($p < 0.05$) .
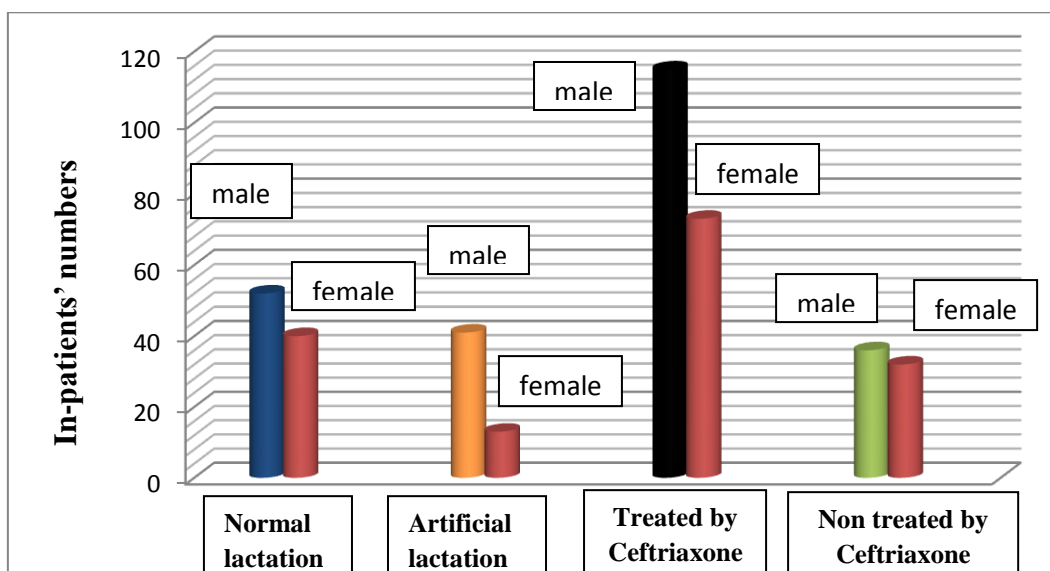

Figure (1), shows the drug – food interaction and its effect of it on the gender (male and female) of peadiatric in-patients.

Discussions

We find agreement with previous study where **Emily** *et al.,* **2010** carried out their trial on 104 cases of patients database. They have found different clinical cases of pneumonia and meningitis and proved the avoiding treatment by medications with another products that contain divalent ingredients (ca^{+2}, mn^{+2}) such as (milk), also such interactions are frequently caused by chelation of antibiotic (Ceftriaxone- $C_{18}H_{18}N_8O_7S_3$) with components in food. In addition, the physiological response to food intake, in particular, gastric acid secretion, may reduce or increase the bioavailability of certain drugs **(Schmidt** *et al.,* **2002; Nekvindová, and Anzenbacher, 2007). (Frankel ,2003) and (Ayo** *et al.,* **2005)** have confirmed that the gastrointestinal absorption of drugs may be affected by the concurrent use of other agents that have a large surface area upon which the drug can be absorbed bind or chelate**,** alter gastric pH **(Nekvindová , and Anzenbacher, 2007; Schmidt** *et al.,* **2002).** This study also agrees with results which show that even a little quantity of milk containing extremely small amounts of calcium severely impair the absorption of the drug, so that the presence of this metal ion should

be carefully controlled in order to avoid decreasing the available cephalosporin. The defferences in effectiveness between male and female about this study are due to different pharmacokinetics and pharmacodynamics, more likely to report adverse events than among of them, or take more medications than another, also may be due to cultural or social variation (**Fishman,Wick, andKoenig, 1999**), and other biological processes (**Chen, 2000).**

Food-drug interactions may reduce the bioavailability of drugs taken after meals (negative food effects). However, enteric-coated tablets that start to disintegrate when they reach the middle-to-lower region of the small intestine could reduce negative food effects. Results indicate that food-drug interactions are avoided by separating the main absorption site of drugs from that of food components (**Tanno** *et al.,* **2008).**

Conclusions

1. There is drug – food interaction between Ceftriaxone and Food containing - Calcium Products (milk) of peadiatric in-patients of the Dedactic Parturition Hospital of al-Zahraa'.
2. Ceftriaxone and non treatment by Ceftriaxone groups have the same average effect on the gender (male and female) of peadiatric in-patients of the Dedactic Parturition Hospital of al-Zahraa' .
3. Superiority of groups of the pediatric in-patients that treated with antibiotic (Ceftiaxone) is more than another groups on the gender (male and female).
4. There are no significant differences ($p<0.05$) between (normal and artificial lactation) in case of effecting on the in-patients (male and female) and both of them have the same average effect on the peadiatric in-patients.

References

Ayo JA, Agu H, Madaki I (2005). Food and drug interactions: its side effects. Nutr Food Sci;35(4):243-252 .10.1108/00346650510605630 [Cross Ref]

Bertram G.,Susan B., Anthony J.,(2009). Basic and Clinical Pharmacology. 11th eddition, University of California, San Francisco.ppt1139, 661t .

Chan E, McLachlan AJ, (1994) . Stereochemical aspects of warfarin drug interactions: use of a combined pharmacokinetic-pharmacodynamic model. Clin Pharmacol Ther; 56:286–294.

Emily S. Dennis W. Raisch,Charles L. Bennett, John S. Esterly, Tischa Becker, Michael Postelnick, June M. McKoy, Steve Trifilio, Paul R. Yarnold, and Marc H. Scheetz. Evaluation of a Potential Clinical Interaction between Ceftriaxone and Calcium. Antimicrob Agents Chemother. Apr **2010**; 54(4): 1534–1540. Published online Jan 19, **2010.** doi: 10.1128/AAC.01111-09 PMCID: PMC2849391

Fishman, J. R., M. A. Wick, and B. A Koenig. (1999). The use of "sex" and "gender" to de. ne and characterize meaningful differences between men and women. Agenda for Research on Women's Health for the 21st Century, vol. 1, 15–18. NIH Publication No. 99-4385.

Frankel EH. (2003). Basic Concepts. In: Hand book of food-drug Interactions, McCabe BJ,   Frankel EH., Wolfe JJ (Eds.) pp. 2, CRC Press, Boca Raton, 2003.

Hansten PD. (2004). Appendix II: important interactions and their mechanisms, In: Katzung BG. (2004). editor, 09th edn, (2004) Basic and clinical Pharmacology, McGraw hill, Boston pp 1110.

Itagaki, S., Ochiai, A., Kobayashi, M., Sugawara, M., Hirano, T., Iseki, K.(2008). Interaction of Coenzyme Q10 with the Intestinal Drug Transporter P-Glycoprotein. J Agric Food Chem. 27; 56(16):6923-7. [PubMed]

Joshi R, Medhi B (2008). Natural product and drugs interactions, its clinical implication in drug therapy management. Saudi Med J. Mar;29(3):333-339 [PubMed]

Kirby BJ, Unadkat JD (2007). Grapefruit juice, a glass full of drug interactions? Clin Pharmacol Ther. May;81(5):631-63310.1038/sj.clpt.6100185 [PubMed] [Cross Ref]

Nekvindová J, Anzenbacher P. (2007). Interactions of food and dietary supplements with drug metabolising cytochrome P450 enzymes. Ceska Slov Farm. Jul;56(4):165-173 [PubMed]

Molden E, Spigset O 2007. Fruit and berries–interactions with drugs. Tidsskr Nor Laegeforen. Dec;127(24):3218-3220 [PubMed]

Schmidt LE, Dalhoff K. Food-drug interactions (2002). Drugs;62(10):1481 150210.2165/00003495-200262100-00005[PubMed] [Cross Ref]

Wayne W. Daniel, (2010). "Biostatics Basic Concepts and Methodology for the Health Sciences," John Wiley &Sons(Asia) Pte Ltd.