

# Potentially hazardous co-prescribing of $\beta$ -adrenoceptor antagonists and agonists in the community

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## SUMMARY

**Aim.** The aim of this study was to investigate the co-prescribing of  $\beta$ -antagonists and  $\beta$ -agonists in the community, and to assess the potential hazards of such co-prescribing.

**Methods.** The study was set in the population of Tayside, Scotland (population approximately 400 000), between January 1993 and March 1993. An automated person-specific prescribing database was used, which could also be linked to hospital admissions. Patients who were co-prescribed  $\beta$ -antagonists and  $\beta$ -agonists on the same day or within 30 days were selected. A model was used to identify those who showed an asthmatic profile, on the basis of age, and previous prescribing and hospitalization history, and for whom the co-prescribing was judged to be particularly hazardous.

**Results.** Altogether, 0.9% of 15 824 patients who received a  $\beta$ -antagonist during the study period received a  $\beta$ -agonist on the same day. This figure increased to 274 (1.7%) for 30-day co-prescription. A few instances of particularly hazardous co-prescribing were identified, which involved young people who had previously received prescriptions for corticosteroids and been hospitalized for asthma.

**Conclusion.** Potentially hazardous co-prescribing of  $\beta$ -agonists and  $\beta$ -antagonists occurs despite labelled warnings, even in patients who appear to be at high risk. These events are quite rare but probably should not occur at all.

**Keywords:** co-prescribing;  $\beta$ -antagonists;  $\beta$ -agonists; asthma.

## Introduction

SINCE their introduction in the 1960s, beta-adrenoceptor blocking drugs ( $\beta$ -antagonists) have been implicated in the precipitation of problems in asthmatics, including marked reduction in forced expiratory volume (FEV),<sup>1-3</sup> wheezing,<sup>1,2,4-8</sup> and near-fatal<sup>7,9,10</sup> and fatal<sup>9,10</sup> asthma attacks. Even those  $\beta_1$ -antagonists such as atenolol, betaxolol, bisoprolol and metoprolol that have lesser effects on the  $\beta_2$ -receptors and airways resistance<sup>11</sup> are not  $\beta_1$ -specific and free of such side-effects.<sup>12</sup> Therefore,  $\beta$ -antagonists are contraindicated in asthmatics<sup>13</sup> and should be prescribed to them only when no other treatment is available.<sup>2,11</sup> If such treatment is essential,  $\beta_1$ -selective antagonists are recom-

mended over those that are less  $\beta_1$ -selective, such as propranolol.  $\beta$ -Antagonists should also be avoided in patients who have chronic obstructive airways disease.<sup>2</sup> In particular,  $\beta$ -antagonists are contraindicated in patients receiving  $\beta_2$ -adrenoceptor stimulants ( $\beta$ -agonists) as they have opposing effects.

The Medicines Monitoring Unit (MEMO) is a university-based organization that was set up to carry out pharmacoepidemiological research in the population of Tayside (population approximately 400 000).<sup>14,15</sup> Data on prescriptions that have been dispensed in the community are collected and stored on a database. MEMO currently has records of 8 million prescriptions dating from January 1989. The information can be linked to the hospitalization database for Tayside, which represents records of all episodes of hospitalization for Tayside residents, with diagnostic and procedure codes. The record linkage is achieved using the Community Health Index Number (CHNo.). This is a 10-digit number allocated to all patients in Tayside when they register with a GP.

MEMO has strict confidentiality agreements and does not disclose person-specific or general practitioner (GP)-specific data without written agreement from the individuals concerned. For publication purposes, data from MEMO are considered in aggregate and anonymized form, so that no individual patient or GP identification is possible.

Using purpose-written software, the prescribing database was interrogated to investigate patterns of co-prescribing of  $\beta$ -antagonists and  $\beta$ -agonists to patients in Tayside likely to have asthma or chronic obstructive airways disease.

## Method

Co-prescribing of  $\beta$ -antagonists and  $\beta$ -agonists was investigated in the population of Tayside between January 1993 and March 1993. To begin with, the number of patients potentially at risk from co-prescribing was established by determining how many received prescriptions for  $\beta$ -antagonists and  $\beta$ -agonists during the time period. The number of co-prescription events was then determined for these patients.

Two definitions of co-prescribing were used in the study:

- (1) Same day co-prescription:  $\beta$ -antagonist and  $\beta$ -agonist prescribed to the same patient on the same day.
- (2) Thirty-day co-prescription:  $\beta$ -antagonist and  $\beta$ -agonist prescribed to the same patient within a 30-day period.

It was judged that the co-prescribing of  $\beta$ -antagonists and  $\beta$ -agonists was particularly hazardous for patients who were likely to have asthma. Patients were therefore stratified into their likelihood of having asthma according to the following assumptions:

- (1) Patients who had previously received a prescription for an inhaled corticosteroid were more likely to have asthma rather than chronic obstructive airways disease. These data were available from August 1992.
- (2) Patients were more likely to have asthma if they were under the age of 45 years, and more likely to have

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© British Journal of General Practice, 1996, 46, 423-425.

chronic obstructive airways disease if they were over this age.

- (3) Patients who had been hospitalized (since January 1980) with a diagnostic code for asthma were likely to be asthmatic.

The co-prescribing events were also stratified into whether the  $\beta$ -antagonist was  $\beta_1$  selective or non-selective, and for the 30-day co-prescribing analysis whether it was prescribed before or after the  $\beta$ -agonist.

The hospitalization database was then searched to identify any evidence of hospital admissions resulting from co-prescribing in the patients studied.

The results of this study were circulated to all GPs in Tayside to seek their permission to publish the results. The local medical committee of the British Medical Association also sent a newsletter to all GPs suggesting that they check their prescribing records for instances of co-prescribing of  $\beta$ -agonists and  $\beta$ -antagonists. Any GPs in Tayside who requested information on co-prescribing in their patients were supplied with the relevant study data.

## Results

Between January 1993 and March 1993, 15 824 patients in Tayside received prescriptions for  $\beta$ -antagonists and 16 330 for  $\beta$ -agonists.

Table 1 shows the results of the search for co-prescription of  $\beta$ -antagonists and  $\beta$ -agonists on the same day during this period. There were 201 instances of co-prescription to 149 of the above patients. Fifty-three of these patients, seven of whom were below the age of 45 years, had previously received prescriptions for corticosteroids. There were eight instances of co-prescribing to these seven patients, of which half involved a non-selective  $\beta$ -antagonist. One had previously been admitted to hospital with asthma.

When the definition of co-prescription was broadened to 30 days (Table 2), 579 instances of co-prescribing to 274 patients were identified. Ninety-four had previously received prescriptions for corticosteroids and 17 were under the age of 45 years. These patients had 30 instances of co-prescribing, 20 of which involved a non-selective  $\beta$ -antagonist. Two had previously been admitted to hospital with asthma.

Of those co-prescribing events which did not occur on the same day (59% of the 203), the  $\beta$ -agonist was prescribed first in over half (59%) and the  $\beta$ -antagonist first in 41%.

No records of hospital admissions resulting from co-prescribing were identified in the patients studied.

## Discussion

In Tayside, 149 (0.9%) of the 15 824 patients who received a  $\beta$ -antagonist between January 1993 and March 1993 received a  $\beta$ -agonist on the same day. Within 30 days, this figure increased to 274 (1.7%). The aim of this study was to assess the potential hazards of such co-prescribing. To do this, it was necessary to make certain assumptions because the precise indications for the drugs were not known.

There are two possible scenarios within which co-prescribing could occur. If a patient is not known to be asthmatic and a  $\beta$ -antagonist is prescribed, asthma symptoms might develop, thus disclosing asthma. The  $\beta$ -antagonist might then be withdrawn and a  $\beta$ -agonist prescribed. Such prescribing is reasonable. On the other hand, if a patient is already known to be asthmatic, the co-prescription of  $\beta$ -antagonists and  $\beta$ -agonists is less rational. For this reason, we defined co-prescribing as hazardous if it occurred in patients who were likely to have asthma. Given that use of corticosteroids is recommended in patients even with mild asthma<sup>11,16</sup> and that differentiation between asthma and chronic obstructive airways disease can be attributed to age,<sup>17</sup> patients were considered to be asthmatic if they had received prescriptions for corticosteroids from August 1992 and were under the age of 45 years. This model for asthma has its limitations, especially given the availability of recent data only for corticosteroid prescribing. Therefore, the number of asthmatic patients might be underestimated. Whether the  $\beta$ -antagonist was  $\beta_1$ -selective or non-selective was also assessed, as was whether there had been any previous hospitalization episodes for asthma.

Using this rationale, several instances of hazardous prescribing were identified in young patients who had previously received therapy for asthma and been admitted to hospital with asthma. One such example involved a young person who had previously been admitted to hospital with asthma on three separate occasions, had received prescriptions for corticosteroids, and was subsequently prescribed a non-selective  $\beta$ -antagonist and a  $\beta$ -agonist on the same day. Such prescribing seems difficult to justify, as even the use of a  $\beta_1$ -selective antagonist may precipitate severe bronchospasm owing to the effect of a relatively small degree of  $\beta_2$ -blockade.

When 30-day co-prescribing was investigated, the  $\beta$ -agonist was prescribed first in the majority of events. These events can-

**Table 1.** Co-prescription on same day in Tayside, January 1993 to March 1993.

201 events (149 patients)			
Prescriptions for corticosteroids?			
84 events (53 patients)			
Aged <45 years		Aged >45 years	
Eight events (seven patients)		76 events (46 patients)	
Selective $\beta$ -antagonist	Non-selective $\beta$ -antagonist	Selective $\beta$ -antagonist	Non-selective $\beta$ -antagonist
Four events (three patients)	Four events (four patients)	63 events (36 patients)	13 events (10 patients)
Previous hospital admissions for asthma?			
—		One patient	One patient

**Table 2.** Co-prescription within 30 days in Tayside, January 1993 to March 1993.

579 events (274 patients)			
Prescriptions for corticosteroids?			
203 events (94 patients)			
Aged <45 years		Aged >45 years	
30 events (17 patients)		173 events (77 patients)	
Selective $\beta$ -antagonist	Non-selective $\beta$ -antagonist	Selective $\beta$ -antagonist	Non-selective $\beta$ -antagonist
10 events (six patients)	20 events (11 patients)	128 events (53 patients)	45 events (24 patients)
Previous hospital admissions for asthma?			
—		Two patients	Three patients

not be explained by the presence of asthma being disclosed by the use of a  $\beta$ -antagonist.

Data error should be considered in such an automated study. CHNo. allocation to prescriptions within MEMO has an error rate of approximately 1%. It could be that a  $\beta$ -antagonist appearing in the prescribing record of an asthmatic is caused by such misallocation. However, this is unlikely to account for all the instances of co-prescribing, especially as many patients experienced more than one co-prescription event and the probability of the error occurring twice in the same patient is low.

In this study, only a few instances of particularly hazardous co-prescribing were identified during a 3-month period, none of which resulted in hospital admissions that could be attributed to such co-prescribing. Nevertheless, the overall prescribing of  $\beta$ -antagonists to asthmatic patients was probably underestimated, given the limitations of the model for asthma and the definition of co-prescribing. It could also be argued that such co-prescribing should not occur at all, and the study perhaps serves as a reminder of the potential consequences of such actions.

The study also shows how the data in MEMO served as a resource for local GPs. Many requested information on co-prescribing in their patients and used it for clinical review.

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## Acknowledgements

We would like to acknowledge the Local Medical Committee of the British Medical Association and all the general practitioners in Tayside who agreed that this paper should be published. MEMO is supported by the Medicines Control Agency.

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