Reproductive BioMedicine Online (2012) **24**, 206–210

www.sciencedirect.com
www.rbmonline.com

ARTICLE

Sperm parameters and male fertility after bariatric surgery: three case series

Nathalie Sermondade [a,b,*], Nathalie Massin [c,1], Florence Boitrelle [d,1], Jérôme Pfeffer [e], Florence Eustache [a], Christophe Sifer [a], Sébastien Czernichow [f], Rachel Lévy [a,b]

[a] *Service d'Histologie-Embryologie-Cytogénétique-CECOS, Hôpital Jean Verdier (AP-HP), Avenue du 14 Juillet, 93143 Bondy, France;* [b] *Unité de Recherche en Epidémiologie Nutritionnelle, INSERM U557; INRA; CNAM; Université Paris 13, CRNH IdF, 93017 Bobigny, France;* [c] *Assisted Reproduction Technology Unit, Department of Obstetrics and Gynecology, Intercommunal Hospital, University of Paris 12, 40 Avenue de Verdun, 94000 Créteil, France;* [d] *Department of Reproductive Biology and Gynecology, Hospital of Poissy, 78303 Poissy, France;* [e] *Laboratoire ZTP, Centre AMP Clinique de la DHUYS, 93170 Bagnolet, France;* [f] *Department of Nutrition, Ambroise Paré Hospital (AP-HP), University of Versailles Saint Quentin en Yvelines, 9 Avenue Charles-de-Gaulle, 92100 Boulogne-Billancourt, France*

[*] Corresponding author. *E-mail address:* nathalie.sermondade@jvr.aphp.fr (N Sermondade). [1] Both authors equally contributed to the manuscript.

Dr Nathalie Sermondade completed her medical studies at the Paris VI University in 2008. Her 4-year residency in medical biology specialized in reproductive biology, especially assisted reproductive technologies, and her MD was supervised by Dr Jacqueline Mandelbaum in Tenon Hospital, Paris. She has also obtained a Master's degree in Science in Paris V University. She is currently following a fellowship in Jean Verdier Hospital (Bondy, France) and working on her PhD in Paris XIII University about the impact of nutrition on fertility.

Abstract Recent studies have underlined the impact of obesity on sperm parameters, but very few data are available on the effect of weight loss on male fertility. This article reports the case series of three male patients who underwent rapid and major weight loss following bariatric surgery and the consequences of this surgery on semen parameters and fertility. A severe worsening of semen parameters was observed during the months after bariatric surgery, including extreme oligoasthenoteratozoospermia, but azoospermia was not observed. This effect may hypothetically be the result of two opposite mechanisms: (i) the suppression of the deleterious effects of obesity; and (ii) the negative impact of both nutritional deficiencies and the release of toxic substances. Information about potential reproductive consequences of bariatric surgery should be given to patients and sperm cryopreservation before surgery proposed. However, for one case, the alterations of spermatogenesis were reversible 2 years after the surgical procedure. Finally, intracytoplasmic sperm injection with fresh spermatozoa after male bariatric surgery can be successful, as demonstrated here, where clinical pregnancies were obtained for two out of the three couples.

KEYWORDS: azoospermia, bariatric surgery, ICSI, IVF outcome, male infertility, obesity, sperm analysis, weight loss

1472-6483/$ - see front matter
doi:10.1016/j.rbmo.2011.10.014

Introduction

Obesity has progressively become a worldwide concern, affecting not only reproductive-age women but also men (Finucane et al., 2011). Recent data pointed out an association between high adiposity and subfertility in men. Data from three large-scale epidemiological studies have suggested an elevated risk for infertility among couples when the male partner is overweight or obese (Nguyen et al., 2007; Ramlau-Hansen et al., 2007; Sallmen et al., 2006), with a plateau for body mass index (BMI) higher than 32 kg/m^2 (Nguyen et al., 2007; Sallmen et al., 2006).

A negative, but controversial, correlation between BMI and sperm count has been reported (Hammoud et al., 2008b; MacDonald et al., 2009; Magnusdottir et al., 2005). Data strongly suggest that excess bodyweight affects sperm production, but it is currently unclear whether weight loss can reverse this effect.

Due to exponential incidence of morbid obesity, bariatric surgery is an increasingly frequent treatment (Colquitt et al., 2009; Sjostrom, 2005), with long-term effectiveness on weight loss, comorbidities and mortality (Buchwald et al., 2004; Sjostrom et al., 2004, 2007). It also concerns younger patients, thus of reproductive age. Although bariatric surgery could constitute a possible strategy to manage obesity-linked male infertility, di Frega et al. (2005) reported secondary azoospermia after Roux-en-Y gastric bypass for six healthy previously fertile males. The authors postulated a developmental block of spermatogenesis due to malabsorption of essential nutrients.

This article reports the cases of three male patients who underwent rapid and major weight loss from bariatric surgery and the consequences on sperm parameters and results of assisted reproductive treatments.

Patient 1

Patient 1 was a 30-year-old man with a 4-year history of primary idiopathic infertility. His partner was 29 years old and had a normal BMI (19.4 kg/m^2); her ovulatory status, hormonal profile (including FSH, LH, oestradiol, anti-Müllerian hormone and prolactin) and hysterosalpingography were normal. No alcohol intoxication or smoking and no medication were reported for both partners. At the time of first visit, male BMI was 65.7 kg/m^2, hormones including FSH, LH, testosterone, oestradiol and inhibin B were within normal values and sperm parameters showed isolated teratozoospermia (sperm concentration 48×10^6/ml, 35% progressive motility and 7% normal spermatozoa, according to David's modified classification (Auger and Eustache, 2000)). The patient underwent a sleeve-gastrectomy procedure, resulting in the reduction of the gastric volume. After the surgery, he received supplementation for iron, vitamin B_{12} and vitamin D. He lost 108 kg in 9 months and reached a BMI of 33.4 kg/m^2. Assessment of sperm parameters 10 and 13 months after surgery showed drastic worsening, resulting in severe oligoasthenoteratozoospermia (sperm concentration 0.9×10^6/ml and 0.56×10^6/ml, 10% and 15% of progressive motility, 6% and 1% of normal spermatozoa, respectively). Hormonal pattern remained within normal values. At this time, the couple underwent two IVF with intracytoplasmic sperm injection (ICSI) cycles with long agonist protocols. In the first cycle, seven oocytes were retrieved, including five metaphase II, but no embryo was obtained. In the second cycle, eight oocytes were retrieved, including five metaphase II, and three oocytes were fertilized. Two good-quality cleavage-stage embryos, classified according to previously described criteria (Van Royen et al., 1999), were transferred at day 3, but no pregnancy occurred. Assessment of sperm parameters 2 years after surgery showed semen improvement with normalization of both concentration and motility (sperm concentration 41×10^6/ml, 40% progressive motility and 8% normal spermatozoa), with no evidence of dietary or pharmacological changes since the last examination. The couple underwent a third ICSI cycle. A long agonist protocol was used allowing the retrieval of 11 oocytes, including nine metaphase II, and five oocytes were normally fertilized. Two top-quality cleavage-stage embryos were transferred at day 2, resulting in an ongoing singleton clinical pregnancy. Three good-quality supernumerary embryos were cryopreserved.

Patient 2

Patient 2 was a 41-year-old man with a 6-year history of primary infertility related to female dysovulation and male factor. His partner was 23 years old and had a normal BMI (20.7 kg/m^2) and polycystic ovary syndrome with normal hysterosalpingography. No alcohol intoxication or smoking and no medication were reported for both partners. At the time of their first visit, male BMI was 53.5 kg/m^2, hormones including FSH, LH, testosterone, oestradiol and inhibin B were within normal values and sperm parameters showed extreme oligoasthenoteratozoospermia (sperm concentration 0.8×10^6/ml, 25% progressive motility and 13% normal spermatozoa, according to David's modified classification). The patient underwent a Roux-en-Y gastric bypass procedure, which both restricts the gastric volume and reduces the absorption of nutrients. After the surgery, he received supplementation for vitamin D. He lost 79 kg in 5 months and reached a BMI of 30.4 kg/m^2. Control of sperm parameters 6 months after surgery showed severe worsening with cryptozoospermia (presence of 25 non-motile spermatozoa in the centrifugation pellet of the whole ejaculate). Hormonal profile remained within normal values. Fifteen months after surgery, and after multiple sperm collection for cryopreservation, the couple underwent an IVF with ICSI attempt using the antagonist protocol. Five oocytes were retrieved, including five metaphase II, all fertilized after ICSI with fresh spermatozoa (sperm concentration 0.2×10^6/ml and 10% of progressive motility). Two top-quality cleavage-stage embryos were transferred at day 2, resulting in an ongoing clinical twin pregnancy. Three good-quality supernumerary embryos were cryopreserved.

Patient 3

Patient 3 was a 30-year-old man with an 18-month history of primary infertility related to a male factor. His partner was 27 years old with normal BMI (22.2 kg/m^2) and her fertility tests were normal. No alcohol intoxication or smoking and

no medication were reported for both partners. At the time of their first visit, male BMI was 38.6 kg/m^2 and his obesity was complicated by obstructive sleep apnoea, recently treated by nocturnal positive airway pressure. Sperm parameters showed severe oligoasthenoteratozoospermia (sperm concentration 6×10^6/ml, 6% progressive motility and 1% normal spermatozoa, according to David's modified classification). The couple underwent an ICSI attempt with long agonist protocol: eight oocytes were retrieved, including eight metaphase II, and four oocytes were fertilized after ICSI. Two top-quality cleavage-stage embryos were transferred at day 2, resulting in a clinical pregnancy, but with spontaneous miscarriage at 5 weeks of gestation. Two good-quality embryos were cryopreserved. After sperm cryopreservation, the patient underwent a Roux-en-Y gastric bypass procedure. After the surgery, he received multivitamin (B_1, B_6, B_9, B_{12}, D) and dietary mineral supplementation (calcium, magnesium, potassium, zinc, iron, selenium, iodine). He lost 36 kg in 6 months and his BMI reached 27.5 kg/m^2. Assessment of sperm parameters 3 and 6 months after surgery showed worsening of oligozoospermia (sperm concentration 0.9×10^6/ml and 0.3×10^6/ml, 4% and 7% progressive motility, 0% and 0% normal spermatozoa, respectively). No pregnancy was achieved after a frozen–thawed embryo transfer. A second ICSI attempt is planned.

Discussion

Recent studies evaluated the impact of obesity on sperm parameters (see for review Du Plessis et al., 2010; Hammoud et al., 2008a). However, few data are available about the effect of weight loss on male fertility or sperm parameters.

After weight loss through natural methods (diet and/or exercise), a decrease in leptin and insulin associated with an increase in sex hormone-binding globulin and total or free testosterone were observed (Kasturi et al., 2008; Kaukua et al., 2003; Niskanen et al., 2004) and a potential improvement in sexual function was reported if erectile dysfunction was present at baseline (Esposito et al., 2004). Progressive weight normalization could also improve sperm parameters and male fertility, allowing spontaneous pregnancy (unpublished case report). Different pathophysiological mechanisms could be implicated: (i) correction of obesity-linked alterations of the hypothalamic–pituitary–gonadal axis, especially hypogonadotrophic hyperoestrogenic hypogonadism (Schneider et al., 1979); (ii) removal of direct spermatogenesis and Sertoli cell-function alterations (Winters et al., 2006); (iii) decrease of scrotal temperature (Shafik and Olfat, 1981); and (iv) decrease of ghrelin peptide after surgical procedure that is inversely correlated with testosterone concentrations (Ishikawa et al., 2007). However, no data are available in the literature.

After bariatric surgery, some authors suggest that an improvement in sex-life quality (Hammoud et al., 2009) and a correction of hormonal profile (Bastounis et al., 1998; Hammoud et al., 2009) could be expected. Only one team published a case series describing sperm parameters after Roux-en-Y gastric bypass, with azoospermia for six cases, irreversible after a follow up of 12–15 months and

Table 1 Follow up of patients with weight loss and consequences on sperm parameters and results of IVF procedures.

Time to treatment	*Patient 1 (30 years old; sleeve gastrectomy)*			*Patient 2 (41 years old; bypass)*			*Patient 3 (30 years old; bypass)*		
	−12 months	*+10 months*	*+24 months*	*−12 months*	*+6 months*	*+15 months*	*−9 months*	*+3 months*	*+6 months*
BMI (kg/m^2)	65.7	33.4	33.4	53.5	30.4	30.4	38.6	31.5	27.5
Sperm concentration (10^6/ml)	48	0.9	41	0.8	<0.01	0.2	6	0.9	0.3
Progressive sperm motility (a + b) (%)	35	10	40	25	0	10	6	4	7
Normal sperm morphology (%)[a]	7	6	8	13	NA	NA	1	0	0
Hormonal profile	Normal	Normal	NA	Normal	Normal	NA	NA	NA	Normal
Assisted reproductive treatment	None	2 ICSI	1 ICSI	None	None	1 ICSI	1 ICSI	Frozen–thawed embryo transfer	1 ICSI
Outcome	No pregnancy	No pregnancy	Clinical pregnancy	No pregnancy	No pregnancy	Clinical pregnancy	Spontaneous miscarriage	No pregnancy	In progress

BMI = body mass index; ICSI = intracytoplasmic sperm injection; NA = not available.
[a]Morphology according to David's modified classification (Auger and Eustache, 2000).

associated with spermatogenic arrest at testicular biopsy (di Frega et al., 2005).

The present study reports, as far as is known for the first time, the follow up of three male patients who underwent rapid and major weight loss after bariatric surgery and the consequences on sperm parameters and results of assisted reproductive treatments (**Table 1**). A worsening of their semen parameters was observed, at least during the first year following the procedure. However, contrary to the only previously published report (di Frega et al., 2005), azoospermia was not observed.

The relationship between weight loss from bariatric surgery and alteration of sperm parameters is likely multifactorial, and different pathophysiological hypotheses can be raised. First, major and rapid weight loss may be compared with a relative undernutrition status, so disrupting the normal pulsatile gonadotrophin-releasing hormone secretion (Tsutsumi and Webster, 2009) and leading to reproductive disorders. Second, nutritional deficiencies constitute well-known complications after bariatric surgery, especially after malabsorptive surgery such as Roux-en-Y gastric bypass, with deficiencies concerning iron, calcium and vitamins B_1, B_{12} and B_9 (Coupaye et al., 2009; Poitou Bernert et al., 2007). Thus, diverse deficiencies in spermatogenesis-required nutrients may contribute to sperm alterations, even if supplementation for vitamins and minerals is recommended after all types of bariatric surgery. Lastly, some toxic substances and liposoluble endocrine disruptors present a preferential accumulation in fatty tissue, as indicated by the correlation of serum organochlorine concentrations with BMI (Magnusdottir et al., 2005). It can be postulated that a rapid and massive release of such liposoluble toxic substances could occur after bariatric surgery, in association with the rapid and major weight loss, leading to alterations in spermatogenesis. However, ICSI with fresh spermatozoa after male bariatric surgery can be successful, as demonstrated in the current report, where clinical pregnancies were obtained for two of the three couples. Finally, the resulting effect of opposite hypotheses (positive influence related to the suppression of the deleterious effects of obesity on semen parameters versus negative impact of both nutritional deficiencies and toxic release) needs further evaluation. Thus, sperm DNA fragmentation could constitute a relevant marker in upcoming studies. The impact of various surgical procedures on spermatogenesis may also differ, especially according to the malabsorption degree, and should be investigated.

Whatever the causes of male infertility are, interestingly some of them seem to lead to severe but possibly reversible alterations in spermatogenesis, as suggested by patient 1, whose sperm parameters normalized 2 years after the surgery. This reversibility may result from the correction of nutritional deficiencies and the removal of exposure to toxic substances, as has been, for example, previously described for alcohol intoxication (Sermondade et al., 2010).

In conclusion, even if the number of patients is limited, these original findings may suggest that information about potential reproductive consequences of bariatric surgery should be given to the patients and sperm cryopreservation proposed before surgery. Further longitudinal prospective studies and randomized trials will be required to evaluate whether weight normalization through diet modification and physical activity and/or bariatric surgery could have an impact on sperm parameters and male fertility.

References

Auger, J., Eustache, F., 2000. Standardisation de la classification morphologique des spermatozoïdes humains selon la méthode de David modifiée. Andrologie 10, 358—373.

Bastounis, E.A., Karayiannakis, A.J., Syrigos, K., Zbar, A., Makri, G.G., Alexiou, D., 1998. Sex hormone changes in morbidly obese patients after vertical banded gastroplasty. Eur. Surg. Res. 30, 43—47.

Buchwald, H., Avidor, Y., Braunwald, E., Jensen, M.D., Pories, W., Fahrbach, K., Schoelles, K., 2004. Bariatric surgery: a systematic review and meta-analysis. JAMA 292, 1724—1737.

Colquitt, J.L., Picot, J., Loveman, E., Clegg, A.J., 2009. Surgery for obesity. Cochrane Database Syst. Rev. CD003641.

Coupaye, M., Puchaux, K., Bogard, C., Msika, S., Jouet, P., Clerici, C., Larger, E., Ledoux, S., 2009. Nutritional consequences of adjustable gastric banding and gastric bypass: a 1-year prospective study. Obes. Surg. 19, 56—65.

di Frega, A.S., Dale, B., Di Matteo, L., Wilding, M., 2005. Secondary male factor infertility after Roux-en-Y gastric bypass for morbid obesity: case report. Hum. Reprod. 20, 997—998.

Du Plessis, S.S., Cabler, S., McAlister, D.A., Sabanegh, E., Agarwal, A., 2010. The effect of obesity on sperm disorders and male infertility. Nat. Rev. Urol. 7, 153—161.

Esposito, K., Giugliano, F., Di Palo, C., Giugliano, G., Marfella, R., D'Andrea, F., D'Armiento, M., Giugliano, D., 2004. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial. JAMA 291, 2978—2984.

Finucane, M.M., Stevens, G.A., Cowan, M.J., Danaei, G., Lin, J.K., Paciorek, C.J., Singh, G.M., Gutierrez, H.R., Lu, Y., Bahalim, A.N., Farzadfar, F., Riley, L.M., Ezzati, M., 2011. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. Lancet 377, 557—567.

Hammoud, A., Gibson, M., Hunt, S.C., Adams, T.D., Carrell, D.T., Kolotkin, R.L., Meikle, A.W., 2009. Effect of Roux-en-Y gastric bypass surgery on the sex steroids and quality of life in obese men. J. Clin. Endocrinol. Metab. 94, 1329—1332.

Hammoud, A.O., Gibson, M., Peterson, C.M., Meikle, A.W., Carrell, D.T., 2008a. Impact of male obesity on infertility: a critical review of the current literature. Fertil. Steril. 90, 897—904.

Hammoud, A.O., Wilde, N., Gibson, M., Parks, A., Carrell, D.T., Meikle, A.W., 2008b. Male obesity and alteration in sperm parameters. Fertil. Steril. 90, 2222—2225.

Ishikawa, T., Fujioka, H., Ishimura, T., Takenaka, A., Fujisawa, M., 2007. Ghrelin expression in human testis and serum testosterone levels. J. Androl. 28, 320—324.

Kasturi, S.S., Tannir, J., Brannigan, R.E., 2008. The metabolic syndrome and male infertility. J. Androl. 29, 251—259.

Kaukua, J., Pekkarinen, T., Sane, T., Mustajoki, P., 2003. Sex hormones and sexual function in obese men losing weight. Obes. Res. 11, 689—694.

MacDonald, A.A., Herbison, G.P., Showell, M., Farquhar, C.M., 2009. The impact of body mass index on semen parameters and reproductive hormones in human males: a systematic review with meta-analysis. Hum. Reprod. Update 16, 293—311.

Magnusdottir, E.V., Thorsteinsson, T., Thorsteinsdottir, S., Heimisdottir, M., Olafsdottir, K., 2005. Persistent organochlorines, sedentary occupation, obesity and human male subfertility. Hum. Reprod. 20, 208—215.

Nguyen, R.H., Wilcox, A.J., Skjaerven, R., Baird, D.D., 2007. Men's body mass index and infertility. Hum. Reprod. 22, 2488—2493.

Niskanen, L., Laaksonen, D.E., Punnonen, K., Mustajoki, P., Kaukua, J., Rissanen, A., 2004. Changes in sex hormone-binding globulin and testosterone during weight loss and weight maintenance in abdominally obese men with the metabolic syndrome. Diabetes Obes. Metab. 6, 208—215.

Poitou Bernert, C., Ciangura, C., Coupaye, M., Czernichow, S., Bouillot, J.L., Basdevant, A., 2007. Nutritional deficiency after gastric bypass: diagnosis, prevention and treatment. Diabetes Metab. 33, 13—24.

Ramlau-Hansen, C.H., Thulstrup, A.M., Nohr, E.A., Bonde, J.P., Sorensen, T.I., Olsen, J., 2007. Subfecundity in overweight and obese couples. Hum. Reprod. 22, 1634—1637.

Sallmen, M., Sandler, D.P., Hoppin, J.A., Blair, A., Baird, D.D., 2006. Reduced fertility among overweight and obese men. Epidemiology 17, 520—523.

Schneider, G., Kirschner, M.A., Berkowitz, R., Ertel, N.H., 1979. Increased estrogen production in obese men. J. Clin. Endocrinol. Metab. 48, 633—638.

Sermondade, N., Elloumi, H., Berthaut, I., Mathieu, E., Delarouziere, V., Ravel, C., Mandelbaum, J., 2010. Progressive alcohol-induced sperm alterations leading to spermatogenic arrest, which was reversed after alcohol withdrawal. Reprod. Biomed. Online 20, 324—327.

Shafik, A., Olfat, S., 1981. Scrotal lipomatosis. Br. J. Urol. 53, 50—54.

Sjostrom, L., Narbro, K., Sjostrom, C.D., Karason, K., Larsson, B., Wedel, H., Lystig, T., Sullivan, M., Bouchard, C., Carlsson, B., Bengtsson, C., Dahlgren, S., Gummesson, A., Jacobson, P., Karlsson, J., Lindroos, A.K., Lonroth, H., Naslund, I., Olbers, T., Stenlof, K., Torgerson, J., Agren, G., Carlsson, L.M., 2007. Effects of bariatric surgery on mortality in Swedish obese subjects. N. Engl. J. Med. 357, 741—752.

Sjostrom, C.D., 2005. Systematic review of bariatric surgery. JAMA 293, 1726 (author reply 1726).

Sjostrom, L., Lindroos, A.K., Peltonen, M., Torgerson, J., Bouchard, C., Carlsson, B., Dahlgren, S., Larsson, B., Narbro, K., Sjostrom, C.D., Sullivan, M., Wedel, H., 2004. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N. Engl. J. Med. 351, 2683—2693.

Tsutsumi, R., Webster, N.J., 2009. GnRH pulsatility, the pituitary response and reproductive dysfunction. Endocr. J. 56, 729—737.

Van Royen, E., Mangelschots, K., De Neubourg, D., Valkenburg, M., Van de Meerssche, M., Ryckaert, G., Eestermans, W., Gerris, J., 1999. Characterization of a top quality embryo, a step towards single-embryo transfer. Hum. Reprod. 14, 2345—2349.

Winters, S.J., Wang, C., Abdelrahaman, E., Hadeed, V., Dyky, M.A., Brufsky, A., 2006. Inhibin-B levels in healthy young adult men and prepubertal boys: is obesity the cause for the contemporary decline in sperm count because of fewer Sertoli cells? J. Androl. 27, 560—564.

Declaration: The authors report no financial or commercial conflicts of interest.

Received 4 July 2011; refereed 18 October 2011; accepted 19 October 2011.