Impact of pre-packaging antimalarial drugs and counselling on compliance with malaria treatment at Port Moresby General Hospital
Adult Outpatient Department

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SUMMARY

We investigated the impact of pre-packaging antimalarial drugs and counselling on compliance with treatment of malaria at the Adult Outpatient Department of Port Moresby General Hospital. Adult patients who were prescribed standard antimalarial drugs following clinical and microscopic diagnosis of malaria were randomly assigned to one of three groups: an intervention group, where pre-packaging and counselling instructions were applied; control group A, with counselling but no pre-packaging; and control group B, with neither counselling nor pre-packaging. Patients were interviewed on two occasions, day 1 of treatment and day 4 post treatment. Of a total of 436 patients, 322 patients (179 males and 143 females) completed the study. Our data indicate an increase of 18% in compliance with treatment in the intervention group and 16% in control group A, when compared with control group B. While compliance with treatment was gender independent, the language spoken and used for giving instructions and counselling may have influenced patients' behaviour on prescribed medication. The results of our study indicate that a simple pre-packaging system and proper counselling could improve compliance with antimalarial drug treatment. As an additional beneficial observation, pre-packaging is likely to eliminate errors and possible contamination of the products during dispensing.

Introduction

Malaria continues to be a major health problem in the world (1), including Papua New Guinea. In spite of the establishment of standard malaria treatment guidelines in Papua New Guinea (2), malaria is listed as the second leading cause of mortality and morbidity (3). Resistance of *Plasmodium falciparum* to the first-line antimalarial drugs, chloroquine and amodiaquine (4-6), led to the establishment of new combination therapies for malaria in 2000 (7,8). Patient non-compliance with malaria treatment regimens may also be another factor contributing to the high morbidity and mortality of malaria in Papua New Guinea, as observed elsewhere (9). Drug resistance and non-compliance with malaria treatment are factors likely to impact on disease management costs and on the selection of antimalarials for drug resistance respectively.

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Studies on pre-packaging of antimalarial drugs in a number of countries have demonstrated a reduction in incidence of severe malaria as a result of improved compliance (9-12). Sirima et al. (9) in Burkina Faso showed a reduction in the risk of progression to severe malaria by 6% when pre-packaging was used. Studies by Anssah et al. in Ghana (10) and of blister-packed daily doses by Shwe et al. in Myanmar (11) also showed improved compliance with pre-packaging. Despite these benefits, medicine pre-packages have been found to be relatively more expensive than dispensing from bulk product. Pre-packaged drugs also require relatively larger storage space than bulk products. Although these requirements constitute some of the cost implications of the pre-package systems, pre-packaging of drugs is an efficient way to provide effective and safe medication and information to patients (12).

We believe that a simplified method of administering drugs using a pre-packaging system could improve compliance, and hence reduce morbidity and costs. Pre-packaging of the prescribed antimalarial drugs into an organized regimen with clearly delineated daily doses and special counselling instructions could promote patient compliance. In addition, the acceptability of the pre-package by the hospital dispensing staff and other caregivers is a critical attribute in achieving the overall goal of improved patient compliance. Therefore, in this study we investigated the impact of pre-packaging antimalarial drugs and counselling on compliance with malaria treatment at the Adult Outpatient Department of Port Moresby General Hospital (PMGH) using a simple pre-packaging design. We also investigated the acceptability of the pre-packaging concept among health professionals involved in prescribing and dispensing of medicines.

Methods

The study was conducted at the Outpatient Department of Port Moresby General Hospital, the nation’s referral hospital located in the capital city of Port Moresby. The study was an open study where patients, after consenting to participate, were randomly assigned to one of three groups: the intervention group, where pre-packaging and counselling instructions were applied; control group A, with counselling but no pre-packaging; and control group B, with neither counselling nor pre-packaging. Selection criteria included adult patients who were prescribed standard antimalarial drugs following clinical and microscopic diagnosis of malaria, and patients who spoke and understood one of the three commonly spoken languages, English, Tok Pisin or Motu. A guardian (close relative) was requested where a patient was unable to read and/or understand any one of the languages. Patients who indicated their inability to return for follow-up interview on day 4 of the study were excluded. Antimalarial drug treatment followed standard national malaria treatment guidelines for uncomplicated malaria, which consisted of chloroquine (25 mg/kg over three days) plus a single dose of sulphadoxine-pyrimethamine combination (3,7,8).

The pre-packaging of antimalarial drugs and instructions on how to take the medications were prepared as depicted in Figure 1. Briefly, a transparent polyethylene bag of about 10 x 18 cm dimension was partitioned into three sections by heat-sealing and stapled on to a hard card base. Names of the drugs and instructions for use were printed on the card under each section of the polyethylene bag, which were colour coded differently. Appropriate tablet quantities of the malaria treatment regimen were counted and packaged such that each of the three sections of the package contained treatment supplies for one day.

Patient interviews were conducted in two stages in the language spoken and understood by the participating patients. The interview and data collection were carried out by trained assistants using a structured and pre-validated questionnaire. Before the first interview, patients were given their appropriate medication in packages, the intervention group received the pre-package with special instructions, while control groups A and B received drug packages with and without special instructions, respectively. In order to ensure uniformity in counselling, the research assistants (intern pharmacists) read to the patients a written script containing information, questions and special instructions. This activity was repeated across patients and across time. The special instructions included information on the risks associated with malaria if it was not quickly
and appropriately treated, and on the need to adhere to medication directions, to complete treatment, to seek further medical attention if adverse effects were experienced and to return to the Outpatient Department if there was no improvement after completion of medication. Patients were interviewed thereafter employing a structured pre-validated questionnaire. The second follow-up interview was conducted on day 4 of starting treatment, from which compliance and cure rates were assessed. Compliance was rated ‘good’ on the basis of patients’ ability to remember instructions and to complete the medication as prescribed or directed; compliance was ‘poor’ if patients were unable to recall instructions, or failed to complete or adhere to the medications as prescribed. Patients’ perceptions of feeling better and cured or not cured were recorded, and the Outpatients clinical notes were also used to confirm whether patients were cured of malaria or not.

Health professionals (n=40) who were involved in prescribing or dispensing were

Figure 1. Design of the pre-package with labels and instructions.
also interviewed, in order to understand their attitude and behaviour towards pre-packaging of antimalarial drugs for malaria treatment, using a separately structured pre-validated questionnaire. All the data collected from this study were analyzed using the WHO Epi-info computer program. Chi-squared tests were performed on comparable data and the level of statistical significance was set at a p value of less than 0.05. The School of Medicine and Health Sciences Research Committee and the Medical Research Advisory Committee, Papua New Guinea Ministry of Health, gave the ethical approval.

Results

The study was conducted between March and July, 2003. A total of 436 patients, 242 (56%) males and 194 (44%) females, were recruited into the study initially, but 322 patients (179 males and 143 females), representing 74% of initial enrolment, completed the study. Table 1 provides demographic data on patients who were enrolled initially, and data on those who completed the follow-up interview (returned on day 4 for interview) are provided in Table 2. Randomization resulted in gender distribution being relatively balanced among the groups. A similar proportion of patients from each group (intervention group 29%, 38/129; control group A 26%, 39/151; and control group B 24%, 37/156) did not return for follow-up interview on day 4.

Patients’ demographics revealed a predominantly Tok Pisin speaker population (97%). Patients who were able to speak and read in English accounted for 44% while only 23% could speak and read Motu. This might reflect the preferable language spoken in Port Moresby. Interestingly, more than 90% of patients in control group B did not understand or have any knowledge about malaria, despite the commonality of the disease. While instructions on dosage were understood by almost all the patients in the three groups, a significant number of patients in control group B still remained oblivious to the dosage instructions (Table 1).

Compliance ratings did not differ much between the intervention group and control group A, but a marked difference was observed between the intervention group and control group B. However, this did not influence cure rates significantly among the three groups. This might have been due to the small sample size. In order to understand the reaction of the health professionals to pre-packaging, 40 health professionals (nursing and dispensing staff) were interviewed. The majority of the health professionals interviewed (95%, 38/40) were in favour of pre-packaging, and 70% (28/40) indicated support for the system because such a system is clearly instructive and convenient.

Discussion

The results of our study indicate that a simple pre-packaging system with appropriate counselling could improve compliance with antimalarial drug treatment. The intervention group and control group A, both with special instructions, demonstrated improved compliance ratings of 18.0% and 16.4% respectively when compared to control group B (Table 2). Although compliance of the intervention group was slightly higher than that of control group A, the difference was not statistically significant. This implies that counselling may also have played a major role in improving compliance in both the intervention group and control group A. The fact that in control group B patients were not subjected to counselling and consequently 94% of them did not have prior knowledge about malaria (Table 1) seems to explain their low level of compliance of 76% (Table 2). These findings stress the need for drug information to be given to the patients by the dispensing staff and patient counselling by prescribing caregivers. Knowledge about the function of drugs and good communication of instructions and information by the physician to the patient have been found to be among important factors that reduced medication errors by patients and thus enhanced compliance (13).

Our findings are comparable to compliance rates obtained from similar studies elsewhere (14,15). For example, in Ghana the pre-packaging of antimalarial tablets and syrups demonstrated an increase in compliance by 21.5% and 22.1% respectively (14). Quingjun et al. (15), who studied the effect of drug packaging on patients’ compliance with treatment for Plasmodium vivax malaria in China, showed that blister packages improved compliance by about 20%. Our data and those of others clearly show that simple pre-packaging with
TABLE 1

NUMBER OF PATIENTS ENROLLED, LANGUAGE PROFICIENCY AND KNOWLEDGE ABOUT MALARIA AND DRUG USAGE IN EACH STUDY GROUP

<table>
<thead>
<tr>
<th></th>
<th>Intervention Group (N=129) (%)</th>
<th>Control Group A (N=151) (%)</th>
<th>Control Group B (N=156) (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>73 (56.6)</td>
<td>78 (51.7)</td>
<td>91 (58.3)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>56 (43.4)</td>
<td>73 (48.3)</td>
<td>65 (41.7)</td>
<td>p &gt;0.05</td>
</tr>
<tr>
<td>Language</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>English</td>
<td>57 (44.2)</td>
<td>57 (37.7)</td>
<td>77 (49.4)</td>
<td></td>
</tr>
<tr>
<td>Tok Pisin</td>
<td>129 (100)</td>
<td>143 (94.7)</td>
<td>153 (98.1)</td>
<td></td>
</tr>
<tr>
<td>Motu</td>
<td>38 (29.5)</td>
<td>10 (6.6)</td>
<td>52 (33.3)</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>Understood about malaria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>85 (65.9)</td>
<td>115 (76.2)</td>
<td>9 (5.8)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>44 (34.1)</td>
<td>36 (23.8)</td>
<td>147 (94.2)</td>
<td>p &gt;0.05*</td>
</tr>
<tr>
<td>Understood instructions on drug usage</td>
<td></td>
<td>142 (94.0)</td>
<td>113 (72.4)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>122 (94.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>7 (5.4)</td>
<td>9 (6.0)</td>
<td>43 (27.6)</td>
<td>p &lt;0.001**</td>
</tr>
</tbody>
</table>

*Intervention vs Control Group A: p >0.05
**Intervention vs Control Group B: p <0.001

appropriately labelled instructions increases compliance.

Though our study was limited to assessment of pre-packaging and counselling on the compliance outcome, there are other variables that have not been given consideration in the study design. Language is an important variable and all medicines prescribed at the Port Moresby General Hospital are usually labelled with directions written in the English language. Yet our data (Table 1) show that only 44% of the study population felt competent to have their instructions/information given in English while the majority (97%) of the study population’s preferable language was Tok Pisin. Although our findings are contrary to the usual practice, our study took into consideration the possible impact of language in understanding directions and thus both oral instructions and printed instructions on the pre-packages were made specifically in languages most understood by the patients. From our analysis, it is not possible to discern how language could have impacted on compliance. However, the finding does not rule out an indirect impact of language, including impacts of other factors such as verbal information and
TABLE 2

NUMBER OF PATIENTS REVIEWED, TREATMENT OUTCOME AND COMPLIANCE RATING FOR EACH GROUP IN THOSE WHO COMPLETED THE FOLLOW-UP INTERVIEW

<table>
<thead>
<tr>
<th></th>
<th>Intervention Group (n=91) (%)</th>
<th>Control Group A (n=112) (%)</th>
<th>Control Group B (n=119) (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>51 (56.0)</td>
<td>59 (52.7)</td>
<td>69 (58.0)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>40 (44.0)</td>
<td>53 (47.3)</td>
<td>50 (42.0)</td>
<td>p &gt;0.05</td>
</tr>
<tr>
<td>Treatment outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cured</td>
<td>77 (84.6)</td>
<td>96 (85.7)</td>
<td>93 (78.2)</td>
<td></td>
</tr>
<tr>
<td>Not cured</td>
<td>14 (15.4)</td>
<td>16 (14.3)</td>
<td>26 (21.8)</td>
<td>p &gt;0.05</td>
</tr>
<tr>
<td>Compliance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>86 (94.5)</td>
<td>104 (92.9)</td>
<td>91 (76.5)</td>
<td>p &gt;0.05*</td>
</tr>
<tr>
<td>Poor</td>
<td>5 (5.5)</td>
<td>8 (7.1)</td>
<td>28 (23.5)</td>
<td>p &lt;0.001**</td>
</tr>
</tbody>
</table>

*Compliance rating Intervention vs Control Group A; p >0.05
**Compliance rating Intervention vs Control Group B; p <0.001
Compliance rating Control Group A vs Control Group B; p <0.001

instructions about the disease itself and effects inherent in the properties of the drug(s) taken, on compliance. We took cognisance of such factors as explaining to the patient how the medication works, frequency of doses, major side-effects and possible adverse reactions, and treatment monitoring procedures, as having important roles in achieving compliance outcomes. These factors, although not evaluated in detail in the study, have been qualitatively investigated by many workers (14-19). From this study it was clear that almost three-quarters (74%) of the intervention group preferred the new pre-package system. In addition, the majority of health workers (70%) interviewed supported the introduction of the new pre-package, while 30% of them were doubtful and undecided.

There are important pre-packaging factors not covered in this study that must be considered in future studies if final development and scaling-up of the new pre-packaging is to be pursued. Stability of the tablet product in the new pre-package form must be studied in order to ensure the product will maintain its integrity and efficacy for a determined length of time. To minimize extensive studies on stability, a known and reputable manufacturer of tablets or capsules employing blister packs could be contracted to package the antimalarial drugs in suitable blister format mimicking the proposed intervention pre-package system. Blisters have been increasingly used to improve compliance (14-19). This trend is likely to continue, given the other benefits associated with blister packs such as prolonged stability of the product. Despite these benefits, drug pre-packages have been found to be relatively more expensive than dispensing from bulk product. They also require much greater storage space than bulk products. Although pre-packages have manufacturing and storage space cost implications, they are efficient in the provision of effective and safe patient management
including shortening dispensing time, reducing the number of dispensing staff, and eliminating errors and excessive exposure of products to potential contaminants during dispensing (12).

Hence, a cost-benefit analysis taking into account the costs of the pre-packages and storage space requirements versus benefits of outcomes must be carried out in the future. One would expect viable outcomes favouring the use of pre-packages given also the stability-related advantages discussed above. These will also improve patient safety, which is of paramount importance.

We therefore conclude that the results of our study indicate that a simple pre-packaging system with proper counselling in the language understood by patients could improve compliance with antimalarial drug treatment. In addition, these results may be used as an important indicator for improving compliance in malaria treatment with antimalarial drugs in this locality, thus reducing the opportunity for development of drug resistance, treatment failure and management costs. However, before the pre-package system is applied on a wider scale a thorough cost-benefit analysis would be warranted.

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REFERENCES

9 Sirima SB, Konate A, Tiono AB, Console N, Cousins S, Pagnoni F. Early treatment of childhood fevers with pre-packaged antimalarial drugs in the home reduces severe malaria morbidity in Burkina Faso. Trop Med Int Health 2003;8:133-139.
18 Rand AD, Michelle R. The impact of language as a