Pharma Sci-The Use of H2-Blockers in Intensive Care- Prabhjot Kaur- Grodno State Medical University

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Introduction

Treatment process in the critical care unit is quite complicated. When a patient is in critical condition, gastro-intestinal tract is often affected in the first place. Conditions like severe burn injury, severe traumas (orthopaedic trauma) sepsis, bacteraemia, acute pancreatitis, patients with pre-existing gastritis or stomach ulcers are highly susceptible to intestinal bleeding caused by stress ulcers. Internal bleeding from the ulcer, contributes a lot to worsen the condition of the patient. In such cases, pharmacological prophylaxis is one of the most effective ways to overcome the situation. Proton pump inhibitors and H_2 receptor blockers are widely used for this purpose. As it is known, each group of drug has its own side effects and contraindications. Superiority of one group of drugs over another group is not documented with proof. Recommended usage of drug should be based on some factors. Such as: condition and probable side effects on a partial patient due to the use of the particular drug, availability and financial benefit for the particular hospital. Taken in account all the above mentioned points, H_2 receptor blockers can be recommended for the prophylaxis of stress ulcers. Of which, the most popular drugs are Ranitidine and Famotidine.

Treatment plan for a patient in ICU is quite complicated as doctors from different specialities take part in it with advanced methods and machines. But the intensive treatment and diseases of the patient also has complications in itself.

GIT gets effected first line in critically ill patients. The pathological studies behind this are still under research. As a whole, pathology under this can be explained by the vasoconstriction due to the ischemia of the gastric mucosa, which gives path for formation of gastric ulcers. Erosive ulcers of stomach and duodenum are noted as high as 75% (40-100%) in patients after the first hour of admission in ICU. The factors which are connected to stress ulcers are as follows:

Very high risk factors:

1. Artificial Ventilation (>48 h)

2. Coagulopathies

3. Thrombocytes <50 000

4. INR>1, 5

5. APTT (R)>2, 0

6. Burn surface area>30%

A. Shock

B. Severe sepsis

C. Severe Trauma

D. Cerebral and Spinal trauma

E. Renal Insufficiency

F. Steroidal Therapy

Gastrointestinal track bleeding directly increases the duration of the treatment and complicates the process. It increases artificial ventilation time, demands blood transfusion, prolongs the time of stay in ICU thereby decreasing hospital-bed capacity and increases the risk of lethal outcome. The average stay for such patients in ICU is 8 days on an average and also a 4-fold increased mortality rate is noted. Of course it should be mentioned that a steep downfall of death -rate in such patients is seen in last decade. In 1970 the rate varied between 5.5-33%, whereas in 2010 it is <5%. Most probably this is due to prophylactic use of pharmaceutical drugs, pulmoprotective lung ventilation and modern methods of hypo and hypovolemic control.

For all the patients in ICU having one or more risk factors for GIT bleeding, pharmaceutical prophylaxis

is must. For this purpose Proton pump Inhibitors and H_2 receptor blockers are used extensively.

There are a lot of research works, publications and discussion regarding the use of proton pump Inhibitors and H_2 receptor blockers. But most of them fail to indicate superior group. Both have nearly same effects over hospitalisation period and end results. However the use of group of drugs must be based upon the particular case of the patient, possible co action, adverse reaction, availability and economic benefit for the patient care.

The fact should be taken under consideration that, prophylaxis of stress ulcers routinely can cause serious side-effects and complications. Near about 70% of the patients without risk factors are treated for stress ulcers, during and even after the ICU setting.

Decreased acidity of gastric juice decreases the natural barrier function from intestinal infections. This can result in inoculation with Nosocomial Pneumonia, infections by *Clostridium difficile*.

The Miano TA et al. showed that use of Proton pump Inhibitors is associated with increased risk of Hospital Acquired Pneumonia (HAP), especially in ICU setting, whereas use of H_2 receptor blockers didn't increase the risk of (HAP).

The research work conducted by Beaulieu, Kwok and colleague refers to the increased risk of clostridia infection with the use of Proton Pump Inhibitors.

According to the Publication in "Pharmacotherapy" H_2 receptor blockers are cheaper than the other, thus treatment expenses becomes less, it increases chances of survival and escapes adverse effects.

Drugs decreasing the acidity of the gastric juice have some side effects, as other drugs.

Proton pump inhibitors present themselves with pharmacological reactions with other drugs, hypomagnesaemia, increased risk for infections, acute interstitial nephritis, increased risk of fractures, risk of iron deficiency and vit-B12 deficiency.

H_2 receptor blockers have the following effects: increased tolerance with time, it does not interfere with

cytochrome P450 system, thrombocytopenia, arrhythmia (bolus i/v dose). Some drugs also have Specific reactions with cimetidine.

Ranitidine and Famotidine are the popular drugs from H_2 receptor blockers. Both of them are available as intravenous form, and are widely used in ICU setting. It is well known that treatment in ICU is a long, complex and expensive process. It is important to take care of pharmaceutical budget. It's very important to understand that price is just a mere factor. All the positive and negative sides should be understood well in order to prescribe a particular drug in order of betterment both the patient and the budget.

Justification of use of famotidine over ranitidine

1. Famotidine suppress basal gastric secretion by 40-150 times than that of cimetidine and 7-20 times of that of Ranitidine, which gives the same effect keeping the pH high. Famotidine binds with Histamine receptors thus providing a long lasting effect. In equimolar doses Famotidine gives 1.3 times more effect than any other H_2 receptor blocker.

2. Serious side effects on cardiovascular system, central nervous system, endocrine and renal system from the use of Famotidine is not documented. Most importantly Famotidine very rarely causes hallucinations, delirium and changes in orientation. As we all know any kind of deterioration in CNS in ICU setting is dangerous for the patient.

3. Famotidine do not go through cytochrome P450 system, which is very important for clinical practice, where patients receive a number of drugs on a daily basis. Drugs like warfarin, theophylline and others don't get interfered.

4. Cimetidine and Ranitidine decrease the activity of alcohol dehydrogenase, but famotidine do not interfere with Alcohol Dehydrogenase. Thus it can be used in patients with alcoholism, or in patients who take alcohol. (In Republic of Belarus, population above 15 years of age consume 17.5 litters of pure alcohol per person per year).

5. Famotidine is injected twice a day, and Ranitidine 3-4 times a day. The number of times of contact with

intravenous catheter is directly proportional to catheter related infections. Also number of sterile gloves usage, syringes decreases if number of dosage decreases. Thus making the treatment a little more economical.

6. On injection of bolus dose of Ranitidine hypotension, bradycardia, arrhythmia and asystolia can occur. But dosage of Famotidine in course of 2 minutes is safe for cardiovascular system. This is very important for high risk cardiac patients, for patients with unstable blood pressure, and for emergency surgeries.

From the above studies we see that use of H_2 receptor blockers is more suitable in critically ill patients. Again, use of Famotidine for the treatment is economic, comparatively with fewer side effects and improved Post ICU results are recommended.

References

1. Marino PL (2014) The ICU Book. ATS 11: 999.

2. Cook DJ, Griffith LE, Walter SD, Guyatt GH, Meade MO, et al. (2001) The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients. Crit Care 5: 368-375.

3. Lucas CE, Sugawa C, Riddle J, Rector F, Rosenberg B, et al. (1971) Natural history and surgical dilemma of "stress" gastric bleeding. Arch Surg 102: 266-273.

4. Anderson ME (2013) Stress Ulcer Prophylaxis in Hospitalized Patients. Hosp Med Clin 2: 32-44.

5. Miano TA, Reichert MG, Houle TT, MacGregor DA, Kincaid EH, et al. (2009) Nosocomial pneumonia risk and stress ulcer prophylaxis. Chest 36: 440-447.

6. Eom CS, Park SM, Myung SK, Yun JM, Ahn JS (2011) Use of acid-suppressive drugs and risk of fracture. Ann of FM 9: 257-267

7. Ro Y, Eun CS, Kim HS, Kim JY, Byun YJ, et al. (2016) Risk of C. difficile infection with use of a PPI for stress ulcer prophylaxis in critically Ill patients. Gut Liver 10: 581-586.

8. Kwok CS, Arthur AK, Anibueze CI, Singh S, Cavallazzi R, et al. Risk of Clostridium difficile infection with acid suppressing drugs and antibiotics. Am J Gastroenterol 107: 1011-1019.

9. Hammond DA, Kathe N, Shah A, Martin BC (2017) Cost-Effectiveness of Histamine2 Receptor Antagonists Versus Proton Pump Inhibitors for Stress Ulcer Prophylaxis in Critically Ill Patients. Pharmacotherapy 37: 43-53.

10. WHO (2014) Global status report on alcohol and health

11. John F, David C, John MD (2013) Wasnick Morgan & Mikhail's Clinical Anesthesiology

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