ORIGINAL RESEARCH PAPER

Volume - 9 | Issue - 7 | July - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A RANDOMISED DOUBLE BLIND STUDY TO COMPARE THE EFFECT OF INTRAVENOUS RABEPRAZOLE VS PANTOPRAZOLE ON GASTRIC pH AND VOLUME IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANAESTHESIA.

Anaesthesiology

Kanchan Chauhan Professor, S.M.S Medical College and Attached hospitals, Jaipur.

Amit Mangal* 3rd year Resident S.M.S Medical College and Attached hospitals, Jaipur. *Corresponding Author

Satyendra Pancholi 3rd year Resident S.M.S Medical College and Attached hospitals, Jaipur.

ABSTRACT

Background And Aims: Laparoscopic surgery is usually associated with high risk of aspiration due to head-down position and increase in intra-abdominal pressure. We planned this study to compare the effect of intravenous rabeprazole and pantoprazole on gastric pH and volume in patient undergoing laparoscopic cholecystectomy under general anaesthesia

Materials And Methods: The present study was conducted in 80 patients of age 20-60years, of either sex, of ASA-PS I&II, undergoing elective laparoscopic cholecystectomy surgery under general anaesthesia in a prospective double blind manner. The patients were kept fasting over night, patients were randomly allocated (Sealed Envelop method) in two groups. Group A received Pantoprazole(40mg) i.v. and Group B Rabeprazole (20mg) i.v. 20 min before induction of anaesthesia One hour after the premedication, gastric contents were aspirated to record volume and pH.

Results: The mean post-intubation volume was 22.05±1.80ml and 20.20±3.31ml in group A and group B respectively. The mean pre-extubation volume in group A and group B was 14.70±2.65ml and 11.33±2.19ml respectively. The mean pH of post-intubation gastric aspiration contents in group A was 4.84±0.84 and in group B was 6.67±0.58. The mean pre-extubation pH in group A was 5.53±0.81 and group B was 7.24±0.53.All values were statistically significant ($p<0.05$).

Conclusion: Intravenous rabeprazole is more effective than pantoprazole in reducing the gastric volume and increasing the gastric pH.

KEYWORDS

Rabeprazole, Pantoprazole, Gastric volume, pH

INTRODUCTION

Laparoscopic surgery is usually associated with high risk of aspiration due to head-down position and increase in intra-abdominal pressure. In laparoscopic cholecystectomy secretion of gastric acid is increased and patients may regurgitate or vomit bile-stained fluid. There are many reports of pulmonary aspiration in patients undergoing laparoscopic cholecystectomy[1]. Acid aspiration syndrome (AAS) occurs mainly during general anaesthesia, so regional techniques are the most effective prophylactic measure . Other measures for prevention of aspiration of acid gastric contents during general anaesthesia, include preoperative fasting, non- particulate antacids, H2 receptor blockers, gastro kinetic drugs like metoclopramide, rapid-sequence induction with cricoid pressure and awake extubation during emergence from general anaesthesia[2]. Many published articles are available about intravenous use of H2 receptor antagonist and prokinetics, however reports about use of proton pump inhibitors (PPI'S) in prevention of acid aspiration in patients undergoing laproscopic surgery are relatively few.Therefore we postulated that a single dose of IV rabeprazole 20 mg would cause greater inhibition of acid secretion and a higher pH when compared to IV 40 mg pantoprazole.

Aim Of Our Study

We planned this study to compare the effect of intravenous rabeprazole and pantoprazole on gastric pH and volume in patients undergoing laparoscopic cholecystectomy under general anaesthesia. Pantoprazole and rabeprazole both are substituted benzimidazole derivatives and irreversible proton pump inhibitors which have been shown to effectively reduce gastric acid secretion.[3,4,5] However Rabeprazole has been shown in vitro to be more readily converted to its active form than omeprazole, pantoprazole or lansoprazole.[5] Furthermore no trials to date have evaluated the effect of specific proton pump inhibitors on gastric volume and pH. With this background this study was undertaken to compare the effect of intravenous rabeprazole and pantoprazole on gastric pH and volume in patient undergoing laparoscopic cholecystectomy under general anaesthesia.

METHODOLOGY

After obtaining written informed consent from patients and approval from institutional ethics committee, 80 adult patients aged 20 to 60 years, ASA grade I-II, undergoing elective laparoscopic cholecystectomy under general anaesthesia were included in the study. Complete preanesthetic evaluation was performed in each patient including detailed history taking, thorough physical examination and routine preoperative investigations. Patient refusal,allergy to study drugs, emergency surgery, obese (>20%of ideal weight), diabetic patients, patients with history of any GIT disorder and patients receiving any medication known to interfere with gastrointestinal function were excluded.

On arrival in OT, routine non invasive monitors were attached and baseline parameters in form of systolic and diastolic BP, ECG, SpO2 ,ETCO2 were noted and drip started with Ringer lactate.Twenty minutes before the induction of anaesthesia, 10mL study drug was given intravenously (IV) in the form of either Pantoprazole 40 mg (Group A) or Rabeprazole 20 mg(Group B) by an anaesthesia resident who did not know the contents of the IV injection. Patients were premedicated inj. Midazolam 0.05mg/kg and inj. Fentanyl 2mcg/kg iv. After preoxygenation with 100% O2 for 3 min, anaesthetic induction was performed with inj. propofol 2mg/ kg, and tracheal intubation was facilitated with inj. atracurium 0.5mg/ kg. IV Direct laryngoscopy was done and patient was intubated with ETT of appropriate size. B/L air entry was checked and tube was fixed. The lungs were ventilated, taking care to avoid inflation of the stomach. Anaesthesia was maintained with nitrous oxide in oxygen and isoflurane. Muscle relaxation was maintained with 0.1mg/kg atracurium IV SOS. After tracheal intubation and before start of surgery, an anaesthesiologist who did not know which drug has been given to the patient, inserted a 16 G multiorifice nasogastric tube (NGT) into the stomach. Its placement within the stomach was verified by auscultation over the epigastrium during the introduction of 10ml of air. Great care was taken to avoid epistaxis, vomiting, oxygen desaturation or any other serious complication during insertion of NGT. Gastric fluid samples were obtained by gentle aspiration with a 50ml syringe by an investigator who was unaware of the patient's pre-anaesthetic medication. The volume of gastric contents were measured with a syringe. The pH of the gastric fluid was determined immediately using a pH meter (Range 0.0 to 14.0 pH, resolution 0.1 pH, accuracy ± 0.1 pH). A pH of < 2.5 and volume of >25 ml was regarded as clinically significant and if both present, then this was regarded as placing the patient at risk of acid aspiration.The time interval between the injection of study drug and post intubation aspiration was estimated. Haemodynamic parameters was monitored throughout including SpO2 at regular intervals of 10 min till the end of surgery.

Aspiration was repeated before extubation and its volume and pH was measured as previously. The time interval between injection of study drug and pre-extubation aspiration was estimated. We looked for the following findings to rule out aspiration: 1) the presence of foreign material in the mouth or posterior pharynx; 2) sudden coughing or laryngospasm; 3) dyspnea, tachypnea, hyperpnoea or apnea; 4) chest

retraction or obvious airway obstruction; 5) cyanosis, particularly if not relieved by oxygen;6) tachycardia and signs of shock; 7) development of pink frothy exudates At the end of surgery all anaesthetic agents were discontinued and pt. was taken on 100% O2 .On regaining spontaneous respiration, patient was reversed with inj. Neostigmine 0.05 mg/kg and inj. glycopyrolate 5mcg/kg. Patient was extubated when fully awake and breathing spontaneously. All patients were observed in the recovery room and then in the postoperative ward for 24 hours to rule out any complications due to acid aspiration and also side effects of drug injected. The particulate and non-particulate nature of aspirate was also noted. A pH of ≤3.5 and volume of >25 ml were regarded as clinically significant and a combination of two was regarded as placing the patient at risk of acid aspiration. The sample size calculated was 36 in each group at 95% confidence and power 80% to verify the minimum expected difference of 6.38 (±4.33)ml in gastric volume variation from baseline in both groups. This sample size was large enough to include all other variables of this study. So for the study purpose 40 subjects were taken for both groups that is 40 subjects for rabeprazole group and 40 subjects for pantoprazole group. Statistical data was coded and entered into microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPPSS statistics inc.chicago, illinosis USA) windows software program. Descriptive statistics included computation of percentages, means and standard deviations. The data were checked for normality before statistical analysis using Shapiro-wilk test. All the quantitive data were analysed using paired and unpaired student t-test while nonparametric data were analysed using wilcoxon signed –rank test and mann U test. Chi-square test and fisher exact test were used for qualitative data whenever two or more than two groups were compared. Level of significance was set at P<0.05.

RESULTS

The study groups were statistically comparable in terms of age, weight, sex ratio and ASA grade between the study groups shown in Table 1.

There was no statistically significant difference in the duration of surgery ,SPO2 and ETCO2 between the two groups. There was no statistically significant difference in hemodynamic parameters (SBP,DBP, MAP, PR) at different time intervals between the study groups. Post-intubation and Pre-extubation pH of gastric aspirate showed statistically significant difference between pantoprazole group (4.84+/-0.84) and (5.53+/-0.81) and rabeprazole group (6.67+/-058) and (7.24+/-0.53.) as shown in Table 3.

Post-intubation and Pre-extubation volume of gastric aspirate showed statistically significant difference between pantoprazole group (22.05+/-1.80) and (14.70+/-2.65) and rabeprazole group (20.20 +/-3.31) and (11.33+/- 2.19) shown in Table 2. There was no statistically significant difference in mean time interval between drug given and 1st gastric aspirate in group pantoprazole (24.72±0.54 min) and in group rabeprazole (24.65±0.56 min). There was no statistically significant difference in mean time interval between drug given and 2nd gastric aspirate in group pantoprazole (48.07±0.67 min) and in group rabeprazole (48.17±0.56 min). There was no statistically significant difference in nature of gastric aspirate between the two groups.

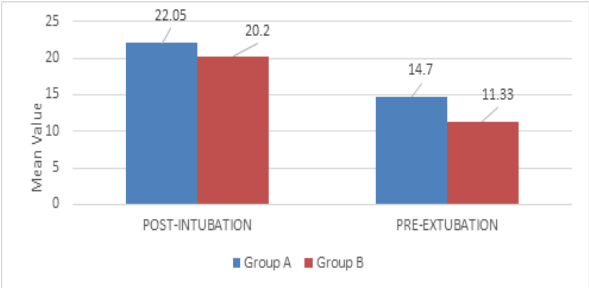
Table 1: Demographic Data

	Group A	Group B	P value	Significance
Age	41.70±10.16	40.43±9.85	0.570	NS
Weight	53.08±4.80	55.43±7.18	0.09	NS
Sex(M/F)	7/33	8/32	0.77	NS
ASA grade I/II	32/8	29/11	0.47	NS
Duration of surgery	46.97±0.69	46.42±0.74	0.78	NS
Time interval between drug given and 1st gastric aspirate	24.72±0.54	24.65±0.56	0.61	NS
Time interval between drug given and 2nd gastric aspirate	48.07±0.67	48.17±0.56	0.46	NS

Table 2: Post-intubation And Pre- Extubation Volume

Volume	Group A	Group B	P value
	Mean(ml±SD)	Mean	
Post-intubation volume(ml)	22.05±1.80	20.20±3.31	0.023*
Pre-extubation volume(ml)	14.70±2.65	11.33±2.19	0.000*

A – Pantoprazole; B- Rabeprazole; * - significant(p<0.05);

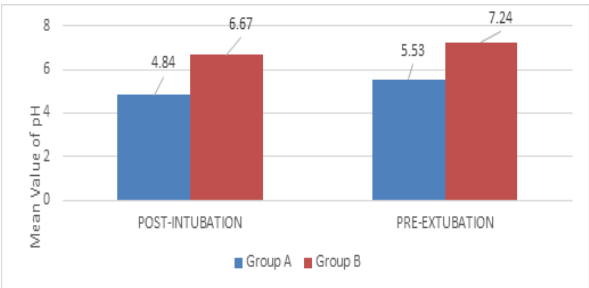


Comparison Of Volume Of Gastric Aspirate Between The Study Groups

Table 3: Post-intubation And Pre-extubation Gastric Aspiration pH

pH	Group A	Group B	P value
	Mean	Mean	
Post-intubation	4.84±0.84	6.67±0.58	<0.001*
Pre-extubation	5.53±0.81	7.24±0.53	<0.001*

A – Pantoprazole; B- Rabeprazole; * - significant(p<0.01);



Comparison Of pH Of Gastric Aspirate Between The Study Groups

DISCUSSION

Regurgitation, vomiting and aspiration may occur quite unexpectedly in association with anaesthesia and may have serious sequelae. Aspiration/regurgitation was ranked fifth and comprised over 5 per cent of a large collection of incidents that arose during general anaesthesia[6]. While attention has been usually focused on aspiration as the major consequence of regurgitation and vomiting, other sequale such as laryngospasm, desaturation and bronchospasm are also important. These problems are encountered by all practicing anaesthetists and present as emergencies requiring instant recognition and a rapid as well as appropriate response.

Pulmonary aspiration of gastric contents during anaesthesia is a small but important cause of anaesthesia related deaths, especially in obstetrics. Although precise numbers are not known, it is probable that many patients suffer nonfatal aspiration with considerable morbidity. Any safe treatment that reduces this hazard is desirable.

Perioperative morbidity and mortality secondary to aspiration of gastric contents is avoidable complication during induction of general anaesthesia reported by Meril and Hingson et al 1951)[7]. 33% morbidity has been reported by Hall et al (1940)[8]. Lunn and Mushin (1982)[9] have found pulmonary aspiration of gastric contents to be leading cause of death directly related to general anaesthesia.

The current study was designed to be performed on laparoscopic cholecystectomy patients, as these patients are proven to be at a higher risk of aspiration[10]. Generally, patients who are undergoing upper abdominal surgery should be considered at risk, as surgical manipulation may push gastric contents back up to the mouth. Moreover, patients who are undergoing laparoscopic surgery are at a higher risk of aspiration, because of the increase in intra-abdominal pressure and lithotomy or the head-down position that may encourage residual gastric contents to regurgitate, as well as increase in secretion of gastric acid. Also, these patients may regurgitate or vomit bile-stained fluid[11]. In fact, pulmonary aspiration has been reported in patients undergoing laparoscopic cholecystectomy[12]. The high

incidence of regurgitation after laparoscopic cholecystectomy comes as no surprise even when patients are fasting and in spite of all the measures taken, where an orogastric tube is introduced at induction of anesthesia and during surgery, to empty the gas from the stomach. This risk is due to the presence of pockets within the stomach far from reach of the tip of the gastric tube[13].

Various measures have been described which prevent aspiration.(14) The condition of aspiration pneumonitis and its dreaded sequelae are well known to the anesthesiologists. Although it is not absolutely preventable, but by adopting some precautions or preventive measures, the chance of aspiration or if it occurs, its sequelae can be brought down to an absolute minimum. Patients especially undergoing upper abdominal surgery present a greater risk during induction and recovery(15) Therefore in our study we have taken in to consideration post intubation and preextubation aspiration volume and pH for analysis. Recently proton pump inhibitors are shown to have better efficacy in preventing acid aspiration(omeprazole, rabeprazole, lansoprazole, pantoprazole, esomeprazole). PPI'S after activation, concentrate in the secretory canaliculus of the parietal cell. The protonated molecules undergo a conversion to an active sulfenamide compound and, in this state, form covalent inhibiting disulfide bonds with surfaceexposed cysteine's of the active parietal cell H+/K+ATPase. However, the five available PPIs differ in terms of acid stability. Due to the modified functional

substituents on the rabeprazole, it can be activated at higher pH levels much faster than other PPIs. At acidic pH rabeprazole is activated faster compared to pantaprazole and other PPI'S. At pH 5.1 (the pH during fasting), the activation half-life was again the shortest one for rabeprazole. In addition, rabeprazole is known to have a faster onset of action in patients with heartburn leading some to suggest that rabeprazole may have efficacy as an on-demand or abortive therapeutic agent.(16) In an isolated hog vesicle model, rabeprazole confirmed its potent and fast onset of action but pantoprazole could only inhibit the 50% of the pump by the end of the 50 minute test.(17)Therefore, rabeprazole sodium produces a dose-related sustained inhibition of both basal and peptone meal-stimulated gastric acid secretion. (18,19)

In our study The mean post-intubation volume and pre-extubation volume in pantaprazole was 22.05±1.80and 14.70±2.65ml respectively which was in consistent with previous studies which concluded that intravenous 40 mg pantoprazole is effective in reducing gastric volume and pH.(41,42,43) In rabeprazole group the mean post-intubation and pre-extubation volume was 20.20±3.31ml and11.33±2.19ml respectively which was statistically significant. Similarly the mean value of post-intubation and pre-extubation aspiration pH was higher in group B compared to group A which was statistically significant.

Our results match with the findings of Ahmed SMN (2016) et al(20) who compared the efficacy of drugs in decreasing gastric volume and pH and found that mean volume of gastric aspirate was less and pH was more in proton pump inhibitors group as compared to control group. Our results are also in concordance with Miner et al(21) who conducted a study to compare the effects of single doses of rabeprazole 20mg and pantoprazole 40 mg on 24 hr intragastric acidity and esophageal acid exposure.They concluded that rabeprazole 20mg was significantly more effective then pantoprazole 40 mg in raising intragastric pH. Our results are similar to study done by Celebi A et al(22) who compared the acid inhibitioneffectsof esomeprazole,rabeprazole,lansoprazole and pantoprazole on days 1 and 5 of treatment in patients with GERD and concluded that rabeprazole was superior to others on first day of treatment. Padmaja R (2014) (23) et al, compared the effectiveness of intravenous rabeprazole 20mg and intravenous ranitidine 50mg on gastric fluid properties in patients undergoing elective surgery under general anaesthesia. Their results are consistent with the results of our study in terms of effectiveness of rabeprazole in reducing the gastric aspiration volume and pH but their study differs in methodology as they compared the pre intubation, post-intubation and pre-extubation volume and gastric pH. But in our study we have taken into consideration only post-intubation and pre-extubation gastric volume and pH.Similar result was reported in another study by Wang HS et al(24) .In other comparative trial by Pantoflickova D et al(25) rabeprazole has shown to be more potent acid inhibitor compared to pantaprazole. Similarly in patients with acid peptic ulcer disease rabeprazole 10 mg compared to pantoprazole 40 mg decreased the incidence of nocturnal acid break through (NAB),decreased persisting time of NAB and increased mean pH of NAB(26) . In another cross over study using 5 different PPI'S, the intragastric pH was measured following PPI treatment for 5 consecutive days. On day 5 assessment revealed that rabeprazole maintained pH>4 for greater percentage of time compared to pantoprazole and other PPI'S except esomeprazole.

Limitations of the current study included the use of otherwise healthy participants and surrogate endpoints (gastric fluid pH and volume); it would have been better if we had used high-risk patients (e.g., obese, diabetics, esophageal dysfunction) and the outcome data included e.g., incidence of aspiration pneumonia.

Another limitation of the study may be directed toward the fact that the gastric volumes in this study are not representative of the total volume of gastric contents, because emptying the stomach with a nasogastric tube has not been shown to ensure complete emptying of gastric contents.

Most common restriction of the study was that there was limited study material and data available for comparison.

REFERENCES

1. Keller C, Brimacombe J, Bittersohl J, Lirk P, Von Goedecke A. Aspiration and the laryngeal mask airway: three cases and a review of the literature. Br J Anaesth 2004;93:579–82.
2. Shaikh JM, Sabbar S, Aziz N et al.; acid aspiration prophylaxis during anaesthesia for Caesarean section: a survey among anaesthetists at Hyderabad; J Ayub Med Coll Abbottabad 2009;21(4).
3. Bardhan KD. Pantoprazole: A new proton pump inhibitor in the management of upper gastrointestinal disease. Drugs Today. 1999;35:773–808.
4. Fitton A, Wiseman L. Pantoprazole: A review of its pharmacological properties and therapeutic use in acid related disorders. Drugs. 1996;51:460–82.
5. Pace F, Pallotta S, Casalini S, Porro G B. A review of rabeprazole in the treatment of acidrelated diseases. Therapeutics and Clinical Risk Management 2007:3(3).
6. Webb RK, Van Der Walt JH, Runciman WB, Williamson JA, Cockings J, Russell WJ, et al. Which monitor? An analysis of 2000 incidents reports. Anaesth Intensive Care 1993; 21 : 529-42.
7. Merill RB, Hingson RA. Studies of incidence of maternal mortality from aspiration of vomitus during anaesthesia occurring in major obstetric hospitals in the U.S. Anaesth and Analg 1951;30(3):121-35.
8. Hall CC. Aspiration pneumonitis as an obstetric hazard. JAMA 1940;114(9):728-33
9. Lunn JN, Mushin WM. Mortality associated with anaesthesia. Anaesthesia 1982;37(8):856
10. MALTBY J.R., BERIAULT M.T., WATSON N.C. and ASAI T.: Use of the laryngeal mask is not contraindicated for laparoscopic cholecystectomy. Anaesthesia, 56: 800- 2, 2001.
11. MESSAHEL F.M. and AL-QAHTANI A.S.: Pulmonary Aspiration Of Gastric Contents In Anesthesia: A review over 15-year period. The Internet Journal of Anesthesiology, 19 (1), 2009.
12. WARNER M.A., WARNER M.E. and WEBER J.G.: Clinical significance of pulmonary aspiration during the perioperative period. Anesthesiology, 78: 56-62, 1993.
13. Wendy King; Pulmonary aspiration of gastric contents; Update in anesthesia Dec 2010;26:28- 31.
14. Engelhardt T., Webster NR. Pulmonary aspiration of gastric contents of anaesthesia. BJA 1999;83:453-60.
15. Wendy King; Pulmonary aspiration of gastric contents; Update in anesthesia Dec 2010;26:28- 31.
16. Kromer W, Kruger U, Huber R, et al. Differences in pH- dependent activation rates of substituted benzimidazoles and biological in vitro correlates. Pharmacology, 1998;56:57–70.
17. Besancon M, Simon A, Sachs G, et al. Sites of reaction of the gastric H,K-ATPase with extracytoplasmic thiol reagents. J Biol Chem, 1997 272:22438–46.
18. Lew EA, Barbuti RC, Kovacs TO, et al. An ascending single-dose safety and tolerance study of an oral formulation of rabeprazole (E3810). Aliment Pharmacol Ther, 1998;12:667–72.
19. Ohning GV, Walsh JH, Pisegna JR, et al. Rabeprazole is superior to omeprazole for the inhibition of peptone meal- stimulated gastric acid secretion in Helicobacter pylori-negative subjects. Aliment Pharmacol Ther, 2003;17:1109–14.
20. Ahmed SMN, Patil YW, Deshpande SG, et al. Effects of proton pump inhibitors on gastric volume and gastric PH in adult patients posted for elective operative procedures. J.Evolution Med. Dent. Sci. 2016;5(62):4346-4350
21. Miner P J, Orr W, Filippone J, et al. Rabeprazole in nonerosive gastroesophageal reflux disease: a randomized placebo-controlled trial. Am J Gastroenterol, 2002;97:1332–9.
22. Çelebi A, Aydın D, Kocaman O, Konduk BT, Şentürk O, Hülagü S. Comparison of the effects of esomeprazole 40 mg, rabeprazole 20 mg, lansoprazole 30 mg, and pantoprazole 40 mg on intragastrıc pH in extensive metabolizer patients with gastroesophageal reflux disease. Turk J Gastroenterol 2016; 27: 408-14
23. Padmaja R, Kumar K GTS, Murali YV. Study on intravenous rabeprazole and intravenous ranitidine for improving perioperative gastric fluid properties in patients undergoing elective surgery under general anesthesia. Asian Pac. J. Health Sci., 2014;1(4):559-565.
24. Wang HS; Oh DS; Anderson A; Nieto J; Tien P; Ohning G et al. Comparative Efficacy of Rabeprazole and Pantaprazole in the control of Nocturnal Acid Output and Intragastric acidity. Gut and Liver Vol 2. No 1, June 2008,p-30-38.
25. Pantoflickova D, Dorta G, Ravic M, Jornod P, Blum AL. Acid inhibition on the first day of dosing: comparison of four proton pump inhibitors. Aliment Pharmacol Ther 2003;17:1507-14.
26. Luo JY, Niu CY, Wang XQ, et al. Effect of a single oral dose of rabeprazole on nocturnal acid breakthrough and nocturnal alkaline amplitude. World J Gastroenterol, 2003;9(11):2583–6.

PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr