Patient perspectives on multiple medications versus combined pills: a qualitative study

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Received 9 August 2005 and in revised form 25 September 2005

Summary

Background: A growing number of patients are taking multiple medications. Unfortunately, adherence may fall as drug numbers and procedural complexity increase. While there are plausible theoretical reasons why combining pills might improve non-adherence, patients’ attitudes are unknown.

Aim: To explore attitudes and practices to medication regimens among patients already in receipt of multiple medications, and to assess whether a combined tablet would be perceived as advantageous.

Design: Qualitative study.

Methods: Ninety-two men and women aged >40 years currently receiving both antihypertensive and cholesterol-lowering medications took part in 14 focus groups.

Results: Drugs were seen as unwelcome but necessary. Some took drugs flexibly by changing dose timing, thereby increasing the complexity of their regimen. A routine was seen as the key to coping with multiple medications, although it was sometimes threatened by changes in prescriptions and life circumstances. While some participants welcomed a combined pill, there was uncertainty about whether a combination that mirrored their current doses would be available. There were also concerns about tablet size, allergies, the attribution of side-effects, timing of tablets throughout the day, and the ability to alter dose levels.

Conclusions: While some patients would be willing to try a combined pill and would appreciate the associated convenience, they are likely to have a number of concerns that prescribers should address. Willingness to move to combined therapy may be hindered if drug combinations that mirror personalized and trusted regimens are not available.

Introduction

General practitioners see large numbers of patients with hypertension and raised cholesterol. Since most are aged over 40, and many have comorbidities such as diabetes, daily drug regimens can be large and complex. Furthermore, the introduction of a link between funding and evidence-based targets under the new GP contract1 may increase prescribing, as practitioners strive to achieve recommended levels of control. Unfortunately, a number of studies have suggested that adherence may fall as drug numbers and procedural complexity increase, potentially threatening clinical outcomes.1,2

There is both empirical evidence and a plausible theoretical explanation for why combining separate...
drugs into a single tablet may improve adherence, and thus clinical outcome. Reducing the discomfort of swallowing multiple tablets is likely to lower dissatisfaction with care, which in turn has been linked to non-adherence. A number of studies have also shown that reducing the procedural complexity of drug regimens can improve adherence. How and why this occurs is unproven, although it seems likely that simpler regimens are easier to understand, harder to forget, and impact less on daily activities. Patients’ attitudes to changing to combined tablets are currently unknown, and the recent debate on the potential merits of ‘polypill’ formulations suggests that new research is warranted. We therefore conducted this study to explore (i) whether patients taking multiple medications would welcome taking a combined antihypertensive and cholesterol-lowering drug in order to reduce the number of medications they take, and (ii) the likely reasons why combination therapy might or might not be successful in improving adherence.

Methods

We conducted 14 focus groups with people aged between 45 and 72 years who were receiving current prescriptions for both hypercholesterolaemia and hypertension. Focus groups were chosen for three reasons. Firstly, they would allow individuals to comment on views expressed by others that they would not otherwise have thought about. This was particularly important given that some discussion was to focus on a possible future experience (the use of a combined pill) rather than past or current practices or experience. Secondly, we believed that focus groups would enable individuals to see that their possible ‘non-adherent’ medication behaviours were not unusual, thereby facilitating a more open discussion of past and current practices. Finally, focus groups enabled us to explore the views of a larger number of individuals than in-depth interviews would have allowed in the time available for the study.

Our sample was drawn from urban and rural practices in Tayside, Scotland and the South East of England. Patients who were in receipt of both antihypertensive drugs and lipid-lowering drugs were identified from the MEMO prescribing database in Scotland and the Primary Care Data Quality programme, largely based in the South-East of England. Individuals were then purposively sampled in order to ensure a range of age, sex and use of drugs for either primary or secondary preventive reasons (Table 1). Approximately half of the sample were taking medication for primary prevention and half as a secondary prevention measure. We did not exclude people with comorbidities. Consequently, almost half of the sample suffered from diabetes. Letters were sent to potential participants to inform them of the study; a researcher (AS or RD) then telephoned them to provide further details and answer any questions. In Tayside, five groups were conducted in GP surgeries and three in a room at the Medical School, University of Dundee. All groups in the south-east were conducted in a general-practice setting.

Data collection

Focus groups lasted between 45 and 75 min, and were conducted by RD and BW in Scotland and AS and IC in England. Two pilot focus groups were conducted prior to the study in order to identify appropriate ways of generating dialogue. Discussion initially centred around people’s knowledge of their hypertension and hypercholesterolaemia before moving on to the medications that they were being prescribed, how these were being taken, barriers to use as recommended, and whether prescribers or manufacturers could do anything to improve things (Box 1). The possibility and potential benefits of a combined pill was only raised if a group had not already suggested it.

Analysis

All focus groups were transcribed in full, and the analysis was based on the transcripts. We used ‘Framework’ for our analysis. This method has been used widely, although it originated in the context to applied policy research. It includes five analytic stages: familiarization (reading and rereading the transcripts); identifying a thematic framework (a key list of codes); indexing (applying these codes to the transcripts); charting (creating tables of quotes and comments to compare data from across interviews or groups); and mapping and interpretation (the integration of the key findings into a meaningful whole). These stages of analysis were facilitated by the use of the software package NVivo. The data gathered from the interviews were

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wide-ranging; here we focus only on medication use, and the possible benefits and problems associated with a combined pill. The index was created in three stages. RD and AS checked all transcripts for accuracy. BW and RD then read and produced initial themes and concepts for the Scottish data; IC and AS did the same for the English groups. The researchers then met, compared codes and ideas, and produced a common coding framework. This was then applied to a small number of the groups, revised and then applied to the whole dataset. This enabled the relationship between themes to be explored fully across the entire dataset, and deviant cases identified in order to refine and test the findings.16

Results

Participants’ drug regimens varied widely. Different medications, combinations and doses were taken for different clinical conditions and side-effects at a varied number of times throughout the day. Pill numbers ranged from a low of 6 per day to $>20$; individuals who reported larger numbers of pills often had difficulty in recalling the exact number of tablets they were taking. Almost all respondents described the central importance of developing a stable daily routine organized around social activities, work and essential domestic tasks (Box 2). Some drugs were taken at fixed times, while others were varied depending upon their possible impact on planned daily activities. For example, ‘water tablets’ tended to be taken flexibly in order to avoid being ‘caught out’ (requiring the toilet when none was available).

Pill numbers, dissatisfaction and adherence

While some participants did not like the general idea of ‘putting chemicals into their body’, almost all respondents had reconciled themselves to its long-term necessity. However, the experience of taking the drugs and implementing the regimen was frequently characterized by discomfort or underlying anxiety (Box 3: Angus, Frank).

Side-effects (sleep disturbance, bodily aches, nausea, indigestion and heartburn, and excessive urination) were the most commonly reported aspect of discomfort or dissatisfaction with the regimen. Marginally less common, but more strongly felt and unanticipated by the researchers, was the difficulty and discomfort associated with opening large
amounts of packaging and organizing each day’s pill combinations. Much of this centred on coping with the increasing number of medications that were packaged in sealed, blistered sheets (Box 3: Norman).

Less common and less strongly felt were fears about addiction, increased drug interactions (as numbers increased) and a concern that some drugs may be ‘counteracting each other’ (Box 3: Iain, Frank). The experience of swallowing did not arise as a major area of discomfort or dissatisfaction.

Despite these areas of discomfort and difficulty, there was little indication to suggest that they were a significant cause of non-adherence. Most participants regarded their drugs as essential for their health and well-being, while others said it was important to do what the doctor said. Discomfort was largely tolerated, although a few individuals shared strategies for reducing them. Swallowing difficulties were addressed by chewing or spreading tablets throughout the day, while pharmacists were sometimes asked to transfer tablets from sealed sheets to bottles.

Drug numbers and complexity

The complexity of prescribed regimens varied with the number of medications, number of pills, dose frequency, the combination and degree of fixed or flexible consumption points, and the changeability of drugs, doses and tablet appearance over time (Box 2). Complexity could be potentially managed if a routine was developed; this was often supported through the use of memory aids and drug dispensers. However, a routine was dependent upon stability in both prescribing and the key anchor points in the individual’s daily life. A shift in either of these routine structures caused problems. More complex regimens demanded more routine, but the instability of drug type, dose frequency and colour and shape of individual medications that characterized this complexity also made routines more difficult to develop and maintain. The reported relationship between complexity and low adherence therefore appeared to stem from the need for more frequent behavioural change, threatening stability, damaging routine and therefore lowering adherence.

While patients had little control over most of the elements that resulted in complexity, they did alter dose frequency and the times of the day when drugs were taken. This meant that there was an important difference between the complexity of a prescribed regimen and the complexity of the patient’s drug-taking routine. While some patients simplified routines by reducing dose frequency, others made it more complex by spreading pills out over the day. The latter strategy was used to avoid having to
swallow a large number of tablets at once, to limit side-effects and to manage key daily events (Box 2: Anthony). The groups stressed the importance of ‘doing what the doctor says’ but still talked about these variations (and swapped ideas and strategies) as if they were unproblematic. Most respondents therefore implied that they were broadly free to manage their medications throughout the day as long as all the pills were consumed. Adherence was defined in terms of whether drugs were taken rather than when or how.

**Attitudes to combined tablets**

When asked what improvements could be made to their current medication regimens, two groups suggested the idea of combined pills without prompting. Many respondents were initially favourable towards the idea, and suggested that it would be more convenient, might reduce mistakes, may be easier to remember and could possibly save money on prescription charges (Box 4: Ron, John, Greg).

Some individuals had no problem with their current regimen and were thus less enthusiastic, while others raised concerns about tablet size, allergies, tolerability, reduction in daily flexibility, a possible increase in the consequence of consumption mistakes, and the difficulty of knowing which drug was responsible for particular side-effects. Individuals on a larger number of pills perceived less benefit, since a combined tablet would only marginally reduce the total needed to be taken each day.

After a few moments of consideration and discussion almost all groups expressed scepticism as to whether pills could be manufactured that covered all the drug and dose combinations of participants (Box 4: Nigel). This therefore raised the question as to whether they would be willing to trade off an element of their unique current regimen for a reduction in complexity and the associated benefits. The stability of a regimen that was tolerable, manageable and apparently effective appeared to be of central importance to patients. Consequently, most respondents were not keen to change,
although some said that they would if their doctor recommended it.

Discussion

Main findings

While many respondents were not keen on taking drugs, most had managed to establish a relatively complex medication routine within their daily lives. Drug complexity was not necessarily problematic, and was in fact sometimes introduced by patients themselves in order to cope with specific problems. Changes in medication type, dose, frequency or changes to daily life routines all potentially threatened established routines and thus adherence.

We found that while some respondents saw the potential convenience of combined pills, most could see little clinical benefit in changing an established, effective and tolerable regimen and routine to one that contained less flexibility and might not mirror their current dosages. Despite mixed attitudes, some people indicated that they would probably agree to try a combined pill if it was suggested by their doctor.

Strengths and weaknesses of the study

Our sample was sufficiently large and diverse for us to be reasonably confident that most key beliefs and attitudes to multiple medication taking and combined tablets were been identified. Although the proportion of participants from lower age groups was less than hoped for, the larger sample size means that the actual numbers are comparable to other studies, and would probably not limit the breadth of issues identified. However, the study population was focussed on people already on a multitude of medications and who were generally older. It is therefore possible that patients newly prescribed with antihypertensives or statins may

Box 4. Attitudes to a combined pill

**Increased convenience**

Ron (70 yrs): Well perhaps, I’ve heard talk about maybe where you’re on two or three different tablets getting a tablet that contains, one tablet that contains the three drugs that you’re on. That would make matters easier for a lot of people – especially people that are on these drugs because they are long term so they’re not going to change very often. So that’s one way that would help.

**Reduction in errors**

John (51 yrs): One of the things I get confused with is, when I look at the tablets I don’t know why but I always seem to take my beta blockers before anything else, you stick with the same sequence, some reason or not, and always panic at the end of the month or because seem to have more ACE inhibitors left and aspirin and that and I know I don’t any more, so as a result of that I end up screaming at the surgery or whatever, emergency, prescription quick and having to go to the chemist for it and I think to have them all one tablet, that would be an advantage, you know you’re going to see clearly just how many you’ve got left.

**Reduction in forgetting**

Greg (61 yrs): Oh.. combined pill, oh I am all in favour on that.

David (65 yrs): Because the less you have to take the better. I think you know its better if you are taking say entinnil one time and (other drug name). I am only taking two as an instance say a couple of hours later but then you are combining them you are not going to forget them you know you can take that one and forget that one whereas if you take them combined and you are not going to forget them.

**Titration problems**

Wendy (60 yrs): I think it would be wonderful but I can’t see it working because you know you’re, I mean I was on 100 mg of one drug, they done a blood test and they dropped me down to 75 so you’re going to be changing it all the time.

Mary: Or you could be taking it before you get your test results back when you’re maybe shouldn’t be taking that amount of doses.

Wendy: They chop and change.

Anita (70 yrs): Cos I know mine goes up and down.

**Limited combinations may mean less suitability**

Moderator: If there was a combined pill and I’m talking about for high blood pressure and high cholesterol would that be something you would feel you would like to take or would be happy to take?

Nigel (66 yrs): I don’t honestly think so because there are different heart tablets and different cholesterol tablets and it is difficult enough to find the one that suits you rather than suddenly finding that they put two together and you can’t find one that suits you. If they were asking for a recommendation then I would say no.
have other, potentially more favourable, views on fixed-dose combination medications.

The free and open discussion within groups, and the common admission of non-adherence, did not suggest any significant response or social desirability bias. In addition, findings relating to the use of current medication are sufficiently congruent with existing literature suggest that their views on a combined drug may be generalizable outside of this study.

This study explored participants’ current attitudes, concerns and beliefs about combined therapy. These data may be useful in identifying reasons why people may or may not wish to switch from multiple to combined pills. However, the actual experience of combined therapy may be different from that expected or imagined by patients before commencement, and our results must be interpreted with this in mind.

Explanations and evidence from other studies

It has generally been thought that increased drug complexity is disliked by patients and is detrimental to adherence and clinical outcome. However, many trials of regimen simplification have failed to include measures of satisfaction or acceptability. In addition the proportion of people who refuse to enter the study, or their reasons for refusal, are frequently unreported. Our data suggests that patients may agree to try switching, if advised to do so by their doctor, although they may do so reluctantly. Longer-term adherence may depend on whether they feel that it has worked for them.

While simplification through reduced dose frequency generally leads to improved adherence rates, there is less evidence that complexity is problematic to all patients, or that simplification necessarily leads to clinical improvement. Patients themselves may introduce some complexity by spreading out or delaying doses in order to manage every day events and the discomfort of side-effects. There is evidence that increased frequency of low doses can reduce side-effects and improve adherence. Adherence studies typically find that while overall adherence can be 80–90%, timing compliance is usually 20–30% lower, suggesting a large amount of forgetfulness and/or a degree of intentional drug spreading during the course of each day. Unfortunately, since no studies have managed to separate unintentional from intentional non-compliance in this context, it is difficult to determine whether patient-instigated complexity is beneficial or harmful in terms of clinical outcome.

Respondents saw adherence in terms of whether drugs were taken rather than when or how. The answer as to whether drug complexity leads to lower adherence therefore depends on whose definition of adherence is used. While these strategies may deviate from formal recommendations, they may improve overall adherence by increasing the probability that all drugs will be taken. It may also be hypothesized that such strategies empower patients, which may confer additional benefits in terms of self-care and health outcomes, thereby supporting the potential benefits of the ‘expert’ patient.

Our data suggest that where drug numbers and complexity are problematic to patients, the perceived benefits of simplification will be related to the proportional decrease rather than the actual numerical change. A reduction from 20 to 19 tablets is less likely to seem as attractive as a reduction from 2 to 1. Unfortunately, trials of drug simplification may have inadvertently omitted patients on larger numbers of medications by excluding patients with comorbidities. Consequently, the generalizability of these studies may be limited.

Our data suggest that many patients have a clear rationale for their behaviour and may react differently to simplification by combining drugs as compared to simplification through reducing dose frequency of individual medications. Combining different medications may reduce the ability of the prescriber to tailor drug regimens to suit individuals’ precise needs or preferences. Titration may also be problematic and there have been few trials comparing the efficacy of fixed drug combinations (FDCs) with free combinations. A review in 2003 identified three studies, but commented that the strength of evidence of any benefit was currently weak.

Implications for practice

Since drug numbers and complexity are not always problematic to patients, new fixed drug combinations should be targeted primarily at individuals where difficulties with adherence and/or dissatisfaction with the current regimen are known, those starting the relevant medications for the first time, and those where treatment needs to be modified to achieve control. People’s willingness to switch may be hindered if drug combinations that mirror their current, trusted regimens are not available. Consequently, there is an onus on manufacturers to provide a large number of combinations, and a requirement for prescribers to establish patients on equivalent doses of the individual drugs before the move to a combined tablet is suggested.
Further research will be required to assess the cost-effectiveness of this approach.

Since developing an established routine appears to be of key importance to patients, the decision to add, remove or adjust prescriptions should be considered not only in terms of potential clinical benefits and interactions, but also considering ease of integration into current routines. While a number of patients would probably be willing to try a combined pill, and would appreciate the associated convenience this might offer, they are likely to have a number of concerns that prescribers should address. Many patients adjust the dose and timing of drugs throughout the day, and thus it may be more fruitful for prescribers to discuss with patients the time range within which drugs can be delayed while still being effective, rather than trying to establish strict adherence to precise time intervals. The use of blistered packaging for older patients on large numbers of daily tablets should be minimized. The pharmacy industry should consider researching the supply of medication packed in readily transportable (easily opened) daily packs rather than by individual agent.

It is possible that a number of patients will accept combination therapy if recommended to do so by their doctor, despite having concerns that a fixed combination may not adequately mirror their personalized drug regimens. The potential acceptability and uptake of a combined pill is likely to be affected by its proportional impact on patients’ wider drug regimen. Consequently, patients may be more receptive to the possibility of a combined pill where disruption is already seen as inevitable; when patients are first diagnosed or where modifications to the current regimen are already clinically indicated. Patients have personal strategies and routines for managing complex drug regimens, which may be designed to maximize convenience and minimize side effects. While these may not conform precisely to recommendations (for example, dose timing may be different), they may improve overall adherence and increase patient empowerment.

Acknowledgements

We would like to thank all of the volunteers who participated in our focus groups, and the general practitioners who aided recruitment.

The research was instigated by CP and funded by Pfizer UK. However, we confirm that the work was conducted independently and without interference, and the paper accurately reflects our findings. AS’s time spent working on this project has been funded by Pfizer. However, all researchers were employed by their relevant university.

Ethical approval for this study was granted by the Tayside and the South-West Surrey ethics committees.

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