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Review

Sexuality, pre-conception counseling and urological management of pregnancy for young women with spina bifida

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ABSTRACT

A great number of newborns with spina bifida now survive with a growing life expectancy. Support with regard to sexual issues is essential in the management of adolescents with spina bifida, who require specific knowledge of sexual problems related to their disability. Women with spina bifida are usually fertile and need pre-conception counseling. Furthermore, compared to healthy women they have a higher chance of conceiving a child with spina bifida, so they are treated with periconceptional folic acid supplements. In addition pregnancies in women with spina bifida require adequate management of secondary conditions, mainly urological issues, which are exacerbated during pregnancy. This article gives an overview of sexual education, sex functioning and sexual activity among adolescents with spina bifida. Moreover, we aim to support young women with spina bifida, providing pre-conception counseling and practical guidelines essential for the urological management of their pregnancy.

Contents

1. Introduction

The term spina bifida (SB) refers to a group of congenital neural tube defects (NTD) resulting from a lack of vertebral arches in the median line during the 3rd and the 4th weeks of gestation [1]. In SB occulta, the outer parts of some of the vertebrae are not completely closed, but the spinal cord does not protrude, the skin at the site of the lesion is usually normal and the lesion may be asymptomatic in most cases. A common form of SB occulta is lipomyelomeningocele, which does not have associated hydrocephalus but requires a very complex surgical correction of the lipomatous mass that herniates through the bony defect, tethering the cord [2].

Open SB is characterized by a visible protrusion of spinal cord and/or meninges through the defect in the vertebral arch. Myelomeningocele (MMC) is the most significant form of open SB, with lifelong disability, characterized by the extrusion of spinal cord and the development of Arnold-Chiari type II malformations and hydrocephalus in the central nervous system [3]. Higher lesions are correlated with worse walking ability and poorer bladder and bowel control than lumbar or sacral lesions [4].

The incidence of SB is about 0.1–0.3%. If parents have one or more child with SB or if one parent is affected by SB, there is an

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increased risk of recurrence of SB [5]. The multifactorial etiology of SB involves both genetic and environmental factors: socioeconomic status, geographic area, maternal obesity, epilepsy or diabetes, maternal exposure to drugs, alcohol or radiation [6].

Numerous laboratory investigations suggest that defects of enzymes and proteins of folate metabolism may be associated with SB and other NTDs. Moreover a polymorphism of methylene tetrahydrofolate reductase (MTHFR 677C→T) and low folate status are correlated with a higher risk of NTDs [7,8]. Several studies show that a daily periconceptional supplement of folic acid decreases the recurrence rate of NTDs. Women who have had a child with an NTD and women who themselves have NTDs are recommended to consume a higher supplement of folic acid daily. The folate intake can be increased by the diet, by folic acid supplements or by fortification of food with folic acid [9].

Patients with SB need multidisciplinary management of hydrocephalus, Arnold-Chiari II malformation, neurogenic bowel and bladder, latex allergies, precocious puberty and obesity. Thoracic and higher lumbar MMC lesions are more likely to be associated with motor and sensory deficits than those lesions in the lower regions; on the contrary functional defects of the urogenital and lower intestinal tract are likely at all levels [10]. After birth the open spinal lesion needs to be protected from trauma and from the effect of amniotic fluid. Indeed surgical closure within 72 h may reduce the risks of infection and additional spinal cord injury.

Hydrocephalus occurs in above 85% of infants with MMC, with significant problems in learning and cognitive functions. It usually requires ventricular shunt placement, that needs to be monitored regularly for potential malfunctions. Patients with SB are also subject to muscular-skeletal abnormalities (such as kyphosis, scoliosis, deformities of the long bones and feet, joint instability, fractures). The consequences of impaired mobility also require intervention, because the children's physical disabilities can be barriers to social integration [11].

Life expectancy of these patients has been increased by recent improvements of medical and surgical assistance [12]. With their growing life expectancy currently adolescents with SB have prominent emotional, psychosocial and sexual issues. With careful clinical management, young women with SB may now achieve successful pregnancy and delivery [13]. In this article we overview sex education, sex functioning and reproductive health among female adolescents with SB. Moreover we aim to help the young women with SB who want to become mothers, providing a practical guideline for the pre-conception counseling and the urological management of their pregnancy.

2. Sexual function

Sexual function involves a series of phenomena (motivation, arousal, lubrication of the genital area and orgasm) occurring in a hormonally defined environment. Genital innervation is both somatic and autonomic. Somatic sensory information on tactile sexual stimuli is delivered through the pudendal nerve to the sacral spinal cord. The pudendal nerve originates in the sacral plexus from the ventral branch of the second, third, and fourth sacral nerves (S2–4). It innervates the areas around the scrotum and perineum, the penis and clitoris, and the bulbospongiosus and ischiocavernosus muscles: at sexual climax in females, spasms in the bulbospongiosus and ischiocavernosus result in most of the feelings of orgasm.

Activation of the suprasacral regions is also important in sexual awareness and excitation: the hypothalamic centers and limbic-hippocampal structures send out impulses through pelvic nerves to the genital area, causing vaginal lubrication, enlargement of the labia, tumescence and erection of the clitoral glans. Clitoral stimulation, involving pudendal nerve afferents, and vaginal stimulation can result in an orgasmic response [14].

Patients with SB may have sexual dysfunction related to neurological impairment, although Sawyer et al. found that about 80% of women with SB had some genital sensation and 37% of them had experienced orgasm [12]. Vulval sensation and orgasm are, however, rarely described in patients with lesion at or above L2. Females are generally less affected in their sexual functioning than male patients. Moreover in both sexes, altered genital sensation does not prevent arousal patterns and sexual functions [15].

3. Sexual activity

The lack of independence due to physical limitations can impair sexual experience of people with disabilities, even if their sexual desire and sexual feeling are intact [16].

Previous studies have confirmed that almost all women with SB evaluated sex life as important: they also expressed a desire for sexual contact and they manifested sexual fantasies. Sawyer et al. found that 70% of female adolescents with SB had a relationship [12,17]. In the Netherlands Verhoef et al. explored sex education and sexual issues among adolescents with SB, divided into male and female, with or without hydrocephalus. Their study confirmed that female adolescents with SB have more sexual activity than male patients, and that sexual desire, sexual contact and intercourse were lower in both male and female patients with hydrocephalus, because of their impaired social and cognitive skills. About 35% of female SB patients without hydrocephalus had sexual intercourse and about 83% of them had sexual contact. Masturbation or autoerotism was practised by 42% of them and 29% of them had experience of unwanted sexual contact [18].

Lassmann et al. reported that patients with an S1 lesion or lower were more sexually active than patients with a higher level lesion, as a reflection of their neurological and physical impairment [19]. Several studies have verified that urinary continence is a crucial predictor of successful sexual partnering. A very great number of patients with SB suffer from bladder and bowel incontinence, which is an obstacle to starting relationships and having sexual intercourse or contact [18,20]. Moreover, orthopedic problems such as scoliosis or lower limb impairment can prejudice the ability to use specific positions during coitus [21].

4. Sex education

Appropriate sex education for children with disability is important for increasing their social skills and their independence from parents or carers. Discussion of specific sexual problems may generate an ability to take greater responsibility for their sexuality, reducing the risks of sexual abuse, sexually transmissible infections and unwanted pregnancy [22]. Ideally sex education should create a safe environment for discussing these major topics: self-esteem and body image, public and private body parts, changes of puberty (both physical and emotional), menstruation, physical mechanics of sex (including reproduction), sexually transmissible infections, appropriate and inappropriate expressions of sexuality, safer sex and birth control [16].

Accurate counseling should be offered to patients with SB for the control of fertility: latex-free condoms may be required for common latex allergies, the use of estrogen/progestin contraceptives may increase the risk of thrombotic events in these patients with deficient mobility, and finally the use of intrauterine devices is unsafe for the risk of pelvic infections [23].

Verhoef et al. verified that almost all young adolescents with SB received an acceptable level of general sex education, without any difference between males and females. Female adolescents with SB obtained satisfactory knowledge about reproduction, birth control,

sexually transmitted diseases and sexual harassment, but they reported a lack of information about specific problems, such as sexuality and handicap, fertility and heredity of SB. They stressed the need for a practical approach to sexual issues such as latex allergy and condom use, incontinence and sexuality, social aspects of relationships and handicap. For these patients sex education is mandatory in a style and content appropriate to the individual, prior to the onset of sexual activity, due to their high risk of NTDs in pregnancies [18].

Many studies have shown that the main sources of sex education come from school and parents. Gatti et al. demonstrated that only 5% of patients discussed sexual issues with a physician, suggesting the need for qualified sexual counseling in the care of patients with SB [24].

5. Gynaecological issues and fertility

Several studies have reported that the prevalence of true precocious puberty with premature activation of the hypothalamic–pituitary–gonadal axis is higher among girls with SB than in their healthy counterparts. Hydrocephalus and other malformations of the central nervous system may alter the release of growth hormone, and the timing of puberty may be earlier in the patients with shunts than in those without a shunt [25].

In about 15% of girls with SB the average age of menarche occurs between 10.9 and 11.4 years of age [26]. Their mobility impairment may produce difficulties in hygienic management during the menstrual cycle [27]. Disorders of rhythm and intensity of menstruation are not described in these patients and they present an average fertility, currently therefore pregnancies and deliveries are not uncommon events among women with SB [21].

6. Reproductive health and pre-conception counseling

Accurate pre-conception counseling is strongly recommended for those women with SB who want to conceive, because of their increased risk of having a newborn with a NTD. If parents have one child with SB or if one parent is affected by SB, the risk of recurrence increases to 1–5%; if both parents have SB, the chances of having a child with SB increase to 15% [28]. The pathogenic mechanism of NTDs may involve genetic polymorphism related to homocysteine metabolism. The first genetic risk factor for NTDs identified at molecular level is a polymorphism in the gene encoding methylenetetrahydrofolate reductase (MTHFR) 677C→T, which is associated with decreased MTHFR activity, low plasma folate, high plasma homocysteine and high red-cell folate concentrations [29].

Finnell et al. suggested that it makes little sense for potential parents to be tested for MTHFR variants or for variants of other known folate pathway genes, because there is a limited understanding of the genes involved in regulating NTDs susceptibility. Besides they promote the folic acid supplementation and food fortification for the prevention of NTDs, as several pieces of evidence have already suggested [30].

Women who could become pregnant should be advised to take a multivitamin containing 0.4–1.0 mg of folic acid daily from at least 3 months before pregnancy to at least the 12th gestational week [31]. Women with SB or in intermediate high risk categories for NTDs (NTD-affected previous pregnancy, insulin-dependent diabetes, epilepsy treatment with valproic acid or carbamazepine) should be advised that a higher dose of folic acid (4.0–5.0 mg daily) supplementation is required. These women should take folic acid alone, not in a multivitamin format, because of the risk of excessive intake of other vitamins such as vitamin A [32].

Prenatal diagnosis with screening of alfa-fetoprotein (AFP) and ultrasonography has resulted in a reduction of NTDs discovered at birth. The American Congress of Obstetricians and Gynaecologists (ACOG) suggested that maternal serum AFP test should be performed around the 16th week of gestational age: a serum AFP higher than 2.5 multiples of the median (MoM) should be referred as diagnostic test [33]. Ultrasound examinations are useful for detecting the spinal level of the lesion, the type of SB, the presence of cranial associated signs (lemon shaped head, banana cerebellum, ventriculomegaly) and other associated anomalies [34]. An accurate diagnosis in fetal life is very important for parental counseling and for evaluating the prognosis, the degrees of disability, functional motor outcome and the postnatal management of the newborn [35].

MMC must be treated with surgical management in the postnatal period as soon as possible, to cover the exposed spinal cord to prevent infections and to treat hydrocephalus with a ventricular shunt [36]. The Management of Myelomeningocele Study (MOMS) was a randomized trial, performed from 2003 through 2010, which suggested that prenatal surgery performed before the 26th week of gestational age may decrease the risk of death or the need for shunting in the first year of life, improving mental development and reducing hindbrain herniation associated with the Arnold-Chiari II malformation. This technique is also related to an augmented maternal risk, including preterm delivery, placental abruption, pulmonary edema associated with tocolytic therapy and uterine dehiscence in the hysterotomy site [37].

Although there is no special protocol to follow during the pregnancy care of women with SB, a second-level center is required to provide pre-conception counseling and for the management of secondary conditions, such as kyphoscoliosis and respiratory compromise, spinal abnormalities and lower back pain, ventriculo-peritoneal shunt failure, occurrence of pressure sores and urological compromise [13].

7. Urological issues and pregnancy

In the multidisciplinary team of physicians who provide care for patients with SB, the urologist has an important role for the management of their current urinary and bowel issues [38]. The neurological bladder injury creates detrusor/sphincter dyssynergia with high bladder pressure and a serious risk of early upper urinary tract damage. The presence of non-inhibited contractions of detrusor may produce urinary incontinence and unsuccessful emptying of bladder, increasing the risk of vescicoureteral reflux and urinary tract infections (UTI) [39,40].

Ensuring bladder and bowel continence is also crucial for enhancing self-esteem and independence. Medical and surgical management should aim to preserve renal function. Medical therapy involves clean intermittent catheterization (CIC) and antimuscarinic medications. Follow-up management should be regular; periodic urine culture and urinalyses, annual serum creatinine, kidneys/bladder ultrasound and urodynamics are currently the best tools available [41].

Patients with SB and overactive bladder usually make use of oxybutynin hydrochloride, an anticholinergic/anti-spasmodic agent which has been assigned to FDA pregnancy category B. Animal reproductive studies have failed to reveal evidence of impaired fertility or fetotoxicity, but there are no controlled data in human pregnancy, therefore oxybutynin is only recommended for use during pregnancy when benefit outweighs risk [42,43].

Clean intermittent catheterization (CIC) was introduced for neurogenic bladders in 1972 and is carried out with self-lubricating catheters. CIC is a commonly recommended procedure for people with incomplete bladder emptying and urinary incontinence not satisfactorily managed by other methods. This practice may be associated to the risk of UTIs. Pregnant women should apply CIC by themselves, but they must have accurate

hygienic care of the hands and the perineal area; furthermore a microbiological examination of urine should be obtained every month [44].

Patients with SB frequently develop urinary tract infections (UTIs). The most common infecting microorganisms are facultative anaerobic bacteria of the intestinal flora (*Escherichia coli* accounts for 80–90% of asymptomatic urinary infections). Other gram-negative rods such as *Proteus mirabilis* and *Klebsiella pneumoniae* are also common, and group B streptococcus has important implications in the management of pregnancy. UTIs are diagnosed through urine culture (with $>10^5$ colony-forming units/mL) and urinalysis (including positive nitrite and leukocyte esterase test) [45,46].

During the pregnancy these patients have an increased risk for UTIs. In fact almost all pregnant women may develop ureteral dilatation, increased bladder volume and decreased bladder tone, with urinary stasis and uretero-vescical reflux; in addition a large percentage of pregnant women develop glycosuria, which encourages the bacterial growth in the urine [47].

Uncomplicated or asymptomatic UTI in pregnant women with SB should be treated with amoxicillin, oral cephalosporin or nitrofurantoin, in order to reduce the risk of pyelonephritis and preterm delivery. Antibiotic prophylaxis is recommended in the presence of recurrent UTIs, which are a common problem among patients with SB. For the prophylactic treatment of UTIs trimethoprim is approved during pregnancy: it may, however, interfere with the action of bacterial dihydrofolate reductase, inhibiting synthesis of tetrahydrofolic acid, therefore a supplement with 7.5 mg daily of folinic acid is required [48,49].

Salomon et al. described the safety and efficacy of a weekly oral cyclic antibiotic (WOCA) strategy to prevent UTI in six pregnancies with spinal cord injury under CIC. WOCA prophylaxis was recommended at the start of pregnancy with alternate administration of one of two antibiotics once per week, chosen from these (according to the results of recent urine cultures): amoxicillin, cefixime, nitrofurantoin. We suggest that a WOCA program should be adopted by obstetrician to prevent the development of UTIs in pregnancies with SB, preferably with a supplement of probiotics [50].

Additionally many UTIs are caused by gastrointestinal organisms (such as *E. coli*), thus a successful treatment of constipation may avoid the reinfection of the urinary tract from the rectal reservoir [51]. Neurogenic bowel dysfunction (such as chronic constipation) is a common occurrence in patients with SB. Several patients with SB obtain satisfactory treatment both of constipation and fecal soiling with transanal irrigation, which promotes the evacuation of feces by introducing water into the colon and rectum through a catheter inserted into the anus; nevertheless this practice is not allowed during pregnancy [52,53].

Therefore pregnant women with SB and constipation should increase the fiber in their diet, drink a lot of fluids and exercise routinely. Emollient laxatives, such as mineral oil, glycerin suppositories and magnesium hydroxide can be used safely during pregnancy. Osmotic laxatives, such as lactulose or macrogol, should be recommended only in the case of refractory constipation, otherwise they should be avoided as much as possible, because they may possibly lead the pregnant women to dehydration with cramping in the uterus [54,55].

Pregnancy itself and vaginal childbirth may influence pelvic floor function, increasing the presence of urinary incontinence in women with SB [56]. Pelvic floor exercises, used with biofeedback and taught by trained health care personnel, have been described for the treatment of urinary stress incontinence. There is evidence that pelvic floor exercises during pregnancy and after childbirth may prevent urinary stress incontinence decreasing the severity of symptoms at this time [57].

Current recommendations promote vaginal delivery, because a cesarean section can have a higher rate of surgical complications and longer recovery periods. In the case of caesarean section general anesthesia is safer than spinal anesthesia. Arata et al. reported that vaginal deliveries occurred in one out of five women in wheelchairs and in ten out of eighteen independently mobile women; furthermore cesarean sections were accompanied by postoperative complications in 10 women [58]. Rietberg and Lindhout suggested that in the presence of cerebrospinal fluid shunts vaginal delivery is preferable and prophylactic antibiotics and thorough irrigation of the peritoneal cavity are indicated in case of caesarean section [59].

Moreover pregnant women with SB often require delivery by cesarean section for obstetric reasons, including a small deformed pelvis, hip bone abnormalities, lower extremity contractures, severe kyphoscoliosis, vertebral anomalies. In the case of earlier augmentation enterocystoplasty vaginal delivery is possible only in the presence of a close collaboration between urologists and obstetricians [60].

8. Conclusion

Despite their disabilities many adolescents with SB are sexually active or demonstrate sexual desires. Urinary incontinence and orthopedic impairments have a great impact on sexual partnering. Consequently, these patients need accurate counseling about the sexual problems associated with their disease. Female adolescents with SB desire better knowledge about fertility, birth control and heredity of SB. Although precocious puberty is a common problem among girls with SB, disorders of menstruation are not described and these patients are usually fertile. Young women with SB who desire to become pregnant should have accurate pre-conception counseling. Due to the increased risk of having a newborn with SB, they should have an early prenatal diagnosis (by ultrasound or screening of alpha-fetoprotein) and the intake of a higher dose of folic acid (4–5 mg daily) is recommended.

Expert urological management is required for the specific treatment of several bladder and bowel issues, such as recurrent UTIs, constipation and urinary incontinence, which are exacerbated by pregnancy. If secondary contraindications are absent, vaginal delivery is recommended, although it aggravates their urinary incontinence. Pelvic floor exercises are available for preventing or for reducing current urinary incontinence.

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