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Otitis Media with Effusion, Development of Animal Model: Literature Review

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Abstract- *Objective:* Provide a brief review about the development of animal model of otitis media with effusion.

Methods: We studied different methods of inducing otitis media with effusion in animal model published in different journals and try to point out their strong and weak points.

Result: Althought different animal models had been established as model, none of them were able to explain in detail about the disease physiology in animal and further more research is needed to develop a valid animal model of otitis media with effusion.

Conclusion: Otitis media is one of the most common disease in children so further detail study is needed in this disease. Till the date several animal models were established. Before the research detail study on experimental animal and experimental method is necessary for the reliable result.

Keywords: *otitis media, animal model, method, research.*

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I. Introduction

Otitis Media with Effusion (OME) is one of the most common childhood disease defined by the inflammation of the middle ear including middle ear ossicles and Eustachian tube and in some condition mastoid air cells.OME is characterized by the collection of non-purulent nearly sterile fluid in the middle ear cavity. By the age of 3 at least four-fifth of children have experienced at least one or more episodes of OME [1].The pathogenesis of otitis media has been related to malfunctioning of Eustachian tube, which fails to ventilate and drain the middle ear (ciliary dysfunction, mucosal edema, middle ear/nasopharynx pressure gradient, adenoid hypertrophy, chronic rhinitis, sinusitis and tonsillitis, neoplasm and malignant tumors of nose, paranasal sinuses and nasopharynx, cleft palate and palatal paralysis) allergy, unresolved acute otitis media, viral infection and increased secretory activity of middle ear [2].

OME is one of the hot topic in research these days because it effects hearing and balancing causing poor language and development and eventually leading to poor school performance in children [3]. The etiology of OME is multifactorial, it is believed that dysfunction of Eustachian tube (ET) is one of the most important factor in the formation of middle ear effusion [4]. ET has three main functions; pressure regulation, protection and clearance [5]. Any compromise to this function may leads to OME. In recent study in in-vitro and in –vivo it has been found that smoking and air pollution may induce OME. It is very difficult to create a model because of lack of device to control appropriate dosage and time exposure to the smoke and air pollution may be long [6].

OME is creating financial burden in many countries, In United States alone 5 billion USD was estimated annually in OME [7]. This expenditure may will be even high in few years. Studies on human are very difficult because it is very risky to trail newly developed drugs and treatment methods. Further more research on human model require proved hypothesis on animal model, unfortunately such satisfactory animal model of OME has not been developed yet.

Several methods and several experimental animals had been used and still being used to develop a valid animal model of OME. In this review we study different methods used by different researchers and study their strong and weak points. In our study we found following methods.

1. Eustachian tube blockade
2. Use of chemical substances
3. Injury to paratubular muscles
4. Others; creating nasal obstruction and creating cleft palate

II. Eustachian Tube Blockade

To create OME one can block Eustachian tube by ligation of cauterization, this can be done by two surgical approaches; Trans-cervical approach and Trans-palatal approach. In trans-cervical approach ventral incision or anterior cervical incision could be used to expose Eustachian tube, then bony or cartilaginous ET can be obstructed with the use of a small piece of gelofoam or a bite of muscle or dental material or can be obstructed with electrocautery [8-12]. The strong point of this approach is the clear visualization of ET so result obtained is expected to be more reliable and consistent. The week point is this method is comparatively difficult, a good knowledge of anatomy of neck necessary and it is time consuming .Some time may require 30 minutes [13]. In trans - palatal approach mouth is kept open with the use of mouth retractor and electric cautery needle was inserted at the soft palate and hard palate junction and ET pharyngeal orifice was cauterized [14]. This method is easy and relatively fast. The week point is the side effect

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after the surgery due to severe thermal damage around the Eustachian tube pharyngeal orifice can induce severe bleeding and poor oral intake [13]. There is greater chance of animal death after the procedure. In this method ET was not visualized so it is not certain the cauterization was done on the right area. The ET pharyngeal orifice was just estimated, So middle ear effusion may be due to the injury and edema of surrounding tissue not due to ET obstruction so the result may not be always consistent.

Another method to induce OME via trans-palatal approach was transpalatal incision, incision was made on the soft palate of desired side near the perygoid hamulus and visualized the ET pharyngeal orifice which could be obstructed by the use of poly vinyl acetate material [14]. The strong point of this procedure is the better visualization of ET pharyngeal orifice which could be easily closed or obstructed so the result expected may be consistent and reliable. Huang Q et.al. mentioned the use of trichloroacetic acid to create obstruction of Eustachian tube instead of electric cautery [16].

III. Use of Chemical Substances

This method is quite easy and less time consuming and result obtained may be consistent and reliable. Different types of chemical substances were used to induce OME. Till the date we found the use of β-lactamase-producing nontypable Haemophilus influenzae, peptidoglycan-polysaccharide, lipopolysaccharide, E-coli, endotoxin, Streptococcus pneumoniae, non viable heat killed Hemophilus influenza, histamine solution [8, 12,17-23]. The inoculation method may be either directly injection of chemical substances in the middle ear via tympanic membrane or inoculation intransally. The only drawback of this method is the calculation of the suitable dosage of chemical substance. Inoculation of insufficient amount may not induce OME and inoculation of excessive amount may produce undesirable side effects. In a study conducted by Aynali G. et.al. used 0.1 ml. Of histamine solution to induce OME and half of the rats showed middle ear effusion within 24 hours [22].

Some researchers used both ET obstruction and inoculation of chemical substances [8,12]. In our opinion the result could be consistent in such experiment as two parameters causing Eustachian tube dysfunction was used in the research to induce OME.

IV. Injury to Paratubular Muscles

In most of the research tensor veli palatni (TVPM) was used to induce middle ear effusion and compromise Eustachian tube function. Injury to TVPM was created by 3 different methods; (1) Paralyzing TVPM by injecting botulinum toxin injection, (2) Surgical alteration of TVPM (complete excision of muscle, transsection of superficial muscle bundle, and transposition of muscle tendon medial to hamular process, (3) Excision of third branch of Trigeminal nerve [23,24,25]. When TVPM was injured ET function was compromised and was not able to dilate the lumen and increase the luminal cross-sectional area of ET actively and the force required to open ET pharyngeal orifice was not enough so ET pharyngeal orifice remained closed and middle ear negative pressure was created.

In a study conducted by Canteki EI. et.al. studied the effect of LVPM on ET. They excised LVPM bilaterally and after the period of five months no middle ear effusion was observed [27]. But it is still debate whether TVPM or lavetor veli palatni muscle (LVPM). is most important contribute in the ET function. The only drawback is LVPM was excluded from the study. Further study must be done on these two muscles TVPM and LVPM to explain their exact function.

V. Creating Cleft Palate

This method is quite similar to the trans-palatal approach but it is quite simple less time consuming, with little side effect and reversible. To create cleft palate midline incision was made from the uvula to the posterior border of hard palate [28]. The only drawback of this method is difficult in swallowing and poor oral intake, but the swallowing function returns to normal condition after palatal recovery.

VI. Nasal Obstruction

Nasal cavity can be obstructed by use of dental impression material in the nasal cavity and nostrils can be obstructed by use of synthetic resin [29, 30]. In a study conducted by Buchman CA. et.al. created nasal obstruction by using dental material and found no evidence of middle ear fluid in both unilateral and bilateral obstruction group [29].In another study conducted by Scarano E. et.al obstructed nostrils bilaterally using synthetic resin 28 days after birth and after a period of time found that numbers of TVPM muscles fibers progressively decreased in the obstructed rats [30]. OME can be induced by nasal obstruction is still not clear so further research should be conducted to find out whether or not there exists any relationship between nasal obstruction and OME.

Several animal models are availed for OME. But none of these animal models were able to describe the anatomical and physiological effect of the disease, so it has been difficult which experimental method and model is the best. Each experimental methods has its strong and weak points, so selecting appropriate animal model and experimental method is the most important for the better outcome. Although OME is self limiting condition but it has been medical problem and financial burden in many countries so further research is needed to develop a reliable animal model of OME.

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