(12)

EFFECT OF CLINICAL PHARMACOKINETICS CONSULTATION SERVICE ON THE USE OF GENTAMICIN SERUM LEVELS AT A UNIVERSITY HOSPITAL

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Absrtract: To evaluate the impact of the clinical pharmacokinetics consultation service on the use of gentamicin serum levels at a university hospital, a retrospective and two post-intervention audits were carried out over a total period of 38 months. Analysis of gentamicin orders from different hospital's wards was performed. Percentage of the uninterpretable results and the percentage of sub-therapeutic and toxic levels were compared for the retro- spective and post-intervention parts of the study. In addition, acceptance of the pharmacokinetics service recommendations by the medical team were determined. A significant reduction of the total assay wastage was achieved in both post-intervention audits. Inappropriate timing of blood samples reached zero in the second post-intervention part of the study. Acceptance of the clinical pharmacist's recommendations by the medical team increased to reach 85% of overall recommendations. It is concluded that introduction of the clinical pharmacokinetics consultation service had a positive impact on the use of gentamicin assay.It decreased total assay wastage and gained increasing acceptance by the medical team.

INTRODUCTION

Gentamicin is a commonly used drug in the management of serious infections, especially those due to gram negative bacteria. The relatively narrow therapeutic index of gentamicin coupled with a high degree of variability in total drug clearance demonstrate the need for therapeutic drug monitoring (TDM) (1). Drug monitoring has become an increasingly important diagnostic and monitoring tool in the last decade. It aims at promoting optimum treatment by ensuring that the drug plasma concentration falls within a therapeutic range, below which the drug is ineffective and above which toxicity may occur (2-3). However, numerous audits of TDM involving gentamicin have shown a high incidence of drug assay requests that were not indicated, blood samples that were drawn incorrectly, or results that were inappropriately used (4,5).

The appropriate use of serum drug levels offers the benefit of optimizing and individualizing drug therapy. However, the inappropriate use can lead to dangerous and costly therapeutic decisions based on erroneous results (6-9).

In this report we tried to evaluate gentamicin drug levels ordering pattern in king khalid University Hospital (KKUH) and assess the impact of Clinical Pharmacokinetics services on the appropriate use of this laboratory procedure.

METHOD

The study was conducted in a 500 bed, non-profit, university-affiliated, tertiary care hospital in Riyadh, Saudi Arabia. All patients were adults (i .e.,> 20 years of age), receiving gentamicin for more than 72 hours. The Clinical Pharmacokinetics consultation service was implemented after a baseline audit of serum drug levels utilization had been performed.

In the retrospective part of the study, patients population included all inpatients admitted to king khalid University Hospital (KKUH) for a period of twenty months (during 1991-1993)with justifiable gentamicin levels ordered by the physician (s) in charge at that time. All wards were included except MICU, SICU, PICU and NICU that had a Clinical Pharmacist in-charge at the time of the audit. Besides, orders that were not documented correctly in the patient's logbook were not included. Analysis of the gentamicin orders from different wards was performed with ranking of number of orders and number of inappropriate serum levels.

Serum levels of gentamicin were considered uninterpretable if no two levels (pre and post) were ordered (10,11). Trough level was considered toxic if > 2 mg (12-14) and sub-therapeutic peak was considered if < 4 mg% (15,16).

The post-intervention study was carried out for a period of twenty seven months after the introduction of the clinical pharmacokinetics service (during 1994-1996). It consisted of two consecutive post-intervention audits. The first post intervention audit covered a period of nine months (during 1994) and the second post intervention audit was carried over a period of eighteen months (during 1995-1996).

The consultative clinical pharmacokinetics service was carried out by a clinical pharmacist rounding with the infectious disease team in the routine and referral rounds in the hospital and performing full clinical pharmacokinetics monitoring service of gentamicin therapy. All patients receiving gentamicin therapy for > 72 hrs and who were monitored by the clinical pharmacists involved in the study. A multi-disciplinary approach involving patients, laboratory, nurses and physicians as regards dosing, level drawing, assay and monitoring was adopted. The administration protocol for gentamicin and sampling time for plasma for assay were standardized throughout the hospital. The aminoglycoside dose was given in 50 ml of compatible intravenous fluid as a 30 minute intravenous infusion. The " trough" sample was scheduled for 30 minutes before commencement of the infusion (with limits of 0 to 30 minutes before the dose) and the "peak" sample 30 minutes after completion (with limits of 21 to 45 minutes after stopping the infusion).

Serum gentamicin assays were performed by the clinical pharmacokinetics laboratory using the fluorescence polari-

zation immunoassay (TDX, Abbott Laboratories, North Chicago, USA), which is a validated standardized method for gentamicin serum level determination.

All the data was stored and analyzed in the data base management system " FoxPro 6.2". Percentage of un-interpretable results besides percentage of sub-therapeutic and toxic levels were compared for both the retrospective and post intervention parts of the study. Besides, acceptance of pharmacokinetics recommendations of the clinical pharmacist by the medical team was determined.

RESULTS

In the retrospective part of the study, ranking of wards was made in terms of number of gentamicin levels and in terms of number of assay wastage (un-interpretable and sub-therapeutic or potentially toxic levels). Interestingly, those top five wards in terms of number of assay wastage were not from the top five words in terms of the number of assays (Table 1).

As demonstrated in table 2, the retrospective audit of 2848 levels for 2080 patients on gentamicin showed a ratio of 1.37 (pre and post) per patient. Meanwhile, the ratio was (1.46) of 79 levels for 54 patients for the first and (1.3) of 85 levels for 65 patients for and second post-intervention audits respectively. The first post-intervention audit showed that 1.27% of the samples were taken at wrong times with the peak sample collected before complete distribution of gentamicin (30 minute after the dose). In the second post-intervention audit, there were no mistakes in the sampling time, while, this parameter could not be audited in the retrospective part of the study. Assay wastage in terms of un-interpretable assay results was quite high in the pre-consultative audit representing 7.2% of all serum assays compared to 2.53% in case of the first post-intervention audit. Interestingly there was no wastage of the assay in terms of un-interpretable assay results during the second post-intervention audit. Utilization of the Chi square test showed that a significant difference between the pre and post intervention results could be detected only at the second post intervention audit ($P < 0.05$).

During the first post-intervention part of the study, 2.53% of the peak levels were sub-therapeutic and 1.27% of the trough levels were potentially toxic. During the second post-intervention audit, 0.59% of the peak levels were sub-therapeutic and 1.18% of the trough levels were potentially toxic. Meanwhile, in the pre-intervention audit, 6.2% of the peak levels were sub-therapeutic while 7.9% of the trough levels were potentially toxic.

Therefore, the total assay wastage could be easily calculated to be 21.3% in the pre-intervention, 6.33% in the first post intervention and 1.77% in the second post intervention parts of the study. Significant difference between the pre and post intervention audits could be detected using the Chi square test $P < 0.05$).

Seventy four percent (74%) of the recommendations made by the clinical pharmacist were followed and acted upon during the first year after initiation of the consultative service. Acceptance of the recommendations made by the clinical pharmacist increased to 85% during the second year of the service.

DISCUSSION

In the retrospective part of the study data showed that those wards with highest assay wastage did not have the highest rank in terms of number of patients (un-interpretable or outside the normal therapeutic range). This observation showed that highly congested words and increased patient number did not necessarily mean more mistakes in terms of appropriate use of the gentamicin assay.

It seems that the introduction of the aminoglycoside consultative service did not decrease the number of the ordered levels. The number of the ordered levels per patient was 1.37 in the pre-consultative audit compared to 1.5 at the first post-intervention audit and 1.3 at the second post-intervention audit. Such observation comes in agreement with previous studies that documented no decrease in the number of assay orders of gentamicin after initiation of Pharmacokinetics consultative service (17-19).

Introduction of the aminoglycoside Pharmacokinetics consultative service produced beneficial effects on the use of gentamicin assay. Such observed decrease in the percentage of un-interpretable assay results (although it was not statistically significant) from 7.2% in the pre-intervention audit to 2.53% in the first post-intervention part can represent a good saving in the cost of monitoring. Assay wastage was minimal during the second post-intervention period when the service achieved a higher degree of maturity and better communication within other members of the medical process, leading to a statistically significant reduction in the assay wastage ($P < 0.005$).

Other savings after the introduction of the service could be attributed to decreased percentage of sub-therapeutic and toxic levels with less cost of dosing manipulation, frequent levels monitoring and Clinical outcomes of nephrotoxicity. However, we found it impractical to try to calculate the exact cost saving due to the complexity of the Clinical situation. Besides, there are many factors that could contribute to the Clinical outcome and cost of Hospitalization especially in the retrospective part of the study.

Increased acceptance of the clinicians to the Pharmacokinetics recommendations from 74% in the first post-intervention audit to 85% in the second post-intervention audit reflected more confidence and reliability of the Clinical Pharmacokinetics consultative service.

The results of this study showed that the introduction of a Pharmacokinetics consultative service has a positive impact on the use of gentamicin assay. This study reflected also the gradual nature of improvement in the efficacy of the service by time. It also demonstrated the need for further improvement in the efficacy of the service and consequently better reliability and acceptance from other health care professionals.

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Table 1: Rank of the top five wards in terms of assay wastage and in terms of number of patiients.

ward	Ranking in terms of * assay wastage	Ranking in terms of * number of patients
21B	1	22
33B	2	19
23B	3	13
31A	4	15
33A	5	11

* Total number of wards=23

Tablell : Comparison of results from audits of gentamincin levels use at KKUH

Number of levels Number of patients (ratio)	Pre 2848/2080 (1.1)	Post I 79/54 (1.5)	Post II 85/65 (1.3)
Assay wastage in terms of :			
a) Uninterpretable assay results.	7.2%	2.53%	0
b) Results out of the therapeutic levels (%) :			
- Subtherapeutic	4.8%	5.1%	1.18%
- Toxic	6.2%	0	2.33%
Total :	18.2%	5.1%	0
- Appropriate timing of blood saples.	--	1.27%	85%
- pharmacokinetic recommendations were made with clinical acceptance.	-	74%	

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الملخص العربى

يهدف هذا البحث الى دراسة تأثير الخدمة الاستشارية لحركية الدواء الإكلينيكية على استعمال قياسات نسبة دواء الجنتاميسين فى الدم للمرضى بالمستشفى الجامعى. تم إجراء تقييم استرجاعى بالاضافة الى عدد اثنان تقييم مستقبلى بما غطى فترة ٣٨ شهر تم فيها تحليل مستويات دواء الجنتاميسين فى الدم من مرضى بأجنحة المستشفى المختلفة . تم مقارنة النسبة المئوية للنتائج الخاصة تشمل قراءات نسبة الجنتاميسين فى الدم التى لا يمكن ربطها بالوضع الاكلينيكى بالاضافة الى القرارات التى تقع تحت المستوى العلاجى اوعند المستوى السام للدواء. بالاضافة الى ذلك تم تقييم مدى قبول الفريق العلاجى للخدمة الاستشارية لحركية الدواء بالمستشفى . أظهرت نتائج الدراسة انخفاضا فى الفقد الكلى فى طلبات التحاليل لتحديد نسبة معدل الجنتاميسين فى الدم وذلك بعد ادخال خدمة حركية الدواء الاكلينيكية فى المستشفى بالاضافة الى ذلك بلغ سوء التوقيت فى اخذ عينات الدم الى الصفر فى الجزء الثانى من الدراسة بعد ادخال خدمة حركية الدواء وقد ارتفعت نسبة تقبل أعضاء الفريق الطبى لتوصيات الصيدلى الاكلينيكى الى ٨٥٪ من مجموع التوصيات.

من هذه الدراسة يمكننا الاستنتاج ان الخدمة الاستشارية لحركية الدواء تمكنت من إحراز تأثير ايجابى على استعمالقياسات معدل دواء الجنتاميسين بالدم ، فلقد تمكنت من تقليل الفقد فى طلبات القياس واحرزت قبول متزايد عند الفريق الطبى .