Original Article

Utility of noninvasive ventilation in high-risk patients during endoscopic retrograde cholangiopancreatography

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ABSTRACT

Background: There is little evidence on noninvasive ventilation (NIV) preventing respiratory complications in high-risk patients undergoing endoscopy procedures. **Objectives:** The objective of this study is to demonstrate that the application of NIV through a nasal interface can prevent the appearance of ventilatory alterations during endoscopic retrograde cholangiopancreatography (ERCP) in patients with risk factors associated with the development of hypoventilation. **Patients and Methods:** A non-randomized interventional study was performed on 37 consecutive high-risk patients undergoing ERCP. During the procedure, 21 patients received oxygen by nasal cannula (3 L/minute) and sixteen received NIV through a nasal mask. Arterial blood gas analyses were conducted before and immediately after the ERCP. An Acute Physiology and Chronic Health Evaluation (APACHE) score pre-ERCP was recorded. The complications during the procedure were recorded. **Results:** The groups with and without NIV were comparable. A post-ERCP pH of <7.35 was found in eight patients, who did not receive ventilatory support (38.1%) compared to zero patients in the NIV group (P = 0.006). A post-ERCP pCO_2 >45 mmHg was found in one case (6.3%) in the NIV-group and in nine cases in the nasal cannula group (42.9%; P = 0.01). The median pCO_2 post-ERCP was lower (36.5 ± 6.2 vs. 44.5 ± 6.8 mmHg) (P = 0.001) and median pH post-ERCP was higher (7.41 ± 0.4 vs. 7.34 ± 0.5) (P = 0.001) in patients treated with NIV. In the multivariate analysis, after adjusting for gender, the APACHE score, pH and pCO_2 pre-ERCP, age, propofol doses, and procedure duration, the following differences were maintained (pCO_2 difference = 5.54, 95% Confidence Interval (CI) =2.3 – 8.7, pH difference = 0.047, and 95% CI = 0.013 – 0.081). Among the 37 procedures, four complications occurred: One in the NIV group and three in the nasal cannula group. None of them was related to NIV. **Conclusions:** Our preliminary results demonstrate that in high-risk patients undergoing ERCP, hypercapnia and respiratory acidosis are frequent. NIV prevents the appearance of these complications.

KEY WORDS: Endoscopic retrograde cholangiopancreatography, high-risk patients, noninvasive ventilation

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) with sedation and analgesia, performed by well-trained endoscopists, has proved to be a safe procedure, although significant complications may occur as a result of instrumentation or due to the effects of sedation and analgesia.[1-7] These complications are more frequent when patients are deeply sedated, undergo complex or prolonged explorations, or undergo therapeutic procedures.[4,6] Respiratory complications are very significant in high-risk patients. Respiratory insufficiency and clinical hypoventilation are common during the realization of ERCP for patients with hypoventilation risk factors, such as, elderly patients with chronic heart diseases, patients with a history of respiratory failure, patients who are morbidly obese, and patients with obesity-hypoventilation syndrome (OHS).[8-10] Supplementary oxygen is usually indicated in these cases. Oxygen is also provided to patients with severe anemia and to patients in whom desaturation events are observed during exploration.[11,12] There is little evidence of noninvasive ventilation (NIV) preventing respiratory

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Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/0970-2113.142097

complications in high-risk patients undergoing endoscopy procedures, mainly percutaneous endoscopic gastrostomy.[13-15] The purpose of our study is to assess the efficacy and safety of NIV through a nasal mask to prevent gasometric alterations in high-risk patients undergoing ERCP.

PATIENTS AND METHODS

Starting with the hypothesis that the application of NIV through a nasal interface could prevent the appearance of ventilatory alterations during ERCP in patients with risk factors associated with the development of hypoventilation, a non-randomized interventional study in 37 consecutive patients scheduled to undergo ERCP was proposed. The study was approved by the Ethical Committee of our institution and informed consent was obtained from all the study participants.

Patients who presented with at least one of the several previously defined risk factors believed to predispose the patient to ventilatory alterations in this context were included. An advanced age (>70 years), a body mass index (BMI) >35, a New York Heart Association (NYHA) functional class II–IV for congestive heart failure (CHF), prior ischemic heart disease history, and chronic obstructive pulmonary disease stage III–IV according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (FEV_1 < 50%), were considered as risk factors.

The control group, comprising 21 patients, received oxygen through the conventional procedure at the flow rate usually used in our practice (nasal prongs, 3 L/minute) (Group 1). Subsequently, the other sixteen patients (experimental group) received oxygen plus NIV with a BiPAP-Synchrony Ventilatory Support System (Philips-Respironics®) ventilator through a Contour Deluxe nasal mask (Philips-Respironics®) (Group 2).

For sedation, in all cases, propofol was administered intravenously, with an initial dose of 0.5 mg/kg and subsequent bolus doses of 0.25 mg/kg, to maintain an adequate sedation level (grade 3-4 on the Ramsay scale). Simultaneously, meperidine was administered as an analgesic in a 50 mg intravenous dose.

Without disconnecting the patient from the oxygen source, two arterial blood gas analyses were performed, one before and the other immediately after the ERCP. The heart rate, respiratory rate, arterial blood pressure, oxygen saturation, and electrocardiographic trace were continuously monitored during the procedure.

Prior to the start of the exploration, based on the data from the medical history, each patient was assigned a score on the APACHE II scale in order to create groups with equal levels of severity. The duration of exploration was documented for patients of both groups.

Once the patient was placed on the ERCP table, a base arterial blood gas sample was obtained. Next, oxygen was initiated in the control group, and oxygen plus NIV through a nasal mask in the experimental group. In all cases the ventilator was programmed at 7 cm/H_2O inspiratory pressure (IPAP) and 5 cm/H_2O expiratory pressure (EPAP), with good tolerance to these pressures in all patients.

Heart rate and saturation (SaO_2) were continuously monitored and noninvasive measurement of arterial pressure, every five minutes, was begun. Once the monitoring had started and after the patient received positive pressure, he/she was then placed in the left lateral decubitus position to start the procedure. Before introducing the duodenoscope, 50 mg meperidine and 0.5 mg/kg propofol was given. The endoscope was inserted through a glove finger fitted into a mouth guard. The system worked as a valve and did not affect the performance of the bronchoscopy procedure or the pressures administered during noninvasive ventilation.

Once the exploration started, the ventilator settings were reprogrammed to Average Volume Assured Pressure Support (AVAPS) ventilation, to ensure a minimum tidal volume of 500 ml, obtained by means of automatic adjustment of the ventilator's inspiratory positive airway pressure (IPAP). The IPAP range was set at a minimum of 7 and a maximum of 30 cm/H_2O. The expiratory positive airway pressure (EPAP) was set at 5 cm/H_2O. The respiratory rate was determined by the patient with a backup rate of 15. The AVAPS mode was chosen to guarantee the contribution of a volume minute with a backup rate of 15 bpm during the procedure, of about 7.5 liters. Every five minutes, simultaneously with the arterial pressure measurement, the level of sedation was assessed by means of the clinical Ramsay scale. Similarly, the tidal volume, propofol dose used, duration of the procedure, and potential adverse effects were documented.

Once the procedure was completed, a new arterial blood gas sample was obtained, while the ventilatory support continued. Once the ventilatory support was withdrawn, the patient's respiratory capacity and oxygen saturation level were assessed, together with the patient's capacity to respond to verbal, tactile, and pain stimulation. If the patient was capable of breathing by himself/herself and kept at >90% oxygen saturation, with the nasal cannula at 3 L/minute, together with a good response to tactile or verbal stimulation, the patient was transferred to a Recovery Room under a nurse's supervision.

Statistical analysis

For the analysis of the results the statistical package SPSS 11.5 for Windows was used. The absolute and relative frequencies of discrete variables were calculated. Continuous variables were described in terms of mean, median, standard deviation, and interquartile range. Proportions of patients with pH < 7.35, pCO2 >45 or

adverse events in each group were compared using the Chi-square or exact tests. Continuous variables were contrasted with the Student's *t*-test or Mann-Whitney test. Adjusted mean differences of pH and pCO2 between groups and their 95% confidence intervals were estimated by multiple linear regression by using, sex, APACHE score, pre-CPR pH, pCO2, age, propofol doses, and length of the procedure as covariates. The level of statistical significance was $P < 0.05$.

RESULTS

The two groups were comparable before the study in terms of age, APACHE score, and presence of hypoventilation risk factors. They presented baseline pH and pCO_2 values within the normal parameters. Both groups received comparable median propofol doses. However, the NIV group had a larger proportion of men than the nasal cannula group. The patient and pre-procedure characteristics are shown in Table 1.

Endoscopic retrograde cholangiopancreatography could be performed in 87.5 and in 95.2% of the cases, with and without NIV. The procedures lasted longer in the NIV group. Sphincterotomy was performed in 93.7 and 90.4% in each group, respectively. In the NIV group, the median pCO_2 post-ERCP was lower (36.5 vs. 44.5 mmHg; $P = 0.001$) and median pH post-ERCP was higher than in the control group (7.41 vs. 7.34, $P = 0.001$). These differences were maintained after performing a multivariate adjustment by gender, APACHE score, pH and pCO_2 pre-ERCP, age, propofol dose, and duration of procedure (difference of $pCO_2 = 5.54$, CI 95% =2.3-8.7, difference of pH = 0.047, CI 95% =0.013-0.081). The procedure outcomes are shown in Table 2.

A post-ERCP pH of <7.35 was found in eight patients who did not receive ventilatory support (38.1%) compared to zero patients in the NIV group ($P = 0.006$). A post-ERCP $pCO_2 > 45$ mmHg was found in one case (6.3%) in the nasal intermittent mandatory ventilation (NIMV) group and in nine cases in the nasal cannula group (42.9%; $P = 0.01$).

No significant differences were noted in terms of the number of complications associated with ERCP in the two groups: In the NIV group, one patient showed hypotension, while in the nasal cannula group there were two cases of cardiac disturbances: One case of first-degree atrioventricular block and one case of atrial fibrillation. A patient in this group presented with a post-sphincterotomy hemorrhage, which was controlled after sclerosis with 1/10.000 adrenaline. There were no complications related to NIV during the procedure.

DISCUSSION

Our study has shown how in high-risk patients undergoing ERCP, hypercapnia and respiratory acidosis are common problems. In the control group 38.1% of patients presented with respiratory acidosis and a 42.9% had hypercapnia after ERCP procedure. Several studies have demonstrated that the use of sedation gives rise to a higher degree of success and a better acceptance of the exploration by the patient, as well as a global increase of the percentage of completed explorations and comfort for the endoscopist.[5,16-18] However, the increasing use of sedation and analgesia techniques involves an increase in costs as well as morbidity and mortality rates. It is estimated that cardiopulmonary complications currently account for over 50% of all the complications associated with digestive endoscopy and are mainly attributable to the effects of sedation and secondary hypoventilation. They range from mild, temporary hypoxemic events to severe and potentially fatal cardiopulmonary disorders.[10,19,20] In several recent series,[19,20] global morbidity associated with sedation in this context has been estimated between 6 and 54/10,000 patients, with a mortality between 0 and 5/10,000 patients.

Patients with a risk-profile (elderly, obese, chronic cardiac or bronchial disease, and III and IV ASA Grades) may suffer more respiratory or hemodynamic alterations, as we have seen in our study. Our patients were selected according to the above-mentioned risk criteria, and all of

Table 1: Baseline characteristics of the patients included in the study

	Nasal Cannula group (*n*=21)	NIV group (*n*=16)	*P* value
Mean age (years)	79.8±5.99	80.06±6.02	NS
Gender (% male)	75	33	*P*=0.012
APACHE score (mean)	8.61±3.1	8.75±2.4	NS
Age>70 (*n*,%)	20 (95.2)	16 (100)	NS
COPD (*n*,%)	2 (9.52)	1 (6.25)	NS
BMI>35 (*n*,%)	2 (9.52)	1 (6.25)	NS
Congestive heart failure (*n*,%)	2 (9.52)	1 (6.25)	NS
pH pre-ERCP (mean)	7.42±0.4	7.45±0.4	NS
pCO2 pre-ERCP (mean) (mmHg)	35.8±5.0	32.68±7.25	NS
pO2 pre-ERCP (mean) (mmHg)	75±5	73±4	NS
Diagnostic of choledocholithiasis (*n*,%)	14 (66.5)	7 (43.7)	NS
Diagnostic of bile-pancreatic duct malignancy (*n*,%)	5 (23.8)	7 (43.7)	NS

Mean values reported±Standard error, COPD: Chronic obstructive pulmonary disease, BMI: Body mass index, ERCP: Endoscopic retrograde cholangiopancreatography, NIV: Noninvasive ventilation, NS: Not significant

Table 2: Outcomes related to the procedure. The procedures lasted longer in the NIV group. The propofol doses were similar in both groups. The main technique performed was sphincterotomy

	Nasal cannula group	NIV group	*P* value
Duration of examination (minutes)	28.3±14.7	45.3±21.5	*P*=0.013
Propofol dose (mean) (mg)	141±52	130±57	NS
Overall procedure success (*n*,%)	20 (95.2)	14 (87.5)	NS
Sphincterotomy (*n*,%)	19 (90.4)	14 (87.5)	NS

Mean values reported±Standard error, NIV: Noninvasive ventilation

them were administered deep sedation (level 4-5 on the Ramsay scale) with propofol and meperidine. In the NIV group, this treatment was administered and supervised by two physicians from the Emergency Department of our hospital, well acquainted with the management of both drugs and experts in noninvasive ventilatory support and in cardiopulmonary resuscitation techniques.

As we have found in our study, NIV through a nasal mask plus oxygen prevented gasometric alterations in high-risk patients undergoing ERCP compared to the control group. Although they were considered high risk, all patients were normocapnic when they entred of the study. However, there was only one hypercapnic patient in the NIV group compared to nine hypercapnic patients in the control group after the procedure. Similar results were seen in relation to the number of patients with respiratory acidosis. Moreover, the NIV group presented no heart conduction disturbances, while in the nasal cannula group, two patients presented a first degree atrioventricular block and one presented with atrial fibrillation. These data suggest the NIV could be effective regardless of the values of PCO_2. As the number of patients is too small, more studies are necessary to clarify these preliminary results.

Technological advances in NIV over the last decade have produced masks, with an exclusive nasal interface, to ensure efficient ventilation, which allows oral endoscopic explorations to be performed simultaneously. In this context, the application of preset and constant levels of positive pressure on the airway during inspiration and expiration could prevent the occurrence of blood gas alterations. Likewise, CO2 retention secondary to hypoventilation events could be prevented. There are technical issues related to oral air leaks during an endoscopic procedure. The efficacy of endoscopic procedure performed through the mouth with the aid of a mouth guard has been described. Similar to Chiner *et al*.,[21] we placed the mouth guard inside a latex glove, which was then tied off using the conventional suture material around the outer surface of the guard, and a finger of the glove was left protruding from the central part. Once the glove had been tied off, the excess material was cut away and a small incision was made in the glove finger. Endoscopy was performed through this incision. Like other authors's experience, NIV was effective in our patients. As we have mentioned earlier, the system works as a valve and does not affect the performance of the bronchoscopy procedure or the pressures administered during noninvasive ventilation.

Current guidelines (2) recommend the administration of supplementary oxygen during prolonged procedures (ERCP, endoscopic ultrasonography) in those patients in whom hypoxemia could cause or exacerbate myocardial injuries (elderly, severe anemia, previous cardiopathy), or in patients with arterial oxygen desaturation (Grade of Recommendation A, Level of Evidence 1). We think this approach has to change. The results of our pilot study provide encouraging information about the efficacy and safety of NIV applied to deep sedation during ERCP. These data suggest the utilization of NIV associated with oxygen therapy in high-risk patients in order to prevent hypoventilation and appearance of respiratory acidosis.

This study has many limitations. First, it is not a randomized study and this clearly implies a selection bias. Nevertheless, we have studied 37 consecutive high-risk patients scheduled to undergo ERCP, and the group was homogeneous. Second, we have only analyzed the blood gas parameters. There is a doubt if the changes in these levels in the control group will likely result in complications during the procedure. Third, we do not know the real impact of NIV on a patient's morbidity or mortality. A surrogate outcome marker of arterial blood gases post the procedure does not predict decreased complications and it may have been interesting to repeat this after cessation of NIV, to see if applying ventilatory support during ERCP has any lasting effects. Anyhow, the main aim of this study was for it to be a pilot study that would open the door to larger studies.

In conclusion, the present, prospective, interventional study has shown that in high-risk patients undergoing ERCP, hypercapnia and respiratory acidosis are common problems. It provides evidence that NIV with bi-level ventilation can be an efficient technique to prevent cardiopulmonary complications during complex endoscopic procedures under deep sedation. It significantly reduces the occurrence of blood gas alterations in treated patients. The results of our pilot study provide encouraging information about the efficacy and safety of NIV applied to deep sedation during ERCP. Further studies are needed in order to confirm these preliminary results and obtain definitive conclusions on this subject.

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How to cite this article: Folgado MA, De la Serna C, Llorente A, Rodríguez SJ, Ochoa C, Díaz-Lobato S. Utility of noninvasive ventilation in high-risk patients during endoscopic retrograde cholangiopancreatography. Lung India 2014;31:331-5.

Source of Support: Nil, **Conflict of Interest:** None declared.