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Study of Laryngo-Pharyngeal Reflux (LPR) Disease and Combination Medical Treatment of Anti- Acid and Leukotriene Receptor Antagonist

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Abstract

***Background:** Laryngo-pharyngeal reflux disease and laryngo-pharyngeal symptoms and signs are common and increasing disorder mainly in pediatric patients. Frequency of LPR with laryngeal-pharyngeal issues and its response to combination or multiple medical treatment need to be clarified.*

***Objective:** To determine the singes and symptoms LPR in Pediatric patients and to assess its response to combination of medical treatment with anti-acid (H2RA/PPI) and leukotriene receptor antagonist like (Singular; montelukast).*

***Method:** 650 patients were diagnosed as having LPR and medical therapy was given for most of them. then the effect of 1 month of combination treatment of anti-acidand leukotriene receptor antagonist was assessed.*

***Results:** male patients formed 65% of all patients, most of patients have nasal obstruction with snoring and nocturnal cough and vomiting with throat discomfort and above 90% of them improved almost completely and significantly (p> 0.001) on this treatment especially snoring,nocturnal cough, vomiting and voice quality issues after combination treatment for 1 month.*

***Conclusion:** LPR is an increasing disease in pediatric patients may be due newly changing of life style, bad feeding habits in Arab Gulf Ares ,allergy to food, and there was positive impact that combination medical treatment reduce the need for further prolonged treatment and more investigations*

Keywords: *OSA - GERD -LPR- VTI - IDL- RAOM - URT-H2RA - PPI - MZH*

Introduction

The occurrence of Laryngo-pharyngeal reflux disease is strongly associated with snoring and upper respiratory signs and symptoms like: Frequent throat clearing, recurrent Sore throat, recurrent rhino-sinusitis, dental erosion, Halitosis, Chronic recurrent choking cough, Recurrent pneumonia and atypical croup, with multiple hospitalizations or antibiotic,Wet-sounding respirations, 'wet burps' are often present. also hoarseness of voice, Aspiration, Wheezing, laryngospasm, Noisy breathing, Voice fatigue, breaking of voice, Pauses in breathing (apnea), Turning blue (cyanosis) and/or aggravation of pulmonary disease, Reactive airway disease; asthma, Sleep disordered breathing (SDB), irritability. Etc.

It has been found that patients with LPR exhibited more frequent nocturnal reflux symptoms like cough and snoring. It has been supposed that LPR may predispose patients to the development adenoid hypertrophy or other inflammation in URT.

Other airo-digestive symptoms could be found with LPR patient like: Spit up, Hiccups, drooling, Burping, Gagging and Choking, Globus pharynges, Dysphagia, abdominal discomfort, Feeding difficulty,

regurgitation, emesis, Apparent life threatening event (ALTE), Wight loss, failure to thrive (..Less than 5% compared to the expected norm).

Bakr, Mahalawy, Elhabashy, Essa and Saad (2015), study published in Egyption Journal of chest diseases and Tuberculosis at 30 May 2015; they found that:

- Heart burn and regurgitation in patient with OSA were significantly higher than controls (p=0.015 and 0.048 respectively) while the difference in dysphagia was statistically non-significant (p=0.526)

- The frequency of LPR in patients with OSA was significantly higher than in controls (43.3% versus 13.3% p=0.044)

Aim of the Work

The aim of this work was to determine the prevalence of LPR among pediatric patients and to assess its response to combination therapy with anti-acid (H2RA /PPI and leukotriene receptor antagonist) together.

Patient and Methods

This study was performed in on six hundred fifty subjects (patients under 14 years old) in M.Z.H: Madinat Zayed Hospital (referred hospital in ALDhafra region-Abu Dhabi – UAE) department of Surgery during the last 3 years ago (6/2015 till 8/2018) most were case series of retrospective reviews: Studies reporting positive results, taking from electronic archives.

	OP			
Months	2016	2017	2018	Total
January		172	156	328
February		173	105	278
March	26	118	13	157
April	48	186	153	387
May	20	169	162	351
June	55	149	196	400
July	38	172	123	333
August	185	139	115	439
September	160	41		201
October	13	95		108
November	8	4		12
December	38	117		155
Grand Total	591	1535	1023	3149

	IP			
Months	2016	2017	2018	Total
January	2	14	9	25
February	2	12	18	32
March	3	1	1	5
April	11	11	16	38
May	8	12	26	46
June	9	18	17	44
July	16	17	27	60
August	10	8	21	39
September	6	12		18
October	2	21		23
November	1	3		4
December	7	10		17
Grand Total	77	139	135	351

Table1. *all patients came to ENT department during the study period.*

I saw almost 3500 patients during that mentioned time: 1500 patients were under age 14 years, 650 (19%) of all my ENT patients during the last 3 years were complaining from air-digestive signs and symptoms of LPR and GERD.

420 (64%) of them were males and 230(35%) of them were females, clinically diagnosed as LPR due to the underline Patient complaints,history which had been taken from them or in case patients were un-cooperative from their parents.

patients were documented after had been divided into 4 groups, and followed up for at least one month and the development of symptoms and signs monitored especially cough, vomiting, snoring and laryngeal symptoms like hoarseness of voice and throat clearing.

Group 1 (patients): 150 patients were given (H2RA; Histamine 2 Receptor Antagonist): Ranitidin (4 mg / kg) OD alone.

Group 2 (patients): 150 patients were given (PPI Proton Pump Inhibitor): Pantoprazol (1 mg/kg) OD alone.

Group 3 (patients): 150 patients were given combination therapy of Anti-acid (either Pantoprazol or Ranitine) and leukotriene receptor antagonist (Montelukast 4-5 mg) OD.

Group 4 (controls): 100 subjects without giving any medications for them, but they have LPR signs or symptoms.

The age of patients were between age :after birth (almost after 6 months of birth till 14 years old) and divided as 2 years for 7 category as follow: after birth till end of 2 years/ 3-4 y / 5-6 y / 7-8 y / 9-10 y / 11-12 y / 13-14 years…

60 patients were obese patients – 10 were have laryngomalacia confirmed by flexible fiber optic – 7 patients have Dawn's syndrome – 6 cerebral palsy – 5 were Autism's patients – 1 only was Kabuki's syndrome diagnosed in USA.

All patients and their families were educated and underwent:

(1) A full history taking and clinical examination was done by either IDL (Indirect laryngoscopy) or Flexible fiber optic laryngoscopy.

(2) Informed their family about the GERD-LPR diet for at least 3 months.

(3) Educated about Life style changing issues to be applied for at least 6 months.

(4) To be followed up with ENT – clinic every 3 month later for at least 2 years.

Respiratory and laryngeal symptoms were almost monitored by family like: nocturnal cough and vomiting, throat clearing, aspiration, OSA, snoring, difficulty in nasal breathing and open mouth breathing.

Result

Table 1 shows that all patients whom I was seen during time (6/2015 till 8/2018), actually there were 3500 patients during that time 650 of them were pediatric have LPR.

Figure 1 showed numbers of all patients and gender of LPR patients.

Figure 2 showed number of patients regarding the age categories, 2 peaks between 5-6 then 13-14 years.

Table 2 showed that most patients improved in their cough and vomiting 95% then aspiration, OSA, difficulty in breathing 85%.

Figure 3 showed total LPR patients and patients whom have congenital or syndromes and neurologic disorders.

Figure 4 showed numbers and percentage of signs and symptoms of LPR during studied period.

Table 3 and **figure 5** shows that patients whom came under group 3 were significantly improved 146 of them (93%) higher than the others groups and the controls subjects.

Discussion

LPR is a condition marked by airway mucosal edema and erythema due to acidic reflux materials and accompanying usually by narrowing airway lumens due to edematous and erythematous mucosa of posterior nasopharynx, oropharynx and tonsillarregion, hypopharynx and laryngeal inlet.

Mostly during sleep which in turn, produces repeated episodes of decreased oxygen saturation due to mucosal edema, cough, nasal obstruction and brief arousals from sleep. Currently, sleep related LPR is underappreciated from aclinical standpoint. LPR disease and OSA are often co-morbid disorder.

The aim of this study was to determine the prevalence of LPR in patients with ENT patients, document signs and symptoms of LPR and to assess its response to combination medical therapy of anti-acid and leukotriene receptor antagonist.

I had seen 3500 patients during the study period,,1500 under age 14 years old, 650 patients (18% of all patients and 435 of all pediatric patients) have LPR, 420(65%) of them were males and 220 (35%) were females.

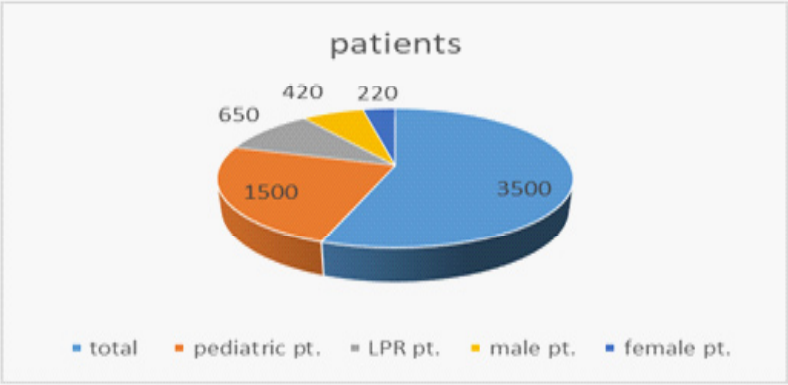

Fig1. *patients study demonstrate their numbers and regarding to gender*

Regarding to age they had been divided as 2 years category for 7 groups as follow: after birth till end of 2 years/ 3-4y / 5-6y / 7-8y / 9-10y / 11-12y / 13-14years ...there were 2 peaks first one on age 5-6 years old may be due the age of entrance to school and the other at 13-14 years old age to start puberty?.

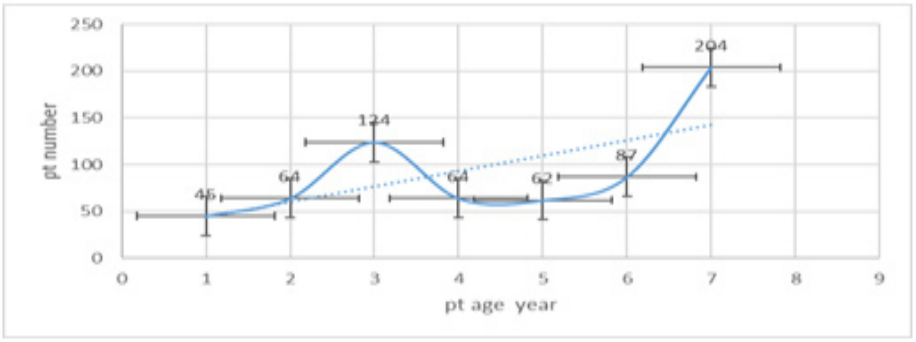

Fig2 *showed number of patients regarding the age categories.*

Most of the patients in study were normal in appearance, some of them have obesitỹ 60 patients few of them have other syndromes and congenital issue, like laryngomalacia in 10 pt. Dawn's syndrome in 7 pt. cerebral palsy in 6 pt. Autism in 5 pt and one patient has Kabuki's syndrome.

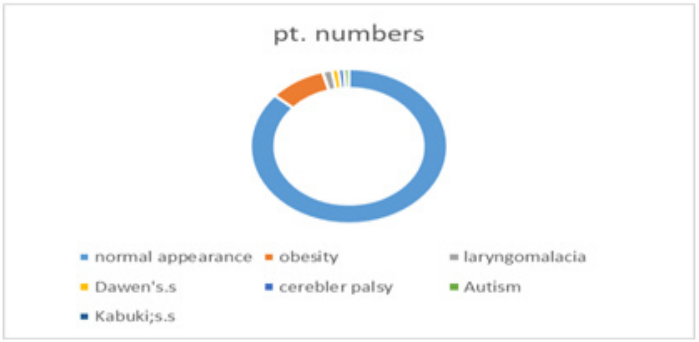

Fig3. *showed total LPR patients and patients whom have congenital syndromes or disorders*

Regarding the signs and symptoms which the patients were complaining from the below figure summarized most S & S, notice that most of patients were complaining from more than symptoms at the same time.

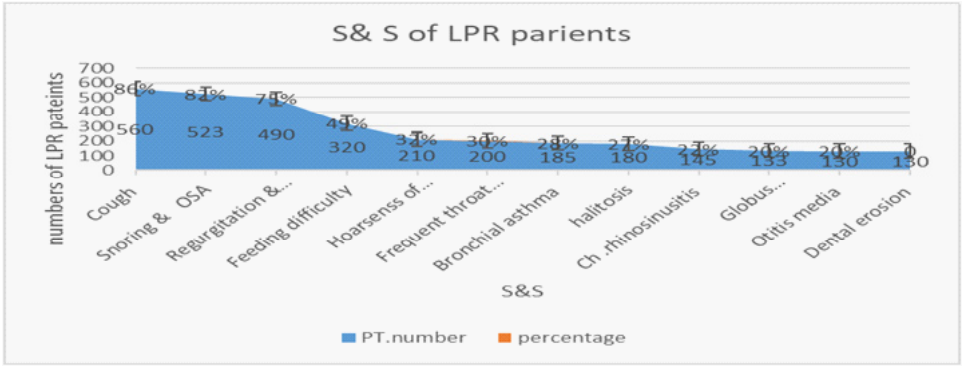

Fig4. *showed numbers and percentage of signs and symptoms of LPR during studied period*

This retrospective study comprised 150 patients to same numbers of other 2 subjects taking other medical treatment and one controls subject (100) patients did not receive medication.

In the present study, the cough and vomiting improved significant completely (95% p=0.001), nocturnal aspiration and OSA improved less than cough (85% p=0.1) and snoring with open mouth breathing were improved only in (60% p=0.4) after using combination medical treatment this confirmed the common existence of classic symptoms of LPR and its relation to improved after conservative combination medical treatment and managements like: life style changing and Diet with proper treatment of anti-acid and leukotriene receptor antagonist for at least 4 weeks and more, may be till 12 weeks.

Table2. *shows that most patients improved in their cough and vomiting 95% then aspiration, OSA, difficulty in breathing 85%*

symptoms	Improved pt %	Not improved pt %
Cough and vomiting	95%	5%
OSA-difficulty in breathing	85%	15%
Other S&S	60%	40%

Cough with vomiting were significant higher than other symptoms in LPR patient and responded well to management if not completely. regurgitation and dysphagia improved with treatment but not mentioned in this study its prevalent.

Group 4, controls subject: improved in their LPR symptoms moderately and not completely but not more 30%.

There were significantly higher frequency of LPR in patients with OSA and other nasal obstruction issues, these were agreement with Penzel et al. (1999) who found LPRin 53.3% (8 out 15)of patients with OSA. Wise et al. (2006) reported that 64.3% of patients with OSA had LPR.

Several other studies showed higher incidence ofLPR in OSA and other studies mentioned in Cummings Otorhinolaryngoogy head and neck surgery text book sixth edition 2015 …

Small studies have suggested that, where LPR is present, anti-reflux therapy may reduce the incidence of recurrent acute otitis media RAOM, and in reduction of adenotonsillar size and resolution of obstructive sleep apnoea (OSA). Children under the age of 2 years undergoing adenoidectomy alone appear to have much higher rates of LPR than their counterparts having grommets alone.

More recently there has been interest in the presence of Helicobacter pylori (HP) in adenotonsillar tissue, Using PCR techniques, HP detection in tonsils has led to the hypothesis that the tonsil is an extra-gastric reservoir for the organism.

In another famous study Little2 created a standard mucosal lesion in canine subglottic larynges, which were then exposed to gastric contents, over 3–4 weeks. This resulted in a nine-fold increase in subglottic stenosis when compared to saline controls.

Reflux control may hasten resolution of recurrent respiratory papillomatosis (RRP). There is also evidence that reflux control reduce anterior commissure web formation.

Eryuksel E et al.J Asthma. 2006; 437@539-4232: Prevalence and Treatment of LPR and Asthma : Pantoprazol 40 mg/day x 3 months – 21/28 (75%) had LPR – Treatment improved both LPR ($p<0.001$) and asthma symptoms ($p=0.001$)

In our study, due to combination therapy which consists of (H2RA/PPI +leukotriene receptor antagonist) the results were as follow below and the percentage of improving almost 93% ($p>0.001$) and it is considered as significant result in this study.

Table3. *shows that patients whom came under group 3 were significantly improved 140 of them (93 %) higher than the others groups.*

Group number	Improved pt.	Not improved pt.	Improved Percentage %
1- using Ranitidine	107 pt	43 pt	71%
2- using PPI alone	125 pt	35 pt	83%
3- combination T.	140 pt	10 pt	93%
4- controls subjects	30 pt	70 pt	30%

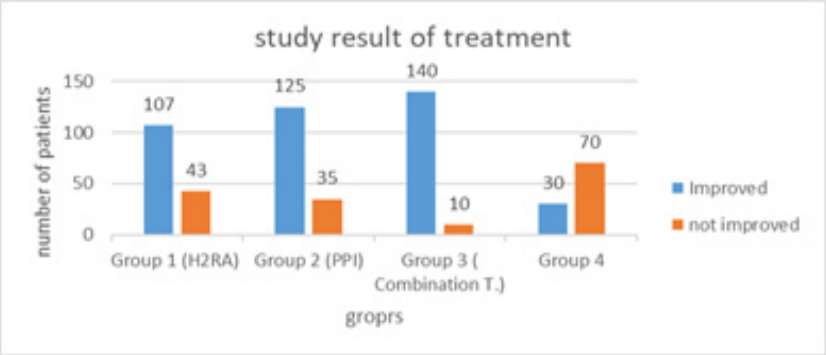

Fig5. *result of study; improved patient under group 3 percentage of improvement on combination study >93% (p>0.001)*

Conclusion

From the present study we can conclude that LPR increasing in occurrence in pediatric community patients as compared to many years beforein pediatric patients may be due newly life style changing, bad feeding habits in Arab Gulf Ares, allergy to food.

there was a positive impact that combination treatment of anti-acid and leukotriene receptor antagonist which They have an unique profile in that they are a hybrid of an anti-inflammatory and bronchodilator drugreduces LPR symptoms and signs in most patients >90%.

We suggested that As there were approved external allergens considered in allergic and asthmatic patients, We considers an internal allergens from the vapor of acid reflux or the Refluxed materials itself, so after using combination treatments most LPR S&S were improved..

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[3] Cummings Otorhinolaryngology head & neck surgery, sixth edition, 2015.

[4] electronic and manual Archives of MZH-ALDhafra region Abu Dhabi –UAE :between 2015 till 2018.

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