Available online at www.elixirpublishers.com (Elixir International Journal)

Pharmacy

Elixir Pharmacy 109 (2017) 48002-48007

ISSN: 2229-712X

Compliance to resupply date of Gutt. Ciclosporin 0.5% preparation after the implementation of SMS (Short-Messaging System) reminder system

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ARTICLE INFO

Article history:
Received: l6 May 2017;
Received in revised form:
5 August 2017;
Accepted: 16 August 2017;

Keywords
Gutt Ciclosporin 0.5%,
Morisky scale,
Adherence.

ABSTRACT

This study was designed to determine the compliance of patient to resupply date in using 'short-messaging-system' as medication collection reminder system.Patient receiving Gutt Ciclosporin 0.5% was included in the study. Patient with collection date of Gutt. Ciclosporin 0.5% preparation from January 2015 to August 2015 was classified as pre-intervention data while collection date from September 2015 to April 2016 was classified as post-intervention data. The intervention consists of messaging patient 1 day before of the production day. Patient's collection date was recorded. The difference in production date and collection date was weighted and categorised according to modified Morisky scale. There was significant improvement in patients adherence to collection of Gutt Ciclosporin $\chi 2=6.19$, P=0.012 on production date after implementation of the SMS. The compliance means score have increased by from 7.28±2.09 to 7.61±2.39. There was also increment by 47.8% to High adherence category and reduction by 47.8% in low adherence category post-implementation. Furthermore there was reduction of 80% in production wastage. This study has shown that the implementation of SMS will have significant improvement in adherence by patient to collection Day 0. Furthermore there was increase in patients Morisky adherence and cost saving in production.

1. Introduction

The ocular exterior covers the entire epithelial surface of the cornea, limbus, and conjunctiva. The primary purpose of this tissue t was to maintain corneal clarity. Changes of corneal clarity, such as a reduction of adequate tear film, can contribute to visual disturbances.

Inflammations have been to know to be the main mechanism to cause of injury to ocular surface[1, 2]. The initial injury to ocular surface could be of any etiology including tear film insufficiency, chemical injury, or hypersensitivity mechanisms. Once inflammation was present, ocular injury was increased by mediators released from damaged cells and invading leucocytes. Hence, eyes with ocular surface disease progress in cyclic period of inflammation and injury.

Currently, the anti-inflammatory treatment of ocular surface disorders mainly relies on topical or systemic corticosteroids. Cyclosporine was an established immunomodulation drug that was originally used to prevent rejection after organ or tissue transplantation. Ciclosporin has also been employed as a treatment for a variety of autoimmune diseases, including those with ocular involvement.[3, 4]

Cyclosporine was a neutral, hydrophobic, cyclic metabolite of fungal-derived peptide that inhibits T-cell activation and consequently inhibits the inflammatory cytokine production (selective inhibition of IL-I). Its major clinical effect was the perturbation of expression of interleukin-2 (IL-2) by helper T cells, preventing the proliferation of T cells[4]. Cyclosporine, a powerful T-cell modulator, inhibits the T-lymphocytes from producing the toxic mediators. By preventing the activation of the T-cells, cyclosporine eliminates the source of the cyclic tear gland tissue destruction and release of chemical mediators that lead to the patient's signs and symptoms.

In ophthalmology, topically applied Ciclosporin in various oil based solvents was first used to inhibit experimental corneal allograft reaction in the early 1980s[5, 6]; this was followed by human studies[7]. Later, the drug proved useful for patients with various inflammatory ocular surface disorders[8].

A topical Ciclosporin was commercially distributed as Restasis®. This ophthalmic emulsion (0.05% cyclosporine [Allergan, Inc. Irvine, CA, USA]) was preservative free packaged in unit-dose vials. Restasis has been a prescription drug in the US since April 2003 when it was approved by the FDA for patients whose tear production was presumed to be suppressed due to ocular inflammation associated with KCS.

Patient who partially or don't respond to Ciclosporin 0.05% eye drop might need higher concentration of eye drop preparation at 0.5% .due to inaviability of commercial preparation of Gutt Ciclosporin 0.5% , pharmacist have to compound the preparation .

Pharmacokinetic limitation was that Ciclosporin could not be prepared in a formulation based on aqueous ophthalmic vehicles because of both its hydrophobicity and its low aqueous solubility. Therefore, the agent was dissolved in vegetable oils[9]. Due to issues with the stability and sterility of the preparation, compounded preparation only have a shelf life of 2 week.

Eye drop preparations are prepared once every two week or when the particular eye drops are low in stock. Patients are receiving preparation with short different expiry date and

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are required to come frequently to Pharmacy to get their prescription refilled.

Patient are not adhering to TCA date and hence are getting short expiry date preparation and this lead to frequent visit to pharmacy to refill their eye drop preparation . Patient's compliance to the medication and the safety issue of using expired medication was also an issue.

An observational study by Elizabeth Koshy[10] have shown that SMS reminders for ophthalmology outpatient appointments was associated with a reduction of 38% in the likelihood of patients not attending their appointments, compared to no appointment reminder . A systemic review[11] of 29 studies shows that all studies except one reported a benefit from sending reminders to patients prior to their appointment.

A study by Vervloet M[12] of SMS reminders to improve adherence to oral medication in type 2 diabetes patients , over the six-month study period, have shown that patients receiving SMS reminders took significantly more doses within predefined time windows than patients receiving no reminders. The majority of patients reported positive experiences with SMS reminders. SMS reminders improves adherence of type 2 diabetes patients, especially the precision with which patients follow their prescribed regimen, and was well accepted by patients.

A randomized control study[13] of satisfaction of short messaging service have shown that Participants in the intervention group showed a 2.2-fold higher probability of having a decrease in missed doses compared with participants in the control group. Use of SMS significantly affected the rates of taking medicine on schedule.

There was a need to develop a system to communication with patient to inform on the collection date of new batch of eye drop preparation. The hypothesis was with using 'short-messaging-system (SMS)' as medication collection reminder system for Gutt Ciclosporin 0.5%, patients improvement to adherence to collection date will increase, as well as to supply patient with long expiry date preparation. Eventually to reduce the prescription refill to 2 times a month.

General objective

1. To determine the adherence of patient to resupply date in using 'short-messaging-system' as medication collection reminder system.

1.2.2 Specific

1. To determine the patients adherence to resupply date before and after the implementation of SMS (short-messaging system) reminder system.
2. To determine the number of patients visit to hospital to Day 0 before and after the implementation of SMS (short-messaging system) reminder system.

2. Material and Methodology

Study design

This was an audit of compliance among patients receiving Gutt Ciclosporin 0.5% eye drop of using 'short-messaging-system (SMS)' as medication reminder collection system in Hospital Seri Manjung.

Sample size

The data was collected through universal sampling. All the patient receiving Gutt Ciclosporin 0.5% was included in the study

Study duration

The researchers will collect data from May-June 2016.

Patient's collection date of Gutt. Ciclosporin 0.5% preparation from January 2015 to August 2015 was classified as pre-intervention data while collection date from September 2015 to April 2016 was classified as post-intervention data.

Inclusion criteria

I) Patient prescribed with Cyclosporine 0.5% eye drop

Exclusion criteria

I) Patient's with prescribed Cyclosporine 0.5% eye drop duration to end before the expiry date of the medication.

II) Patients who selected to SPUB their medication to different location.

Data collection

Pre-implementation data collection (January 2015 to August 2015)

I. All prescription with Gutt Ciclosporin 0.5% eye drop received at pharmacy was screened and study subject was selected according to the inclusion and exclusion criteria

II.Selected subject was dispensed with prescribed eye drop (stock) and given next TCA based on the expiry date of the eye drop preparation. A patient's collection card was prepared for pharmacist/pharmacist assistant to record patient name and next TCA.

III.When new batch of eye drop medication was prepared. Respective eye drop was packed according to patient's collection card (table 1) for the particular patient. Patient's adherence to the collection date was scored according to score calculation (refer section 2.1).

Table 1. Gutt Ciclosporin 0.5% card.

Patient Name :		Contact No:	
Rx order date:		**Clinic TCA date :**	
Preparation date	Expiry date	Collection date	Remarks

2.1 Score calculation

Step 1: Patient collection will be given value according to the day that they collect the medication (Table 1). For example: Day 0 is defined as the collection of the medication on production day. Day 1 is defined as the collection of the medication 1 day after the production day and so on.

Table 2. Adherence value [14].

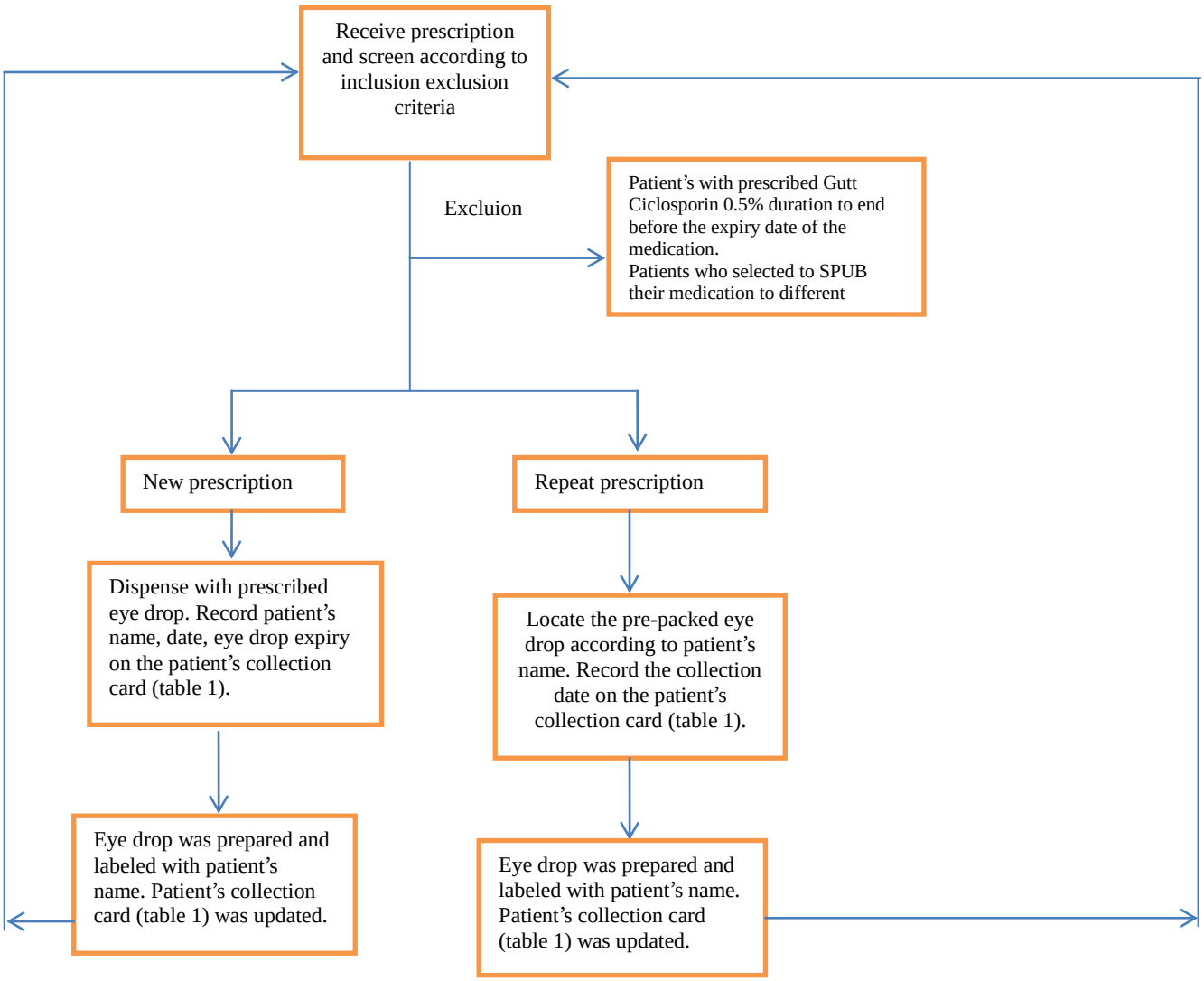
value	Definition
1	collect medication on day 0
0.75	collect medication on day 1-day3
0.5	collect medication on day 4-day7
0.25	collect medication on day 8-day14
0	did not come

Adapted from Morisky medication adherence scale question no8"

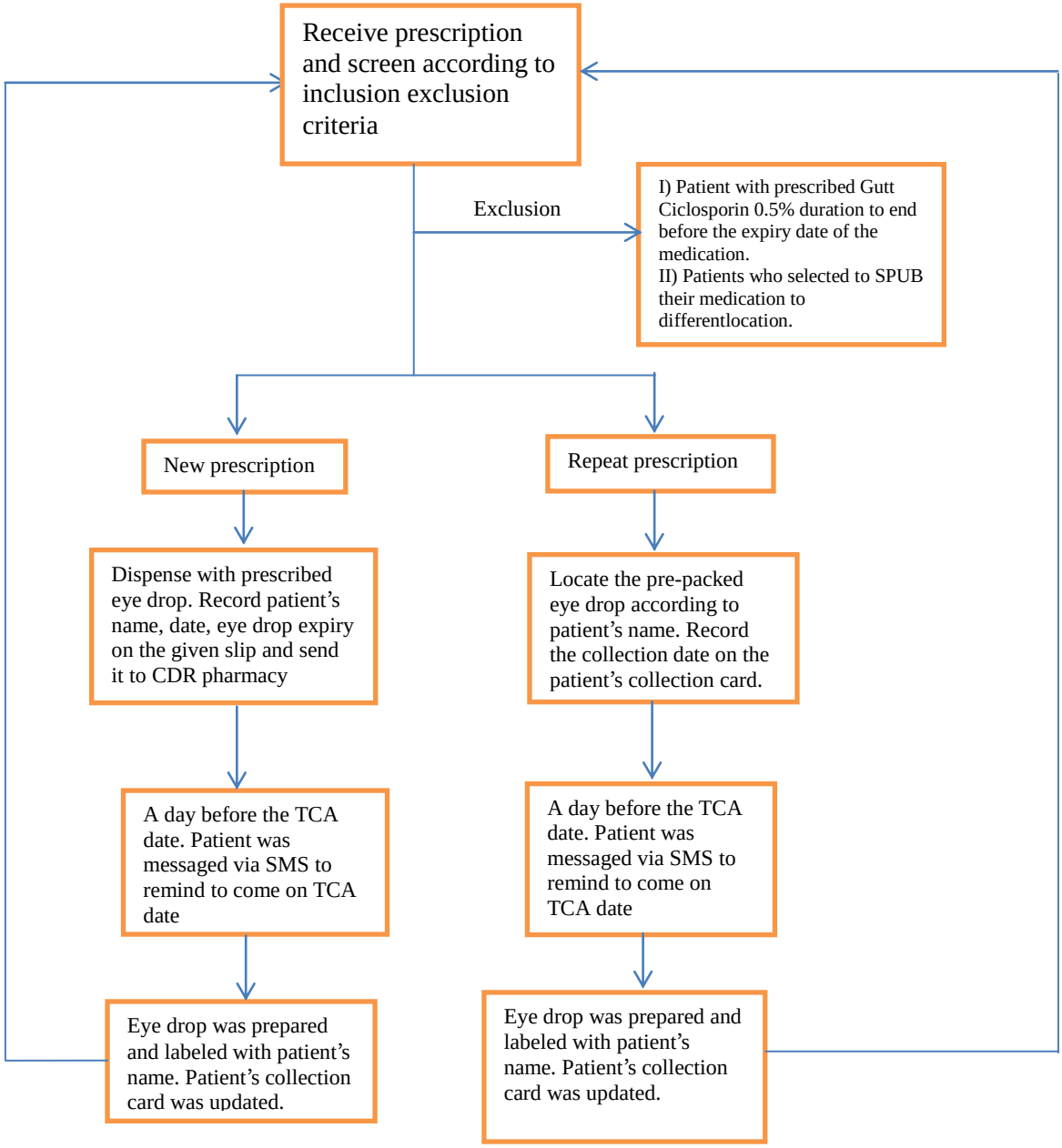
Step 2: The adherence value will be tabulated and calculated according to the formula below.

$$Compliance\ Score^{14} = \frac{[1-\{(\text{no of preparation})-(\text{sum score of each preparation collection})\}]x10}{No\ of\ preparation}$$

Pre-i implementation data collection January 2015-August 2015



Post-implementation data collection september 2015 to April 2016



Step 3: The compliance score will be categorised into adherence category according to the score.

Morisky Score legend[3]

<6	low adherence
6 to <8	medium adherence
>8	high adherence

Post-implementation data collection (September 2015 to April 2016)

I. All prescription with Gutt Ciclosporin 0.5% eye drop received at pharmacy was screened and study subject was selected according to the inclusion and exclusion criteria

II. Selected subject was dispensed with Gutt Ciclosporin 0.5% eye drop (stock) and given next TCA based on the expiry date of the eye drop preparation. A patient's collection card was prepared for pharmacist/pharmacist assistant to record patient name, next TCA and contact information (hand phone number).

III. A day before the preparation of eye drop. patient was messaged with the following :

Salam sejathera. Ubat anda akan luput pada DD/MM/YYYY. Anda boleh mengambil baki ubat baru anda pada DD/MM/YYYY bermula pukul XX.XX pm . Ubat yang baru disediakan akan luput pada DD/MM/YYYY . Sekian terima kasih

Translated to English:

Greeting's. Your medicine will expire on DD / MM / YYYY . You can take your new medicine on DD / MM / YYYY starting at XX.XX pm . The new medicine will be expire on DD / MM / YYYY . Thank you

IV.After new batch of eye drop medication was prepared. Gutt Ciclosporin 0.5% eye drop was packed according to patient's collection card (from II). Patients adherence to the collection date was scored according to score calculation (refer section 2.1) .

3. Ethical consideration

Ethical approval has been obtained from the National Medical Research and Ethics Committee (MREC) of Ministry of Health (MOH) via the National Medical Research Register (NMMR). The research was approved unconditionally with exemption from MREC full board review.

4. Result and Discussion

Table 3. Demographic characteristic of patients.

Characteristics(N=13)	N (%)
Age in years , median, IQR	12 , 10-32
Gender	
Male	12 (92.3%)
Female	1(7.7%)
Ethnicity	
Malay	8 (61.5%)
Chinese	3(23.1%)
Indian	1(7.7%)
Others	1(7.7%)
Prescription duration , mean ± SD (n=36)	13.7 ± 2.45
Min	2 week
Mode	2 week
Max	31 week

A total of 13 patients were involved in the study (table 3). The participant's age ranged between 9 year to 63 year. The median age (n=13) was 12 years. The maximum age was 63 years and the minimum age is 9 years. The middle 50% fell between age of 12 years and 32 years. Majority of patients are male (92.3%) and Malay (61.5%). Participant was prescribed with minimum follow up of 2 week and maximum of 31 week. Mean prescription durations 13.7 week ± 2.45 and mode of the prescription was 2 week (n=10, 28%).

Table 4. The number of preparation and collection pre and post implementation.

pre-implementation		post-implementation
Number of preparation	40	81
number of collection	35	80

Table 5. Production cost pre and post implementation.

pre-implementation		post-implementation
cost of preparation	RM95	RM95
total cost of preparation	RM 3800	RM 7695
total cost collection	RM 3325	RM 7600
wastage	RM 475	RM 95

A total of 40 preparations were done pre-implementation with 35 collections and 81 preparations post-implementation with 80 collection date (Table 4). There was 5 (12.5%) excessive production before implementation and only 1(1.23%) excessive production. although total cost have increased by 100% post implementation the reduction in excessive production have reduced the wastage cost by 80% from RM 475 to RM 95(Table 5). The increment in total cost was due to increment in total number of production and better adherence of patients to collection day.

Table 6. Number of preparation collection according to collection day.

pre-implementation		post-implementation
Day 0	5	30
Day 1	11	21
Day 2	7	19
Day 3	3	6
Day 4	0	0
Day 5	1	2
Day 6	1	0
Day 7	2	0
Day 8	0	0
Day 9	0	0
Day 10	3	0
Day 11	0	0
Day 12	2	2
Day 13	0	0
Day 14	0	0
No collection	5	1
total	40	81

There were significant relationship between patient who collected their medication on production day (day 0) between pre-implementation and post-implementation, χ^2=6.19, P=0.012. However this relationship was not significant between patients who collect their medication between production day and production day + 1 (Day 0 + Day 1) and between pre implementation and post implementation, χ^2=3.26, P=0.07

According to this result, short-messaging-system can significantly improve patient adherence to collection date if the facility or patient need the collect the drug on the particular date (collection must be on day 0). However if the facility or patient are flexible with the collect date (collection can be on day 0 and after that), than the use of SMS to remind patient will not improve patients adherence to collection date.

Table 7.Compliance score between pre and post implementation.

pre-implementation Compliance score ± SD		post-implementation Compliance score ± SD
min	4.5	2.0
max	10.0	9.17
mean	7.28±2.09	7.61±2.39

Table 8. The adherence category pre and post implementation.

Adherence	pre-implementation (n=10)	post-implementation (n=9)
Low	4 (40%)	2 (22.2%)
Medium	3 (30%)	-
High	3 (30%)	7 (77.8%)

According to Table 7, the mean compliance score have increased by 4.5% from 7.28±2.09 to 7.61±2.39. According to modified Morisky scale, the score more than 8 will categorized into high adherence category. There has been an increment of 47.8% in high adherence category from 3 patients pre-implementation to 7 patients post-implementation (Table 8). Better adherence to collection date will be beneficial to the patient as they will be getting Gutt Ciclosporin with longer expiry date.

Table 9: Adherence target achievement pre and post implementation.

pre-implementation		post-implementation
No	7 (70%)	2(22.2%)
Yes	3(30%)	9(77.8%)

The target of this study was to evaluate if the implementation of SMS will increase patients adherence. Patient who achieve high adherence was set to: YES and patient who was in low adherence and medium adherence category was set at: NO (table 9). There was increment of 47.8% from 3 patients in high adherence category pre-implementation to 9 patients in high adherence category post implementation. There was also decrement by 47.8% of patient who failed to achieve target from pre intervention to post intervention.

5. Study limitation

The study sample was too small in size N=13. Statistical analysis failed to show any significant result. Furthermore the gender was heavily biased towards male (n=12).

6. Recommendation and Future consideration

This study should aim for higher number of participant and stratified participant in race and gender category

7. Conclusion

This study have shown that there was significant improvement in patients adherence to collection of Gutt Ciclosporin χ^2=6.19, P=0.012 production date after implementation of the SMS. There was also increment by 47.8% to High adherence category and reduction by 47.8% in low adherence category post-implementation. Furthermore there was reduction of 80% in wastage.

8. Acknowledgement

We would like to thank the Director General of Health Malaysia for his permission to publish this article. The authors are thankful to the team of our study, hospital Seri Manjung and CRC department who supported in all aspect to conduct this study.

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