Management of gastro-esophageal reflux disease in infants less than 3 months old in Ain Shams University NICUs

Thesis

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By

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Contents

Acknowledgment ..... **-**
List of Abbreviations ii
List of Tables iii
List of Figures iv
Introduction 1
Aim of the Work 4
Review of Literature

- History 5
- Embryology 6
- Anatomy 9
- Gastro-esophageal junction 11
- Blood and nerve supply 13
- Esophageal defense mechanisms 16
- Pathophysiology 21
- Clinical picture 23
- Diagnosis 26
- Differential diagnosis 31
- Treatment 32

Patients and Methods **39**
Statistical analysis **50**
Results **51**
Discussion **70**
Summary **77**
Conclusion and recommendation **79**
References **80**
Arabic summary ..... **-**

List of Abbreviations

GA: Gestational age

GI: Gastrointestinal

GER: Gastro-esophageal reflux

GERD: Gastro-esophageal reflux disease

UES: Upper esophageal sphincter

LES: Lower esophageal sphincter

MII: Multiple intraluminal impedance

SIDS: Sudden infant death syndrome

PPIs: Proton pump inhibitors

NICU: Neonatal intensive care unit

ALTEs: Acute life threatening events

BPD: Bronchopulmonary dysplasia

List of Tables

Table (1): Some demographic data 52
Table (2): Duration of medical treatment and resolution of symptoms 55
Table (3): Age and weight at operation 56
Table (4): Comparison between the medical group and the surgical group regarding demographic data at presentation 60
Table (5): Comparison between the medical group and the surgical group regarding the type of feeding and the presenting symptoms 61
Table (6): Comparison between the medical group and the surgical group regarding the final outcome 62
Table (7): Correlation of the gestational age with the duration of medical treatment 63
Table (8): Correlation of age at presentation with the duration of medical treatment 64
Table (9): Relation between the complications and the following (gestational age, age and weight at presentation, duration of medical treatment) 65
Table (10): Relation between mortality and gestational age, age and weight at presentation, duration of medical treatment 67
Table (11): Gestational age as predictors to assess medical and surgical cases 68
Table (12): Age of presentations as predictors to assess medical and surgical cases 69

List of Figures

Figure (1): Anatomy of the esophagus 13
Figure (2): Antireflux barrier of the esophagus 18
Figure (3 a, b): Sandifer syndrome with abnormal neck extension 25
Figure (4 a, b, c): Different upper GI contrast study showing GER 27
Figure (5 a, b): Some anatomical abnormalities 28
Figure (6): The mobilized left lobe of the liver 42
Figure (7 a, b): The mobilized lower 2 cm of the esophagus 43
Figure (8 a, b): The crura of the diaphragm 44
Figure (9 a, b): The 360 degree fundic wrap around lower esophagus 45
Figure (10 a, b): The 3 interrupted non-absorbable sutures of the wrap 46
Figure (11): The floopy nature of the wrap 47
Figure (12 a, b): Stamm gastrostomy 47
Figure (13): Pie chart showing incidence among different forms of feeding 52
Figure (14): Pie chart showing different presenting symptoms 53
Figure (15 a, b): Upper GI contrast study showing evidence of GER 54
Figure (16): Pie chart showing percentage of complications 57
Figure (17): Pie chart showing mortality rate 58
Figure (18): Pie chart showing recurrence rate 59

Figure (19): Graph showing relation between gestational age and duration of medical treatment 63
Figure (20): Graph showing relation between age at presentation and duration of medical treatment 64
Figure (21 a,b,c,d): Relations between complications and some demographic and treatment data 66

Introduction

Gastro-esophageal reflux (GER) is a frequently experienced physiological condition in which there is involuntary retrograde passage of gastric contents across the lower esophageal sphincter into the esophagus ***(Ferreira et al., 2014)***. Gastro-esophageal reflux disease (GERD) occurs when GER causes symptoms that affect the quality of life or causes pathological complications. Around 75-80 % of infants have GER in the first 2 months of life, which usually resolves spontaneously, without intervention, before completing the first year of life. GER is more common in preterm, with an incidence ranging from up to 85 %, while around 50% of full term babies have reflux ***(Czinn and Blanchard, 2013).***

GER is classified into two groups: primary and secondary. Primary GER occurs when lower esophageal sphincter pressure becomes lower than intragastric pressure (unrelated to swallowing and of longer duration than that triggered by swallowing). Secondary reflux may be due to neurological conditions, genetic disorders, congenital anomalies of the gastro-intestinal system (as hiatus hernia, congenital diaphragmatic hernia and primarily repaired esophageal atresia) (***Sherman et al., 2009***).

GER can be suspected when some clinical symptoms are present, such as feeding abnormalities, recurrent attacks of vomiting and regurgitation, repeated respiratory tract infections, abnormal posture (back arching) and hematemesis (***Heine et al., 2006***). Moreover it can be radiologically diagnosed whether by an upper GI contrast study (mainly to exclude secondary reflux and associated anomalies) or scintiscan (used to diagnose aspiration). Lately some physiological and electrophysiological studies may help in the diagnosis of GER such as PH metry and intraluminal esophageal electrical impedance (***Badillo and Francis, 2014***).

Treatment of GERD depends mainly on life style modification including antireflux position, hypoallergenic formulas and thickening of feeds. Some medications may be used as a second line of management, such as antisecretory and surface barrier agents, antacids, and proton pump inhibitors. Sometimes ryle drip feeding may be effective ***(Richard et al., 2014)***. Surgical intervention is usually reserved for patients who didn't respond to medical treatment and have life threatening complications of GERD ***(Yoo et al., 2014).***

Although GER and GERD are very common conditions, caregivers are challenged to differentiate between physiological reflux (which usually resolves spontaneously by the age of 1 year old) and pathological GERD (which usually require more extensive evaluation and treatment). Lack of evidence based medicine in evaluation and management of reflux in neonates and infants younger than 3 months old makes this differentiation difficult. Also there is no clear evidence about the time of surgical intervention and whether early interference would provide good postoperative results or not ***(Jancelewicz et al., 2016).***

Aim of the study

This study is conducted to provide the best treatment plan for the patients (neonates and infants younger than 3 months) suffering from GERD in our community and to identify high risk group patients requiring early surgical intervention.

History

The word esophagus comes from the Greek (oisophagos) that mean gullet. It is derived from eosin i.e to carry and phagos i.e to eat ***(Harper, 2014)***.

The word esophagus has been documented in literature since at least the time of Hippocrates. He noted that the esophagus receives the greatest amount of what we consume ***(Potter, 2010).***

The peristaltic contractions of the esophagus have been documented since the time of *Galen 1916.*

The first attempt at surgery on the esophagus was focussed in the neck and conducted by *Theodore Billroth in 1873.*

In 1877 Czerny carried out surgery in people. By *1908* an operation was performed by *Voeckler* to remove the esophagus, and in *1933* the first surgical removal of parts of the lower esophagus had been conducted ***(Norton, 2008).***

Nissen (1956) published his results, being the first to conduct Nissen fundoplication in which the stomach was wrapped around the lower esophageal sphincter to stimulate its function and control reflux.

Embryology

Gut development takes place in four major patterned axes antero posterior, dorsoventral, left right and craniocaudal. Some endodermal proteins (as Six2/Sox2, Hoxa-2, Hoxa-3 and Hoxb-4) control the development of the esophaus ***(Le Douarin, 2004)***.

Kuo and Urma (2006) reported that esophagus develops from the foregut and is lined by ciliated epithelial cells by week 10. Therefore the endoderm of the foregut is the origin for the esophageal epithelium and submucosal glands.

Tewfik (2017) summarized the development of esophagus in the latter half of the third week of gestation, as the primitive foregut develops a ventral diverticulum.

The rapidly growing heart and liver stretch the esophagus, and therefore it narrows almost to obliteration at the level of Carina.

Between the sixth & eight weeks of gestation, the epithelium becomes 2-5 cells thick and remains stratified columnar. The esophagus becomes surrounded by a layer of undifferentiated mesenchyme and a circular layer of myoblasts.

Later, the longitudinal muscle fibers appeared. By the tenth week, the stratified columnar epithelium becomes ciliated, and by the fourth month it is replaced by stratified squamous epithelium. At either end of the esophagus, the ciliated epithelium gives rise to esophageal glands.

Many blood vessels (which enter the esophagus at week 7) are branches from the inferior thyroid artery, bronchial arteries, and thoracic aorta. The lower oesophageal sphincter receives blood from the left gastric artery and inferior phrenic artery ***(Kuo and Urma, 2006)***.

The smooth muscles of the lower esophageal sphincter are derived from the mesenchyme of the somites surrounding the foregut, while the striated muscles of the upper esophagus and upper sphincter come from the mesenchyme of branchial arches 4, 5, 6. That description explains the innervation of the esophagus by the vagus nerve and recurrent laryngeal nerve ***(Kuo and Urma, 2006)***.

Interstitial cells of Cajal (ICC) emerge from the mesenchyme of the gut around the ninth week, and are crucial to neural transmission within the gut ***(Wallace and Burns, 2005)***.

Esophageal motility patterns have been described in the second trimester of pregnancy, viewed as peristaltic movements in ultrasound images ***(Mallinger et al., 2004)***.

However, at birth the propagation of peristalsis at the LES is immature resulting in frequent regurgitation of food during the newborn period. The pressure at the LES approaches that of the adult at about the sixth week of age ***(Mallinger et al., 2004).***