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Modeling budgetary impact for decision makers

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The budgetary implications of using 5-HT_3 receptor antagonists in the management of patients with chemotherapy-induced emesis is discussed. It was shown that treatment with 5-HT_3 receptor antagonists in the acute phase of emesis resulted in relatively little additional cost when introduced into a normal management pattern of emesis control, and therefore seems justifiable. However, in delayed emesis there is a much more substantial budgetary impact with no proven clinical benefit, and therefore treatment does not appear to be appropriate in this situation.

Key words: 5-HT_3 antagonists, acute emesis, budget, cost, delayed emesis.

Introduction

Most hospitals or oncology units operate within some form of budgetary constraint. Since most new technologies and many new practices are cost additive, it is important for health care professionals to be able to assess the impact new practices are likely to have on their overall expenditure.

The objective of this study is to help physicians, pharmacists and other health care professionals assess how they can make best use of the new 5-HT_3 receptor antagonists within the available resources. The budgetary impact of these new drugs was assessed relative to the total cost of patient management rather than by simply focusing on drug costs. In many units, the cost of drugs is artificially visible, often making it the target of cost-containment measures. This can constrain the flexibility available to the physician and may mean that the available resources are not used optimally to deliver the best possible services to patients.

The current study therefore focuses on the additional costs which might be incurred when 5-HT_3 receptor antagonists are introduced into the normal management pattern of patients being treated with emetogenic chemotherapy and puts these costs in the context of the overall management costs for these patients.

The use of models

Many health care professionals are used to basing their treatment decisions on a thorough assessment of the results of clinical trials; the use of treatment models is not, as yet, a very widespread decision-making tool. Clinical trials are designed to assess the efficacy of therapies in a controlled therapeutic environment. They therefore provide historical data under 'experimental' conditions. They are unable to provide an insight into the future impact of new therapies when used under normal clinical conditions.

Since it is not possible to generate 'data' about the future, the use of treatment models can provide health care professionals with a valuable planning tool which will allow them to assess the likely impact of new therapies, such as 5-HT_3 receptor antagonists, on their treatment practices. Such models need to be based on a thorough assessment of treatment practices combined with what seem to be reasonable assumptions of the likely future impact of new therapies on clinical practice, based on available clinical trial data. Manipulation of the different assumptions can then be used to build a picture of the key factors which are likely to affect outcome, thereby allowing practice decisions to be made. This process is akin to that used by all businesses to make everyday decisions based on what seem to be reasonable assumptions about the future.

For such models to be successful, they need to fulfil two important criteria. Firstly, the basis of the model and the underlying assumptions need to be easily transparent to all users. Secondly, they should be presented in a format which allows users to alter the assumptions to mirror closely their own clinical practice. This allows tailoring to the individual situation in each hospital or oncology unit.

Anti-emetic treatment model

Treatment algorithm

The model is based on an algorithm constructed from a comprehensive review of the literature and

interviews with clinicians to assess actual clinical practice. The detailed assumptions underlying the treatment algorithm have been published previously[1] and will be reviewed only briefly here.

Patients were divided into three groups, according to the chemotherapy they were receiving: low, moderate or highly emetogenic.[2–4] It has been assumed that 5-HT_3 receptor antagonists will generally not be used in patients receiving chemotherapy with low emetogenic potential, except for patients who have persistent emesis not controlled by conventional anti-emetic drugs.

Patients receiving moderate or highly emetogenic therapy were further subdivided into those at high risk of emesis and/or of developing adverse effects from conventional anti-emetics (such as high-dose metoclopramide); and those who are not considered high risk. For the purposes of the model, the high-risk group were defined as patients under 30 years of age, and represented 15% of patients in both the moderate and highly emetogenic chemotherapy groups.[1,5,6]

Treatment strategies

Based on the paper published by Jones *et al.*,[1] six potential usage patterns for 5-HT_3 antagonists were defined. First, three potential treatment strategies were determined (Table 1). These treatment strategies represent an incremental usage pattern for these drugs with an increasing number of patients receiving them as first-line therapy. The likely cost impact of each of these strategies was assessed. The model was then used to assess the budgetary impact of 5-HT_3 receptor antagonists, depending on whether their use was restricted to cases of acute emesis, in the first 24 h after chemotherapy, or extended, in an attempt to control delayed emesis over a 4-day period. Costs for the model were based on the actual cost of managing a cohort of 1000 patients at the United Leeds Hospital Trust in the UK at 1992 prices.

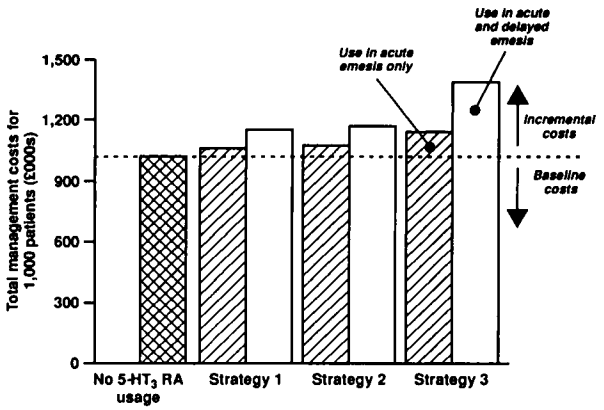

Figure 1. Delayed emesis accounts for most of the potential increase in overall costs. Based on the cost strucure of the Cookeridge Hospital.

Results

The results of the model are shown in Table 2 and Figure 1. When treatment with 5-HT_3 receptor antagonists was restricted to acute phase emesis only, the use of these drugs added between 3.1% and 10.4% to the overall cost of managing these patients. In first-line use (Table 2, Strategy 3), a full 86% of all chemotherapy patients were receiving treatment with 5-HT_3 receptor antagonists.

However, when treatment was extended to cover delayed emesis as well, the budgetary impact ranged from 11.6 to 33.6%.

Applicability of results

The study presented here is based on the cost structure of one regional oncology referral center in the UK. It is therefore legitimate to question the applic-

Table 1. Three treatment strategies representing an incremental usage pattern

Treatment strategy	Usage pattern	% of all patients receiving 5-HT_3 receptor antagonists
Strategy 1	First-line use of 5-HT_3 antagonists in all high-risk patients. Second-line use in all others	28
Strategy 2	First-line use of 5-HT_3 antagonists in all patients receiving highly emetogenic regimens. As per Strategy 1 for moderately emetogenic regimens	34
Strategy 3	First-line use in all patients receiving highly and moderate emetogenic regimens	86

Table 2. Budgetary impact varies according to usage patterns

Treatment strategy	% of all patients receiving 5-HT$_3$ receptor antagonists	Incremental costs	
		acute-phase emesis	acute + delayed-phase emesis
Strategy 1	28	+3.1%	+11.6%
Strategy 2	34	+3.5%	+13.4%
Strategy 3	86	+10.4%	+33.6%

Strategies as in Table 1.

ability of these results to other centers, in the UK and elsewhere. Extensive sensitivity analyses have been conducted where all major assumptions were changed in order to assess the impact on the cost model. Furthermore, the validity of the treatment model has been tested in other European countries, and costs altered accordingly.

Although these changes had an impact on the absolute costs incurred under different conditions, there were no differences in the order of magnitude of the incremental costs for each of the treatment strategies and the overall conclusions did not change.[1] Furthermore, the model is available as an interactive computer model.[7] This enables individual oncology units to assess the potential budgetary impact of different usage patterns of 5-HT$_3$ receptor antagonists under their own specific circumstances.

Potential savings

This study does not take into account any potential health care resource savings which may accrue due to better control of chemotherapy-induced emesis. Our research suggests that such potential savings are likely to be minor in those units where most patients are already receiving chemotherapy as outpatients. Significant savings are likely to occur only where emesis is the determining factor causing inpatient rather than outpatient treatment.

Additionally, any such savings are most important in the first 24–48 h of therapy, when hospital admission would have been avoided. They have little impact on delayed-phase costs after discharge. If such situations do occur in specific units, they are therefore likely to strengthen the conclusion that 5-HT$_3$ receptor antagonists are most useful in acute phase emesis.

Discussion

The cost of introduction of new technology depends on two factors: the cost of the innovation and its pattern of usage. In the past, much attention has been devoted to the former, usually to the exclusion of the latter. This study shows that the cost impact of 5-HT$_3$ receptor antagonists is dependent on their pattern of use. The overall cost impact can vary from +3 to +33%, depending on pattern of use. When used in acute emesis, in up to 34% of patients, the budgetary impact of these new agents is of the order of a 3.5% increase in the overall management costs. Usage can be extended to as many as 86% of patients at an incremental cost of 10.4%. Nausea and vomiting are the symptoms which cause most distress in patients receiving chemotherapy.[7,8] It could therefore be argued that cost increases of this order of magnitude are justified in order to achieve better control of these symptoms.

All health care professionals who are interested in offering the best services to their patients within the constraints of available resources need to balance cost and pattern of use. Clinical trials provide information about the efficacy and safety of drugs. However, they cannot assess the likely future impact of new technologies on overall costs. Furthermore, the results of clinical studies are often not translated into clinical practice. The average doses of ondansetron used in actual practice have remained high, despite clinical trial evidence to show that lower doses may be just as effective in some patients.[9] Models like the one presented here will play a increasing role in decision making which is complementary to that of clinical trials. They will help decision makers plan for the future effect of innovation on the costs they are likely to incur, and on the benefits they can hope to deliver to their patients. Clearly, the largest potential cost impact depends on whether the use of 5-HT$_3$ receptor antagonists is restricted to acute-phase emesis only, or

extended to cover delayed emesis. Clinical opinion based on currently available evidence suggests that 5-HT_3 receptor antagonists are no better than previously used anti-emetic drugs in the control of delayed emesis.[10] In fact, one study suggests that ondansetron is inferior to dexamethasone in the control of delayed nausea.[11] It therefore seems difficult to justify the level of cost increase presented here by extending the use of 5-HT_3 receptor antagonists to the delayed phase of chemotherapy-induced emesis.

In some units, budgeting systems are focused on unit costs of drugs rather than overall costs of management. This study shows one way in which overall costs of management can help decision making about the optimal use of new drugs. Fairly widespread usage of 5-HT_3 receptor antagonists in acute-phase emesis seems justifiable on the basis of costs incurred and benefits provided. Extending the use of 5-HT_3 receptor antagonists to delayed-phase emesis does not currently seem justifiable, because of the substantial increase in cost for no proven clinical benefit.

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References

1. Jones AL, Lee GL, Bosanquet N. The budgetary impact of $5HT_3$ antagonists in the management of chemotherapy-induced emesis. *Eur J Cancer* 1992; **29A**: 51–6.
2. Craig JB, Powell BL. Review: the management of nausea and vomiting in clinical oncology. *Am J Med* 1987; **293**: 34–44.
3. Borison HL, McCarthy LE. Neuropharmacology of chemotherapy-induced emesis. *Drugs* 1983; **25 (Suppl 1)**: 8–17.
4. Triozzi PL, Lazlo J. Optimum management of nausea and vomiting in cancer chemotherapy. *Drugs* 1987; **34**: 136–49.
5. Allen JC, Gralla RJ, Reilly C, *et al.* Metoclopramide: dose related toxicity and preliminary antiemetic studies in children. *J Clin Oncol* 1985; **3**: 1136–41.
6. Kris MG, Tyson LB, Gralla RJ, *et al.* Extrapyramidal reactions with high dose metoclopramide. *N Engl J Med* 1983; **309**: 433–41.
7. Lee GJ, Bosanquet N. *Quality of life in cancer patients.* Health Policy Review Paper No. 3. Cambridge: Daniels Publishing 1992.
8. Cooper S, Gregoriou V. The impact of cytotoxic chemotherapy — perspectives from patients, specialists and nurses. *Eur J Cancer* 1992; **28A (Suppl 1)**: S36–38.
9. Aapro M. A framework for assessing therapeutic innovation. *Anti-Cancer Drugs* 1993; **4(Suppl 3)**: 27–31.
10. Kaye SB, Khayat D, Aapro M, *et al.* Who should receive a 5-HT_3 antagonist? *Lancet* 1992; **340**: 1107–8.
11. Jones AL, Hill AS, Soukop M, *et al.* Comparison of dexamethasone and ondansetron in the prophylaxis of emesis induced by moderately emetogenic chemotherapy. *Lancet* 1991; **338**: 483–7.

Appendix—Discussion

S Kaye (UK): At present, there is no evidence to suggest that 5-HT_3 antagonists have any effect on delayed emesis. We have heard that giving treatment for 5 days triples the cost, since the treatment period is longer. We have also heard from health economic colleagues that it is possible to measure the impact. If the 5-HT_3 receptor antagonists did have an effect in delayed emesis, how would that effect be measured, and would health authorities pay for treatment of delayed emesis? Your figures show very eloquently that the cost of treating acute emesis is moderate, but in delayed emesis treatment would be very expensive. At what point would it become economically viable to treat delayed emesis?

G Rees (UK): The study which has just been presented and the conceptual approaches of methodology are applicable to many other situations, not only in oncology but in medicine in general. Dr Zammit-Lucia started off by saying that the purposes of the study were to identify the optimal use of resources within a confined budget and his talk is entitled 'Modeling Budgetary Impact for Decision Makers'. Almost implicit in that is the fact that the patient is not a decision maker, and I think we have got to consider what is our role as doctors. Are we the patient's advisor, or the patient's best friend? Should we ration information to the patient just as we ration our treatments?

N Bosanquet (UK): The kind of measurement techniques used for acute emesis would certainly be applicable to delayed emesis, in terms of social functioning, anxiety, depression and symptom rating. In addition, studies of longer-term changes affecting patients are required, together with longer-term effects, particularly on work performance and progress, from cancer and ex-cancer patients. Many patients drop out of the work force because of traumatic experiences during treatment. This is extremely expensive, and health authorities will be interested in minimizing this kind of loss.

P Harper (UK): The cost impacts are great because of the budgetary cost of these drugs. The developmental costs of 5-HT$_3$ receptor antagonists are almost certainly largely due to governmental decisions which include the amount of data each nation requires to register the drug. These drugs have to be registered separately in different countries at enormous costs. Central registration would allow better and faster development of the drug. Many of the studies, such as those looking at long-term emesis control, are not yet completed.

J Zammit-Lucia (UK): The model suggests that the cost impact of these drugs is not very high if used in areas where they have been proven to be effective. One has to be aware of what is causing the cost impact. Is it usage patterns, or is it the cost of the drugs themselves? It appears that the cost of the drugs themselves does not seem to have a major impact on overall costs of managing the patients, if their usage is appropriate to the available evidence.

J Carmichael (UK): Since the cost of treating delayed emesis is based on repeated dosing of the drug over 5–6 days, the consequent increase in cost is not unexpected. The evidence suggests that over days 1–3 there is no effect at all and so the compound should be discontinued at that time. The delayed effect seen on days 4–6 could possibly be covered by another tablet or injection administered at this time, thus producing good delayed control with much less administration of the compounds. It would therefore seem unnecessary to disregard 5-HT$_3$ antagonists for delayed emesis solely on the basis that patients are treated twice a day for 5 or 6 days.

MS Aapro (Switzerland): It should be noted, however, that further studies are required to determine whether 5-HT$_3$ receptor antagonists are really effective in delayed emesis. When chemotherapy is divided over 5 days, there are several sets of studies which show that 5-HT$_3$ antagonists are better than the combinations of steroid with metoclopramide. On day 1, acute emesis is seen following the intake of the cytotoxic agent. The delayed effect from day 1 is then seen on day 2. In addition, on day 2 an acute effect following further cytotoxic therapy also occurs. Thus, the benefits of these compounds occur with chemotherapies which are given over 3–5 days. The delayed emesis when chemotherapy is stopped should also be considered. Patients may start to vomit at this time, giving rise to serious doubts that the 5-HT$_3$ receptor antagonists are effective. Perhaps consideration should be given to receptor-blocking agents which operate for much longer periods of time.

J Carmichael (UK): It would appear that the 5-HT$_3$ antagonists do have an effect over standard regimens in fractionated chemotherapy schedules. However, we don't know whether the dose that is given on a daily basis is strictly necessary. Perhaps methods to reduce the amount of drug administered could be investigated in those schedules, to see whether any of that increased benefit is lost with lower doses.

A Stanley (UK): One problem encountered weekly and monthly is the confrontation with managers and accountants when paying acute bills in a cash-limited situation. We have used 5-HT$_3$ receptor antagonists in patients who are having moderate and highly emetogenic therapy in crossover studies and when conventional anti-emetic therapy is inadequate, and the patients seem to do well and like the drugs. However, the 7% increase in cost which arises from the use of 5-HT$_3$ receptor antagonists in this group of patients could not be justified, let alone the 23–25% increase for their use in delayed emesis. An overall decrease in our expenditure is usually required. There is, therefore, an acute problem of paying for the drug today and strategies are required to cope with the problem. An improvement in the ability of patients to return to work is one aspect that requires attention.