Antibiotics for coughing in general practice: exploring, describing and optimising prescribing

Summary

Introduction

The discovery of antibiotics (penicillin) by Alexander Fleming in 1928 triggered enormous progress in the field of medicine. However, as early as 1944 Fleming observed that some bacteria were able to destroy penicillin, and he warned that the misuse of antibiotics could lead to selection of resistant bacteria. This warning was lost in the first flush of the discovery of increasing numbers of antibiotics and the success of these medicines.

At the beginning of the 21st century, infectious diseases again cause more deaths as antibiotics lose their effectiveness. Over the last decade, the causative agent of the most frequent life-threatening bacterial infections, *Streptococcus pneumoniae* - or *pneumococcus* for short -, has become less sensitive to penicillin and other antibiotics. More than 30% of pneumococci isolated in Belgium are resistant to erytromycine and tetracycline, whereas more than 5% show full penicillin resistance.

This increase in bacterial resistance is associated with the increased use of antibiotics, both in animals and in humans. In the case of humans, 80% of antibiotics are prescribed by primary healthcare providers, that is outside the hospital, especially by general practitioners (GPs). The best way of preserving the effectiveness of antibiotics is to use them more appropriately, i.e. in cases where patients will actually benefit. The alternative of continuing to develop new antibiotics will only solve the problem of antibiotic resistance if the principles of judicious use of antibiotics are implemented at the same time. The growth in resistance is progressing faster than the development of newer antibiotics.

This dissertation aims to develop a management model enabling GPs to reduce the prescription of antibiotics without harming their patients. At the same time, our research addresses the very core of primary care, the screening function of general practice, with the missing of diagnoses as Scylla, and the excessive treatment of everyday complaints as Charybdis (**Chapter I**).

The filter function of general practice

General practice has an important role to play in the organization of quality health care. Its main characteristic is to screen various health problems in, on the one hand, self-limiting conditions or conditions to be dealt with in primary care, and, on the other, disorders that require a more specialist approach. For many, even well-known, complaints this function still needs an evidence base.

Missing diagnoses

The fact of working at low cost and with few technological means in order to deal with a wide array of health problems is an inherent feature in general practice. As a result, there is a limited diagnostic certainty. This also applies to the most common complaint, i.e. coughing. Respiratory tract infections (RTIs) are not easy to distinguish from other conditions such as asthma since patients complain about coughing in both cases. Furthermore, there is a low degree of certainty when differentiating between acute bronchitis and pneumonia, and

between viral and bacterial infections. A bacterial pneumonia, however, can be a life-threatening condition, requiring antibiotics, and even admission into hospital.

As a result, the quest for evidence enabling GPs to exclude life-threatening conditions with more certainty should not centre on diagnoses that are difficult to make, such as acute bronchitis, but on symptoms like coughing, for which patients seek help.

Excessive treatment of everyday complaints

For most conditions for which antibiotics are being used, there is no scientific evidence to support their actual benefit. For most patients, the use of an antibiotic in case of an acute cough has no benefit when compared with a placebo. Nevertheless, especially for this condition, (too) many and ever more expensive antibiotics are being prescribed. Apart form the high financial cost and the medicalising effect, this overuse results in an increase in anti-microbial resistance to the antibiotics available.

This dissertation aims to contribute to the development of effective strategies for a more appropriate use of antibiotics. Since coughing is one of the most common complaints in general practice, the appropriate use of antibiotics to treat coughs is a key area of action in order to tackle the resistance problem. Consequently, by describing, exploring and optimising the prescription of antibiotics for coughing we can safeguard a major development in the field of medicine, i.e. the use of antibiotics in the treatment of life-threatening infections. Examining how GPs can identify patients with coughing complaints who will (not) benefit from antibiotics, is another relevant element in this regard.

Part 1: Exploration and description

In the first part of the dissertation we explored the way GPs currently manage patients who consult them with complaints about coughing.

Qualitative part

In a qualitative study (**Chapter II**), we explored the diagnostic and therapeutic decisions by Flemish general practitioners regarding adult patients who consult them complaining about a cough as well as the determinants of their decisions by means of focus groups. Twenty-four GPs participated in four semi-structured group discussions centred on the following questions:

1.You are consulted by one of your adult patients who complains about coughing. Which diagnoses come to mind?

2. How do you differentiate between the various possibilities in your patient?

3. You suspect an infection of the respiratory tract. Do you differentiate in any way? Which distinctions do you make?

4. How do you differentiate between the various possibilities in your patient?

The recordings of these focus groups were transcribed and subsequently analysed in accordance with the principles of "qualitative content analysis". All texts were coded according to the research questions. Interpretation of the coded texts allowed a classification of the codes and the establishment of relationships between the various codes or categories.

In the focus groups, GPs stated that they try to differentiate between infectious and non-infectious causes of coughing, and between various types of RTIs. The most important decision, however, is whether or not to prescribe antibiotics for patients in case of suspected RTI. In terms of the latter decision, we made a distinction between two kinds of determinants after analysis of all codes. Medical determinants, such as signs and symptoms, determine the probability of disease but offer little diagnostic certainty for the patients involved. Non-medical determinants, such as defensive medicine by the GP (doctor-related) and patient expectations (patient-related), help determine the threshold at which to prescribe an antibiotic as well.

Following the analysis of the different codes, hypotheses were set up regarding decisions made by GPs when faced with complaints about coughing and the determinants underlying their decisions:

- The first diagnosis to present itself to a GP is RTI. This diagnosis is reached independently of the patient. Other hypotheses emerge only if they are considered plausible as a result of knowledge of patient history.

- GPs ask routine questions to confirm only the most likely diagnoses. Explicitly ruling out other diagnoses is less often used in decision-making.

- In suspected RTI, GPs want to make a distinction between clinical syndromes such as bronchitis and pneumonia, viral and bacterial RTI and upper and lower RTI. This cannot be achieved with certainty on the basis of medical history and clinical examination. Dealing with diagnostic uncertainty, GPs' decisions are directed at whether or not to prescribe antibiotics.

- For this (therapeutic) decision, doctor- and patient-related factors also come into play. These factors give rise to a shift in the action thresholds in favour of antibiotics, a phenomenon explained by the "Chagrin factor". GPS regret less having unnecessarily prescribed antibiotics than not having prescribed any if afterwards it appears that they were necessary. In this context, 'necessary' does not only mean necessary for curing the patient, but also, for instance, to meet patient expectations and thus retain patient loyalty. The decision to prescribe antibiotics is better explained by both types of determinants than by the conventional diagnostic groups of RTIs.

Quantitative part

A questionnaire (**Chapter III**) was used to quantify and condense the determinants generated in the focus group study. More specifically, we assessed the extent to which GPs consider those determinants when making decisions in the case of suspected RTI in a coughing patient and how strongly the determinants act in favour of or against antibiotic treatment.

Of the 316 Flemish GPs who were sent the questionnaire, 200 replied, with 188 responses being eligible for analysis (59.5 % of overall response rate). Our sample, which included 65.9 % men and an average age of about 43, was typical of the Flemish GP population.

GPs seem to consider all the determinants included in the questionnaire. They nearly always consider 'lung auscultation', but also whether the patient has a fever, is coughing up (coloured) sputum, looks ill and whether s/he has a medical history of COPD or smoking. Moreover, they often watch out for 'anything out of the ordinary'. GPs pay less attention to 'non-medical reasons', whether they be patient- or doctor related.

GPs felt that the deterioration of the general condition of the patient favoured treatment with antibiotics most . There were no items that argued strongly in favour or against treatment with antibiotics. Non-medical reasons support the prescription of antibiotic treatment, albeit to a lesser extent than medical factors.

Validation of qualitative and quantitative studies

In order to validate the focus group and questionnaire findings we recorded GP management of acute cough (**Chapter IV**).

Of the 85 GPs willing to participate in our intervention study (see Part II: Optimisation), 72 included an average of 10 consecutive adult patients who consulted them with acute cough between February and April of 2000 and 2001. They recorded medical as well as non-medical data, including the prescription of antibiotics and the GP's perception of requests for antibiotic treatment on the part of the patients.

These data also revealed that non-medical determinants may have a considerable effect on the decision whether or not to prescribe an antibiotic. After all, the fact that patients requested antibiotics proved to be an equally important, statistically significant, independent predictor of an antibiotic prescription, as were medical determinants, such as for example the presence of sputum. Good clinical practice guidelines and interventions to optimise the prescription of antibiotics have to take into account non-medical reasons such as the patient's request for antibiotics. In order to implement the recommended management approach, this has to fit in with the described, i.e. current, common practice.

Part 2. Optimisation

The second part of this dissertation provides recommendations for changing current practices and specifically for optimising the use of antibiotics for coughing in general practice. We conducted a prospective, cluster-randomised, controlled, 'before-and-after' study. The intervention was based upon a clinical practice guideline.

Recommended management

A group of GPs drafted a guideline for the diagnostic and therapeutic management of acute cough. This text was based upon the available evidence, our own descriptive research, and on a consensus within the author group if evidence was lacking. The text was peer-reviewed by a multidisciplinary panel of experts and subsequently revised.

The revised guideline for acute cough includes the following key points:

- The guideline applies to patients, aged 12 years or older, whose most prominent complaint is acute cough with or without purulent sputum, not patients with recurrent or chronic cough, chronic obstructive pulmonary disease or patients that received antibiotic treatment in the preceding week.

- First, pneumonia, pulmonary embolism, left ventricular failure (pulmonary oedema), pneumothorax, aspiration and irritation by toxic agents should be ruled out by history and clinical examination. Although these are not frequent conditions and acute cough may not

be the most prominent complaint, these potentially life-threatening conditions are treatable. They should not be missed.

- If a cause other than a respiratory infection is present (for example asthma, gastro-oesophageal reflux disease, ACE-inhibitors) management needs to be adjusted accordingly. Even though such conditions may not be obvious in a first encounter, they should not be ruled out.

- If eventually a respiratory infection seems to be the most likely cause, it is not feasible to distinguish between viral and bacterial infections. Nevertheless, the decision whether to prescribe antibiotics has to be made. Antibiotics are only needed for patients whose immunity has been compromised.

- Besides the scientific arguments, we also recommend integrating the GP's own agenda as well as that of the patient in the final therapeutic decision.

An educational package was developed in accordance with the guideline. In addition, this text was further elaborated according to a standardized methodology defined by the Scientific College of Flemish General Practitioners (WVVH) to become the guideline for good clinical practice: acute cough (**Chapter V**).

Implementation

Participants in the questionnaire study were asked whether they were willing to join an intervention study including pre- and post-assessment of the diagnostic and therapeutic management of coughing (**Chapter VI**). The pre-test of the planned intervention study consisted of the previously mentioned registration of the management of acute cough in the period February-April 2000. Before the intervention, all 85 GPs who agreed to participate were divided at random into two study groups.

Our intervention was preceded by a nation-wide public awareness campaign, "Antibiotics: Use them less often, but better." The campaign included TV and radio announcements, booklets and leaflets raising public awareness about the overconsumption and misuse of antibiotics, the resulting resistance problem and the self-limiting character of the most frequent infections.

In January 2001, all GPs in the intervention group received the guideline by mail and were contacted by a facilitator to arrange an outreach visit at their practice. They were asked to read through the guideline in advance of that visit. During the 10-20 minute visit, the educational package was presented. This presentation was adjusted to the needs or observations expressed by the GP. Once all GPs had been visited, each received a written reminder of the key recommendations by post.

Immediately after the intervention period, GPs started the post-test. This consisted of recording data regarding consecutive patients with acute cough in the period February-April 2001. After the first consultation at the GP's practice, the patients involved each day recorded the presence of coughing, sputum, fever, sore throat, headache, muscle ache, runny nose, loss of appetite, shortness of breath, thoracic pain, as well as information about their health status and level of activity. When assessing the intervention, we took into account the amount and cost of the antibiotics prescribed and the time it took for patient symptoms to disappear (symptom resolution).

Results

Of the 42 GPs in the intervention group, 36 received the entire intervention. Fifty-six GPs, 27 in the intervention group, 29 in the control group, participated in both pre- and post-tests. They included 1503 patients eligible for analysis. Patient diaries of 1009 patients eligible for analysis were available. Taking into account clustering of patients (Generalised Estimating Equations analysis), we arrived at the following findings:

Use of antibiotics. The antibiotic prescription rates for acute cough in the intervention group and the control group were 157/365 (43.0%) and 168/445 (37.8%) in the pre-test and 80/292 (27,4%) and 115/401 (28.7%) in the post-test, respectively. When antibiotics were prescribed, these were macrolides, cephalosporines or combinations of penicillins and beta-lactamase inhibitors, i.e. the non-recommended antibiotics, in 94/157 (59.9%) and 105/168 (62.5%), and 37/80 (46.3%) and 72/115 (62.6%), respectively. Without adjustment for the other registered variables, these prescription rates did not differ between the intervention and the control groups, neither in the pre-test nor in the post-test. Although by March 2001 the public awareness campaign no longer had an effect on the use of antibiotics, there was a significant difference between pre- and post-test prescriptions (P=0.005 and P=0.03) in both groups. In cases where antibiotics were prescribed, only the GPs in the intervention group prescribed 14% less of the non-recommended antibiotics (P=0.06 vs. P=0.84).

Unlike the pre- and post-test comparison (cf. the public awareness campaign), the comparison of the intervention and control groups allows a convincing adjustment for the substantial differences in the incidence of acute respiratory infections between 2000 and 2001. If, in addition, we adjust for differences in the other registered variables between patients in both groups and assume the antibiotic prescription rates to be equal in both study groups in the pre-test phase, only GPs in the intervention group prescribed significantly fewer antibiotics in the post-test than those in the control group (OR_{adj} = 0.55 (0.36-0.85)), and compared with their own prescriptions in the pre-test period (OR_{adj} = 0.55 (0.38-0.80)).

The intervention not only influenced the number of antibiotic prescriptions, but also resulted in a better choice of antibiotics for acute cough patients. Since there was a significant pre- and post-test difference only in the intervention group, the public awareness campaign no longer appears to have had an effect on post-test antibiotic prescription.

Cost of antibiotics. During the pre-test, the mean medication cost from the point of view of the National Sickness and Invalidity Insurance Institute (NSIII) was € 12 in the intervention group and € 11 in the control group. In the post-test this dropped to € 8 in the intervention group, and € 9 in the control group.

By limiting the analysis to the subset of patients who were prescribed an antibiotic, the mean medication cost increased to € 22 in the intervention group and € 21 in the control group. This dropped significantly in the intervention group in the post-test, i.e. € 16, in comparison with the control group's € 21 (Mean Difference (MD)adj (95%CI) = -6.89 (-11.77 - (-2.02) €) and with the pre-test figure of € 22 (MDadj = -6.11 (-9.97 - (-2.24) €)

Time to symptom resolution. As far as the use and type of antibiotics are concerned, the same conclusions can be drawn from the subset of patients who completed diaries. Since we are especially interested in public health, the outcome for the patient is of paramount importance. This is why we investigated whether fewer and different antibiotics influenced the time to symptom resolution. However, we found no significant difference between the intervention and control groups in terms of the time to resolution of all symptoms.

Part 3. The patients

In the decision to prescribe antibiotics, patient-related determinants also play a role. International differences in outpatient antibiotic consumption might correlate with differences in patient attitudes. Moreover, the problem of antibiotic overuse is an international problem, which requires international interventions and provides opportunities for international research.

By means of an international postal questionnaire study, in collaboration with Utrecht (the Netherlands), Cardiff (UK), and Barcelona (Spain), 400 patients in each country were asked about their views on respiratory complaints and antibiotic use (**Chapter VII**). Belgian patients reported a higher need for consulting a general practitioner when faced with respiratory symptoms and considered these disorders to be more serious and less self-limiting than did their Dutch and UK counterparts. These results might partially explain the differences in antibiotic use between respondents. Patient counselling should specifically highlight the benign and self-limiting nature of the vast majority of respiratory tract complaints.

Conclusion

This dissertation clearly shows that the prescription of antibiotics for the most frequent (RTI) complaint in general practice, i.e. coughing, requires optimisation (**Chapter VIII**). This can be achieved by means of a guideline for good clinical practice, provided the guideline fits in with current common practice and is implemented by means of academic detailing.

In doing so, we can achieve the goals of the public awareness campaign: ”Antibiotics: Use them less often, but better”. GPs not only prescribed less, but also better because of our intervention. Furthermore, this did not happen at the expense of patient recovery.

There is significant interaction between doctor and patient in the decision to prescribe antibiotics. So, in order to develop effective strategies aimed at a more appropriate use of antibiotics, we need to focus on both the doctor and the patient and, in particular, on doctor-patient communication. More specifically, the discussion of patient expectations about antibiotic prescription and the (in)appropriateness of it, supported by relevant and evidence-based recommendations is the key to success for the GP. Likewise, interventions should focus on both the prescribers and the consumers. Therefore we advise a combination of interventions such as a national public awareness campaign and an intervention like ours, which directly addressed GPs.

Finally, interventions to change behaviour - in this case the prescription behaviour - cannot claim to have a lasting effect. They need to be repeated to preserve the effectiveness of antibiotics in future health care.

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