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Streptococcus Group B (GBS) – Characteristic, Occurrence in Children and Adolescents with Type 1 Diabetes mellitus

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A b s t r a c t

Group B streptococcus causes infections in woman during pregnancy and confinement, perinatal infections in newborns related to mothers carrier-state and in adults, mostly in the elderly, with one or more predisposing to infections conditions. Diabetes mellitus is the most common underlying condition. The aim of the study was to determine the frequency of GBS occurrence and GBS antibiotic susceptibility in children and adolescents with type 1 diabetes mellitus. In years 2000–2002 occurrence of GBS in some clinical materials (urine, swabs from pharynx and urogenital tract) taken from 161 diabetics: 90 girls and 71 boys, hospitalized for newly diagnosed diabetes or insufficient metabolic control/longer duration of diabetes and 37 children with hypostatura (control group) aged from 5–17 years, was examined. Susceptibility of isolated GBS strains to ampicillin, erythromycin and clindamycin was determined. GBS were obtained from different materials from 36 (22.4%) diabetic children – 25 girls (27.8%), and 11 boys (15.5%). In all examined groups GBS was detected significantly in children with insufficient metabolic control/longer duration of diabetes (27 of 36 children; $p=0.029$, $\chi^2=4.773$). GBS in girls was isolated mainly from vestibule of vagina (25 cases) and in few cases (4) from the pharynx. GBS in boys was grown from materials from urethra (6 cases) and pharynx (5 cases). In the control group, GBS colonization was observed only in one case. All isolates (40 strains) were susceptible to penicillins, however lower susceptibility to erythromycin (3 resistant and 1 moderately sensitive) and clindamycin (3 resistant) were observed. High percentage of carriers of GBS both in girls and boys with diabetes mellitus is the potential risk factor of infection caused by GBS.

K e y w o r d s: Diabetes mellitus, children, colonisation GBS, *Streptococcus agalactiae*

Introduction

Streptococcus agalactiae, according to the Lancefield classification group B streptococcus (GBS), caused of bovine mastitis. First reports of infections in human date from the 30. of the XX century, for example: Frey described 3 cases of puerperal fever (Edwards and Baker, 2000). In the 70. in USA GBS was recognized as the main etiological factor of sepsis in newborns and infants up to the 3rd month of life, which was the main cause of death in infants (Edwards and Baker, 2000; Parker, 1984). In other countries the involvement of GBS in infections of newborns is not as big as in USA, but still many countries, including Poland, accepted the rules of prophylaxis of these infections that are in force in USA (Bevilacqua, 1999; Dzierżanowska, 2000; Hryniewicz and Gonera, 1993; Jeljaszewicz and Meszaros, 2001; Lyytikainen *et al.*, 2003; Poulain *et al.*, 1997).

The end part of the digestive tract (ano-rectal area) is the reservoir of GBS. Bacteria are observed in the anal region, urethra and vagina (Edwards and Baker, 2000; Honig *et al.*, 2002; Jeljaszewicz and Meszaros, 2001). The carrier-state of GBS in vagina is not constant, has a changeable character and can be transitional or chronic. Most of the infections in newborns are gained from the mother during the intra-uterine life or labor (vertical infections). Therefore GBS is regarded as one of the main causes of morbidity and mortality

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of newborns and infants up to the 3rd month of life, as well as of pregnant women. These bacteria cause also infections not connected with pregnancy, mainly in elderly people (Gardam *et al.*, 1998; Jackson *et al.*, 1998; Munoz *et al.*, 1997; Opal *et al.*, 1988; Trivalle *et al.*, 1998).

Two groups of infections in newborns and infants up to the 3rd month are distinguished – early-onset disease and late-onset disease. The early-onset disease evolves in the first week of life, usually until the 5th day after birth. The infection mostly develops in children with a low birth weight and in cases of premature outflow of amniotic fluid. As a consequence of a perinatal infection that is connected with colonization of genital passages by GBS, sepsis, more seldom pneumonia or meningitis develops (Edwards and Baker, 2000; Hryniewicz and Gonera, 1993; Jeljaszewicz and Meszaros, 2001; Parker, 1984).

A late-onset disease develops between the 7th day and 3rd month after birth, usually between the 10 and 20th day after birth and occurs mostly in healthy, mature newborns with a normal body weight. This infection is not connected with a carrier-state of GBS in the genital passages of the mother (Edwards and Baker, 2000). The most common clinical form of a late-onset disease is meningitis, more rarely other diseases as inflammation of bones and joints, necrotising fasciitis and bullous skin eruptions (Gardam *et al.*, 1998). In comparison to the early-onset disease the late-onset disease had a better prognosis (Hryniewicz and Gonera, 1993).

Infections of women connected with pregnancy and confinement: Massive infection of the vagina with GBS can lead to asymptomatic bacteriuria and in consequence to streptococcal infection of the urinary tract. Infection with GBS can concern the fetal membranes, mucus membrane of the uteri and as a result of an intra-uterine infection septic aborts can occur. In some of women after labor GBS cause puerperal fever (Edwards and Baker, 2000; Jeljaszewicz and Meszaros, 2001).

Infections of adults not connected with pregnancy: These infections occur in women as well as in men and concern usually elderly people, who have at least one of the risk factors. These is *e.g.* diabetes mellitus, cancer disease, hepatocirrhosis, renal insufficiency, neurogenic bladder, trauma, decubitus ulcer and other (Edwards and Baker, 2000; Jackson *et al.*, 1998; Munoz *et al.*, 1997; Nolla *et al.*, 2003; Opal *et al.*, 1988; Ruoff *et al.*, 1999). GBS belongs to microorganisms that cause hospital infections. The most commonly recognized infections are: infections of skin and soft tissue, inflammation of bones and joints, pneumonia, meningitis, endocarditis, bacteremia and sepsis (Edwards and Baker, 2000; Munoz *et al.*, 1997; Opal *et al.*, 1988; Parker, 1984; Trivalle *et al.*, 1998; Tyrrell *et al.*, 2000). Invasive GBS infections connected with the placement of a central venous line was also described (Jackson *et al.*, 1998). Infections have often a mixed character, beside GBS *Staphylococcus aureus* is isolated.

For prevention of infections in infants applying of ampicillin or penicillin G for women during labor is recommended. Women allergic to penicillin should be given erythromycin or clindamycin (Dzierżanowska, 2000). Until now no penicillin resistant GBS were observed, but there were some strains resistant to erythromycin and clindamycin (Dzierżanowska, 2000; Lin *et al.*, 2000; Munoz *et al.*, 1997; Murdoch and Reller, 2001; Pearlman *et al.*, 1998).

The aim of the study was to determine the frequency of occurrence of GBS in children and adolescents with type 1 diabetes mellitus and to estimate their susceptibility to antibiotics that are in practice used in prophylaxis of perinatal infections.

Experimental

Material and Methods

161 children with type 1 diabetes mellitus (1–18 years old), hospitalized in the period form VIII 2000 to XII 2002 in the Department of Pediatrics, Endocrynology and Diabetology, Silesian University of Medicine in Katowice were examined during this study. The reason for hospitalization was new onset of diabetes (68 patients) or insufficient metabolic control (93 patients). Swabs taken from the pharynx, vestibule of vagina and urine from 90 girls as well as swabs from the pharynx, urethra and urine from 71 boys were examined. Nocturnal urine, obtained with the method of the middle stream, was cultured directly after collection on the transport-culture medium Uromedium or Uromedium PEG (BIOMED – Kraków). In none of the children clinical manifestations of infections of the urinary tract were observed; the biochemical analysis in all cases was correct.

The material from the mucous membrane of the pharynx, ostium of urethra and vestibule of vagina was cultured on Columbia agar with 5% sheep blood. The β-hemolytic streptococci growing on this medium were serologically identified with the lateks agglutination test – Slidex Strepto-kit bioMérieux (France).

Susceptibility of GBS to ampicillin, erythromycin, and clindamycin was performed on the Mueller-Hinton agar Oxoid (England) with addition of 5% sheep blood, according to the recommendations NCCLS (NCCLS, Villanova, 1997). The control group consisted of 37 children hospitalized for hypostatura.

The statistic analysis was performed with the use of the test $\chi 2$, contingency table 2×2.

Results

From amongst 161 examined children GBS was cultured in 36 (22.4%): 25 girls (27.8%) and 11 boys (15.5%) with diabetes. The age of the children was 5 to 17 years; 15 children (11 girls and 4 boys) aged 13 and younger and 21 children (14 girls and 7 boys) older than 13 years. Most of the children, by whom GBS was isolated were hospitalized for insufficient metabolic control (27 patients), while the remaining 9 patients were hospitalized for new diagnosis of diabetes. Table I shows the frequency of GBS occurrence in children and adolescents with newly diagnosed diabetes and those with insufficient metabolic control. GBS colonization was found more often in children – both girls and boys – with insufficient metabolic control/a longer history of diabetes (33.9% girls and 21.6% boys), in comparison to newly diagnosed cases (17.7% girls and 8.82% boys). The analysis of the results forms the whole group of children with diabetes a statistically significant ($p = 0.029$; $P^2 = 4.773$). Colonization was revealed in children with a longer history of the disease. Table II shows the materials, from where GBS was isolated. In girls, these bacteria were mostly found in the swab from the vestibule of vagina (25 cases) and more seldom from the mucus membrane of the pharynx (4 cases). Asymptomatic bacetriuria was revealed in 5 girls with a massive colonization of vagina, in 4 of them the number of bacteria in the urine was above 10^4 CFU/ml, in one above 10^3 CFU/ml.

Table I
Frequency of GBS occurrence in children and adolescents with diabetes

Cause of hospitalization	Girls		Boys		Total	
	total	GBS + (%)	total	GBS + (%)	examined	GBS + (%)
New diagnose of diabetes	34	6 (17.65%)	34	3 (8.82%)	68	9 (14.1%)
Insufficient metabolic control	56	19 (33.9%)	37	8 (21.62%)	93	27 (29.0%) **p = 0.029**
Total	90	25 (27.8%)	71	11 (15.49%)	161	36 (22.4%)

Table II
GBS occurrence in materials

Examined material	Girls (90)		Boys (71)	
	GBS + total	GBS %	GBS + total	GBS %
Swabs from pharynx	4	4.4	5	7.0
Urine	5	5.5	1	1.4
Swabs from vagina	25	27.8	–	–
Swabs from urethra	–	–	6	8.5

Presence of GBS in the region of ostium of urethra was stated in 6 boys, in one of them significant asymptomatic bacetriuria was found – above 10^5 bacteria in 1 ml of urine. From the mucus membrane of pharynx GBS was grown in 5 boys.

In 21 children (10 girls and 11 boys) the microbiological examination was conducted two times (at an interval of few months) and in 4 cases three times. Within the group examined more than once, GBS was isolated in 11–6 girls and 5 boys. These bacteria were isolated two times in the same patient only in two cases (2 boys), in other children their presence was revealed only in one examination.

In the control group – 37 children with hypostatura, GBS was grown neither from the swabs from the pharynx nor from the urine. Microorganisms were not well grown from the swabs from the region of the ostium of urethra of 18 boys from this group. Amongst the examined swabs taken from the vestibule of vagina from girls GBS was grown in one case. The girl was 14 years old.

The susceptibility of the 40 strains of GBS to ampicillin, erythromycin and clindamycin is shown in Figure 1. All examined GBS strains were susceptible to ampicillin, however lower susceptibility to erythromycin (3 strains were resistant and 1 intermediate) as well as to clindamycin (3 strains resistant, which is 7.5%) was observed. Streptococci resistant to erythromycin were also resistant to clindamycin.

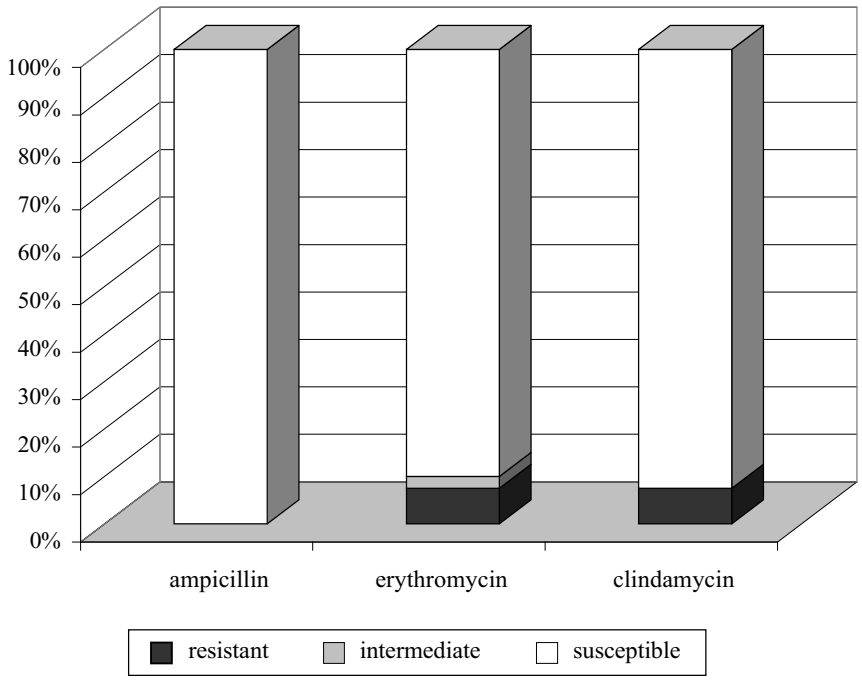

Fig. 1. Susceptibility of group B streptococci to chosen antibiotics

Discussion

After recognizing the dominant role of GBS in perinatal infections of newborns, standards of prophylaxis and treatment of those infections were generated and introduced to hospital practice. Two schemes of procedures were elaborated depending on the presence of risk factors: GBS infection of the newborn from the former pregnancy, infection of the urine tract caused by GBS or asymptomatic bacteriuria and labor before the 37th week of pregnancy. The stated risk factors are an absolute indication for applying penicillin or ampicillin during the labor. From women, who do not have any risk factors, swabs from the vestibule of vagina and anus should be taken between the 35th and 37th week of pregnancy and examined for GBS. Presence of those bacteria in the material (positive result) is an indication for antibiotic prophylaxis during labor. Premature outflow of amniotic fluid above 18 hours before delivery and intrapartum fever (higher than 38°C) is an additional indication for antibiotic prophylaxis. The above mentioned recommendations were published also in Poland (Hryniewicz, 2002).

Owing to the introduction of perinatal antibiotic prophylaxis the frequency of invasive early infections in newborns in USA has decreased (Baltimore *et al.*, 2001; Schrag *et al.*, 2000). The remaining problem is the late infections in newborns and infants and the more and more frequently occurring invasive infections of adults that are not connected with pregnancy. Authors from different countries emphasize the role of diabetes as one of the most common risk factors for GBS infections (Edwards and Baker, 2000; Jackson *et al.*, 1998; Munoz *et al.*, 1997; Nolla *et al.*, 2003; Opal *et al.*, 1988; Parker, 1984; Tyrrell *et al.*, 2000). In women with diabetes more often than in those, who are healthy, GBS colonization of vagina is revealed and that is why these bacteria are the most frequent cause for their septic aborts (Jeljaszewicz and Meszaros, 2001). Although rules of GBS perinatal infections prophylaxis in women and newborns have been known in Poland for a long time (Hryniewicz and Gonera, 1993), not all doctors prescribe screening examinations or they are carried out incorrectly. The high percentage of colonization of vestibule of vagina by GBS strains in girls with diabetes showed in this study justifies the necessity of examinations of pregnant women with diabetes for GBS presence in vagina, anus and urine. In the available literature there are few studies concerning GBS occurrence in children and adolescents with diabetes. Liotta and coworkers (Liotta *et al.*, 1987) while investigating the vestibule vagina flora in girls with diabetes mellitus type 1 revealed GBS in 28.5% of examined, which is comparable with our results – 27.8%.

GBS colonization of mucus membrane of pharynx is observed seldom, it occurs less than in 10% people (Edwards and Baker, 2000; Parker, 1984); in our studies – in children with diabetes the results were similar.

GBS was grown in swabs from pharynx in 4.4% of girls and in 7% of boys (in total in 5.6% children). However GBS was not found in the oral cavity and pharynx of the children from the control group.

All GBS strains isolated by us were susceptible to ampicillin, which is conformable to other authors (Dzierżanowska, 2000; Lin *et al.*, 2000; Pearlman *et al.*, 1988). The percentage of strains resistant to erythromycin and clindamycin was 7.5% and was lower than the resistance of GBS strains isolated in other countries (Lin *et al.*, 2000; Munoz *et al.*, 1997; Murdoch and Reller, 2001; Pearlman *et al.*, 1988). Strains resistant to erythromycin were also resistant to clindamycin, what suggests a type of resistance connected with a modification of the target place – phenotype MLS_B, that manifestates itself by a cross resistance between macrolides, lincozamides and streptogramine B.

Resistance of GBS to macrolides and lincozamides restricts the value of these antibiotics both in prophylaxis of perinatal infections and in empiric treatment of invasive GBS infections in adults.

Conclusion

The high percentage of GBS carrier-state in girls as well as in boys with diabetes is a risk factor for potential infections with this microorganism.

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