

Intravenous Omeprazole versus Ranitidine in Bleeding Peptic Ulcer Patients

Health Technology Appraisal

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• بيانات المستحضر محل الدراسة:

Intervention	Omeprazole
Trade name	Risek vial
Company name	Julphar
Comparator	Ranitidine

• تاريخ عرض المستحضر:

تم تحويل المستحضر من الإجتماع المنعقد مع قطاعات الصيدلة التابعة لوزارة الصحة بتاريخ ٢٠١٦/٦/٢٩ إلي وحدة إقتصاديات الدواء لإجراء دراسة جدوي إقتصادية تقارن كلا المستحضرين omeprazole & ranitidine في علاج قرحة المعدة والأمعاء المصاحبه بوجود دم .

• الهدف:

- تقييم الفعالية لقاء التكلفة لمستحضر omeprazole مقارنة بمستحضر ranitidine في علاج مرض قرحة المعدة والأمعاء المصاحبه بوجود دم وذلك لضمان أفضل النتائج العلاجية بالنسبة للمريض وبأقل تكلفة ممكنة من خلال الإلتزام بالخطوط العلاجية الاسترشادية العالمية وفي ضوء الممارسة الإكلينيكية المحلية.

- علما ان الدراسة التي قامت باجرائها وحدة اقتصاديات الدواء شملت بيانات التكلفة الخاصة بالمستحضرات والتي تم تجميعها من تسعيرة الادارة الفنية لمناقصات الادوية ومناقصات مستشفيات وزاره الصحة ، بالاضافة إلى باقي التكلفة المرتبطة بالإقامة بالمستشفى والأدوية والتبعات المحتملة عن علاج حالات القرح بأنواعها والنتيجة عن استخدام كل بروتوكول على حدة، وطبقا لتسعيرة نفقة الدولة .

قرار اللجنة:

- تم إجراء دراسة الجدوي الإقتصادي لكلا المستحضرين Omeprazole versus Ranitidine في علاج bleeding peptic ulcer علي مدار فترة زمنية قصيرة تتضمن ٣٠ يوم كما هو متبع في الدراسة الإكلينيكية المنشورة وفيها تم إعتبار complete healing الذي يتم تحديده باستخدام المنظار عند اليوم ٣٠ من بدء العلاج ك Intermediate outcome with established link with final outcome لدراسه الجدوي الاقتصادية.

- وقد خلصت الدراسة إلي أن مستحضر omeprazole عند سعر ١١ جنيه لك (40mg) vial هو الأوفر من حيث الفعالية لقاء التكلفة

"Cost saving choice" مقارنة بمستحضر ranitidine عند سعر ٧٢ قرشا لك (50mg) vial، حيث أنه يقدم ميزة علاجه أفضل تتمثل في ارتفاع نسب حالات الـ complete healing بمقدار ٣٧.٥% عن نظيره مع تكلفة إجمالية أقل بنحو ١١٢.٣ جنيه وبالتالي فهو يوفر ٢٩٩.٦ جنيه لكل 1 complete healing episode.

- جدير بالإشارة أن الدراسات الإكلينيكية المنشورة والتي تقارن كلا المستحضرين في هذا الغرض العلاجي محدودة وتعود إلي فترة زمنية بعيدة منذ التسعينات وحيث انه هو الدليل العلمي الوحيد المتاح تم بناء دراسة الجدوي الاقتصادية عليه وذلك للتمكن من الوصول الي افضل النتائج فيما يخص الفعالية لقاء التكلفة للمستحضرين.

English Summary:

Cost-effectiveness study of omeprazole versus ranitidine in the treatment of bleeding peptic ulcer Patients: A decision tree Model

Introduction:

Omeprazole is a potent inhibitor of the ATPase H + / K +, known gastric proton pump. Its efficacy is superior to other H2 blockers for the disease related to the acidity of the upper digestive tract. Despite improvements in endoscopic techniques and the development of new drugs, bleeding peptic ulcers are still addressed to surgeons in 20% of cases and even in intensive care [1, 2].

Although the real effects of acid suppression for the control of bleeding from a peptic ulcer is still the target of controversy, controlled studies with H2 blockers have shown some positive results [3, 4, and 5]

.Omeprazole can cure up to 95% of peptic ulcers resistant to ranitidine. It is an inhibitor of gastric secretion more powerful than the H2 receptor blockers.

Acute upper gastrointestinal hemorrhage is an important cause of morbidity and mortality, with peptic ulcers being the most frequent source of bleeding. The prognosis of bleeding depends on age, underlying diseases, hemodynamics status, and persistence or recurrence of bleeding [6, 7].

The pharmacotherapy of bleeding ulcers attempts to improve the microenvironment at the bleeding point by keeping the gastric pH above the proteolytic range for pepsin to stabilize the clotting process.

Previous studies have shown that, compared with ranitidine, omeprazole is a cost-effective treatment for acid-related disease, and however, since more evidence is continually emerging and since prices vary, both across countries and with the passage of time, re-evaluation is necessary.

Objective:

To evaluate the cost- effectiveness of omeprazole versus ranitidine in bleeding peptic ulcer from health insurance perspective

• Economic evaluation Key Features [8]

Key Features:	
year of the document	October 2016
Affiliation of authors	Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs
Purpose of the document	Evaluation the cost-effectiveness of using omeprazole versus ranitidine in the treatment of bleeding peptic ulcer patients.
Standard reporting format included	yes
Disclosure	yes
Target audience of funding/ author's interests	Public and private payers, healthcare industries and clinicians
Perspective	Ministry of health perspective
Indication	Treatment of bleeding peptic ulcer.
Target population	Those who insured by the Egyptian health care system
Subgroup analysis	No subgroup analysis was done.
Choice of comparator	Ranitidine

Time horizon	Decision tree over 30-days representing the clinical practice.
Assumptions required	yes
Analytical technique	Cost-effectiveness analysis
Costs to be included	Total costs include costs of treatment and managing strategies according to the Egyptian current practice.
Source of costs	Official sources of unit cost data for products (e.g. Tender lists) and MOH hospitals.
Modeling	Decision tree model
Systematic review of evidences	yes
Preference for effectiveness over efficacy	yes
Outcome measure	The outcomes of the two treatments were measured in terms of probability of complete healing from the ulcer.
Method to derive utility	Utility not used.
Equity issues stated	All lives are valued equally, regardless of age, gender, or socioeconomic status of individuals in the population

Discounting costs	Not applicable.
Discounting outcomes	Not applicable.
Sensitivity analysis-parameters and range	Critical component(s) in the calculation is varied through a relevant range or from worst case to best case.
Sensitivity analysis-methods	One-way sensitivity analysis is performed.
Presenting results	Omeprazole is cost-saving compared to ranitidine in management of bleeding peptic ulcer from health insurance perspective.
Incremental analysis	yes
Total costs vs. effectiveness (cost/effectiveness ratio)	yes
Portability of results (Generalizability)	The generalizability and extent to which the clinical efficacy data and the economic data are representative is discussed.

Committee Discussion:

A comprehensive search of PubMed and MEDLINE was conducted for English articles published to retrieve the available published data regarding Randomized controlled Trials (RCTs), systematic reviews, and meta-analyses of RCTs. because they provide the least biased and most robust evidence regarding

treatment. All indirect clinical trials were excluded; only head to head clinical studies comparing omeprazole versus ranitidine in the target indication are included in the economic study.

The clinical parameters were derived from a prospective randomized trial which enrolled 45 patients with bleeding peptic ulcer, the patients were randomized to receive i.v. omeprazole, 40 mg bolus followed by 80 mg/day by continuous infusion for 3 days, or ranitidine 50 mg i.v. bolus followed by 400 mg/day i. v. continuous infusion for 3 days the primary end point was the stopping of bleeding, patients who don't achieve success on ranitidine are shifted to omeprazole then if failed they go for surgery for ulcer treatment.[9]

No utility data are found for patients with bleeding peptic ulcer, as it is a critical case and emergent intervention by surgery is recommended after failure of 3- days' infusion with the drug of choice, and for this reason we depend on the complete healing probability after 30 days as a final outcome in the model.

Direct medical costs regarding cost of treatment, monitoring test performed and cost of management of side effects were obtained from the Ministry of health hospitals in Egypt.

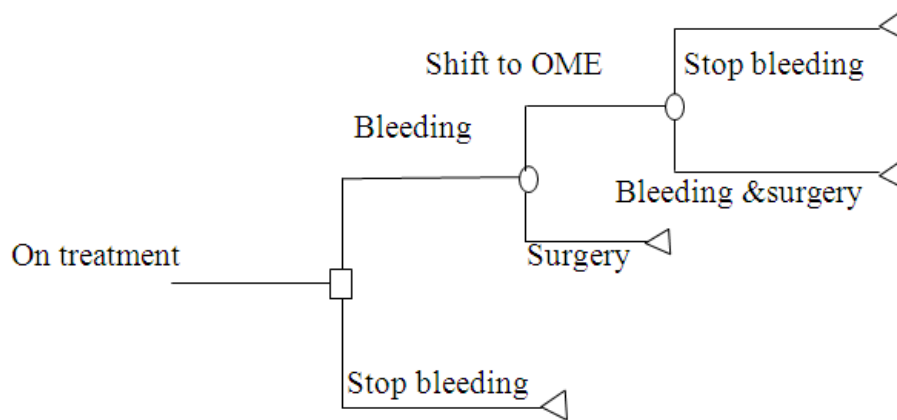
The results of the cost effectiveness study revealed that omeprazole is cost saving compared to ranitidine in bleeding peptic ulcer with an ICER of -159.48 EGP/one complete healing over a 30-day time horizon decision tree model.

Till now no cost effectiveness study has been done for intravenous omeprazole and ranitidine in bleeding peptic ulcer but the available cost effectiveness studies performed for the oral form not the parenteral and revealed that the omeprazole strategy is a superior treatment alternative to ranitidine, with a lower cost and a better effect in achieving more ulcer free days in treatment of duodenal ulcer in Great Britain [10].

The limitation of the economic study is that the trial we depend on for building the model was since 1997, but this was the latest one comparing both interventions in the above mentioned indication, another limitation is the absence of long term data about the efficacy of two interventions in that indication and a short term decision tree model is adopted in the economic study.

As in all modeling exercises, several assumptions were made in this study leading to uncertainties in the results. In this analysis, we explicitly accounted for these uncertainties by assigning confidence intervals and plausibility ranges based on published source for inputs parameters, and monitoring costs in the model. Robustness of results was assessed by using sensitivity analysis. One way sensitivity analysis was conducted and illustrated that the key factor which has the greatest impact on the result was the probability of bleeding in ranitidine arm after shift to omeprazole.

Figure 1: illustrating the decision tree model of the cost effectiveness study.



OME: omeprazole

-Shift to omeprazole occurs in case of patients starts and failed on ranitidine.

-Surgery in case of patients who failed on omeprazole from beginning or after shift to omeprazole upon ranitidine failure.

• Conclusion

It is important to address both the clinical and the economic implications of a new therapy from the payer perspective before deciding on public reimbursement of new therapies. Taking the above-mentioned limitations and uncertainties in consideration the conclusion is that intravenous omeprazole is cost-saving versus ranitidine in bleeding peptic ulcer from health insurance perspective.

• Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

- **Appraisal Committee members**

Each technology appraisal is appraised by the PE Committee, which is one of CAPA's standing advisory committees and consist of members who represent different specialties such as statistics, clinical evidence, economics, medicine, clinical pharmacy and pharmacoeconomics. A list of the Committee members who took part in the discussions for this appraisal appears below:

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