

Extremely High Prevalence of Erythromycin Resistance of Group A Beta Hemolytic Streptococci in Mashhad (Iran)

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Erythromycin has been the classic drug of choice for Streptococcal pharyngitis in case of allergy to penicillin.

To determine the resistance rate of Group A beta hemolytic Streptococci (GABHS) to erythromycin in Mashhad (population 2,500,000), we performed a biphasic research, composed of two retrospective (April 1998- March 1999 and April 2003-March 2005) and a prospective studies. In the first part, we collected GABHS positive cultures and their (disk diffusion) antibiograms from three medical diagnosis laboratories in Mashhad. In the second phase, in April 2005, throat cultures were taken from 204 elementary, high school and college students; antibiograms were done by both disk diffusion and E-test.

In the retrospective study, during 1998-1999, thirty-seven of 62 (59.67%) GABHS isolated samples and during 2003-2005, thirty-six of 44 (81.87%) GABHS isolates were resistant to erythromycin. The mean age of the 2003-2005 group was 25.5 years. The resistance rate in children less than 10 years old was 71.42% and in the older ones 88.23% ($P=0.07$).

In the prospective study, 76 of 204 (37.3%) throat samples were positive for GABHS and both the E-test and disk diffusion method showed that 73.7% (56 of 76) of the isolates were resistant to

erythromycin. The mean age for this group was 14.63 years. Although the rate of erythromycin resistance was higher in the high school students, the difference was not statistically significant ($P=0.07$)(Fig. 1).

The highest rate of erythromycin resistance for GABHS (98.8%) has been reported from China^[1], before that Japan had the first place of resistance (>60% in 1979)^[2]. Japan decreased the rate of erythromycin resistance at early 1990s to the lowest ever reported rate of 0.49%^[3]. In the United States, according to the report of CDC, the rate of erythromycin resistance of GABHS is not high (8%-9%). In Iran, the most recent report (2005) has shown the resistance rate of 40% for throat culture samples from middle school students in Kerman^[4].

In our study there was 100% concordance in the erythromycin resistance of GABHS by disc diffusion and E-test methods. Other studies have also shown such a close identity between the two methods^[5], although in some studies disc diffusion has been reported to be more sensitive^[6].

What is the cause of this high grade of erythromycin resistance? The rate of macrolide resistance is closely related to the extent at which these agents are used; at the time of our study (2005) macrolides were not among the most common antibiotics that were being used in Iran. According to the report of the food and drug organization of the Ministry of Health of Iran (www.fdo.ir), in 2005 erythromycin was the third among suspensions and the fourth among

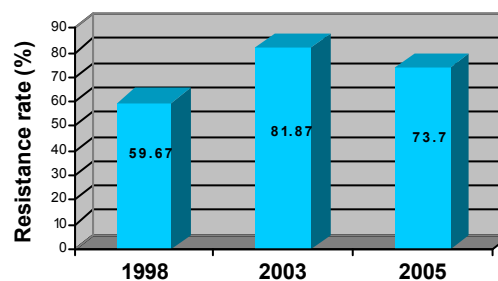


Fig. 1: The rate of Erythromycin resistance among GABHS in Mashhad between 1998 and 2005

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among suspensions and the fourth among capsules in antibiotic production of the country. Amoxicillin possessed the first place, the production of which was more than ten times of erythromycin. The question was, can food industry have a role in this problem? According to the report of Iranian Veterinary Organization (www.ivo.org.ir), lincomycin and erythromycin are the only macrolides used in our meat and dairy industry and none of them is frequently used, erythromycin is the seventh antibiotic (and the only macrolide) used in poultry (Neomycin has the first place). Lincomycin is the 4th drug (and the only macrolide) in cows and sheep husbandary (Penicillin has the first place with a large distance).

Age is an important factor in the rate of antibiotic resistance. Significant negative correlation has been found between the age of patients and the erythromycin-resistance^[7]. Our study however did not show such a relationship between age and erythromycin resistance, we think the reason is that infants and young children (<5 years old) which have the highest resistance rate are not included in this study.

We conclude that GABHS has a high rate of resistance to erythromycin in Mashhad, and although we couldn't find a reasonable explanation for this high degree of resistance, erythromycin can no longer be used for empirical treatment of streptococcal pharyngitis in this city. This project was funded by the Research Vice Chancellor of Mashhad University of Medical Sciences.

Key words: Streptococcus; Drug resistance; Pharyngitis; Erythromycin

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Umbilical Hernia and Ventriculoperitoneal Shunt Complications

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Ventriculoperitoneal (VP) shunt is the standard management of hydrocephalus. A wide range of complications have been reported for this procedure including malfunction, infection, pseudocyst, peritoneal complications, and catheter extrusion^[1]. The incidence of distal shunt migration has been reported 10% with defined causes^[2]. Improvements in surgical techniques and the development of silastic shunt tubing have been helpful adjuncts in reducing the incidence of abdominal complications^[3]. We present two children with umbilical hernia and abdominal complications of VP shunts.

The first patient, a four month old girl, had been seen in emergency department with a history of cerebrospinal fluid (CSF) umbilical fistula since 2 weeks ago and peritoneal catheter extrusion through umbilicus since 3 days ago (Fig 1). Her past history included thoracic myelomeningocele surgery and VP shunt for hydrocephalus. She had



Fig 1: Peritoneal catheter extrusion through umbilicus

small umbilical hernia since birth time. On admission she had low grade fever and CSF leakage from the extruded peritoneal catheter. CSF culture taken from pump was positive for *Klebsiella*. Abdominal sonography was normal. She was managed with shunt removal, 3 week antibiotic therapy and delayed VP shunt. She died 2 months later with sudden stridor and respiratory distress due to probably Chiari type 2.

The second patient, a three month old girl presented with fever, poor feeding and umbilical CSF fistula. At neonatal period, she had undergone myelomeningocele repair and VP shunt. She had a small umbilical hernia that aggravated by crying. CSF examination was positive for infection with low sugar and high white blood cells but negative culture. Shunt system was removed and she was managed with 3-week antibiotic therapy, external ventricular shunt and delayed shunting. Umbilical hernia was repaired too. Follow-up over 3 years has been uncomplicated.

Protrusion of a peritoneal catheter through the umbilicus and umbilical fistula are rare complications of VP shunt. The pathophysiologic mechanism is unclear but several explanations are proposed. Umbilicus location in the median raphe naturally renders it a place of lesser resistance. It must also be considered that a structural malformation of the abdominal wall may be a contributing factor. A persistent umbilical vein and malocclusion of the vitelline duct could be important^[4]. Elevated Intra-abdominal pressure due to increased peritoneal fluid, peritoneal adhesions around the catheter in relation to the parietal peritoneum producing a fibrous tunnel,

bridging the distance between the end of the catheter and the umbilicus, periumbilical nonhealing granulation lesion may be contributing factors^[5]. Thus it may be rational to correct an umbilical hernia before VP shunting in such cases to reduce the risk of umbilical fistula or extrusion. Weakness of abdominal wall muscles consequent to paresis in high level myelomeningocele can be another cause for shunt extrusion or CSF fistula in our patients.

Umbilical perforation and concomitant CSF infection need shunt removal and antibiotic therapy. Due to concomitant infection, both of our cases were managed with shunt removal, antibiotic therapy, external ventricular drainage and delayed VP shunting.

Shunt infection subsequent to CSF fistula or umbilical perforation must be considered even if ascending infection through shunt is rare. Further, it seems that umbilical hernia may increase risk of umbilical fistula or extrusion of shunt catheter especially in paraplegic myelomeningocele children; thus it is better to consider the correction of umbilical hernia before performing VP shunting.

Key words: Ventriculoperitoneal Shunt; Fistula; Umbilical Hernia; Perforation

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