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CASE REPORT



Applicability of biological fertility indicators for effective birth control after orthotopic liver transplantation

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In young women, a return to normal life after organ transplantation includes the possibility of fulfilling her possible motherhood wishes. Immediately after transplantation, pregnancy should generally be avoided, and the use of reliable and safe birth control methods counselled for at least 12 months (McKay et al. 2005). The choice of a recommended method is not exempt from difficulty. Reliable and safe methods applicable to healthy women are not universally recommendable after liver transplantation (Curtis et al. 2016). Doctors should carefully balance which methods to propose, and decide on grounds of individual medical, safety and patient-derived conditions (Hilger et al. 2018).

Some of these methods, based on the identification of biological fertility indicators (BFI) and periodic continence during fertile phase, have the best possible efficacy to side effect ratio in general population: the symptothermal method (STM) has shown minimal methodological failure rates, comparable to that of modern combination anovulatory drugs (Trussell 2011; Peragallo Urrutia et al. 2018). Nevertheless, there is no evidence-based recommendation for applicability of such methods in transplanted patients, which explains why guidelines dismiss their usefulness. This case report first describes an eight-year follow-up of the use of BFI after liver transplantation used for pregnancy postponement.

The 31-year-old woman received a liver allograft due to fulminant idiopathic hepatic failure 6 weeks after delivery of her first offspring. At week 13 post-transplantation the couple was admitted to our family orientation unit, seeking advice for birth control using fertility awareness-based methods. For highest possible efficacy in avoiding pregnancy, our staff recommended the use of STM originally proposed by Rötzer (1968) and adapted later by others (Frank-Herrmann et al. 2007). Training, monitoring, documentation and analysis were performed according to our local practice (Soler et al. 1995). During the first 3 cycles, the patient became autonomous in identifying her clinical fertility window (CFW), by using calculations plus cervical mucus evaluation as preovulatory double

check and mucus plus basal temperature raise as postovulatory double check. After that training period graphs were only checked for confirmatory purposes and filing.

At the time of first presentation, lactation had already been discontinued. End of amenorrhoea at week 29 postpartum (23 post-transplantation) was preceded by an ovulation, as evidenced by the characteristic biphasic pattern of body temperature. Despite being ovulatory, the first ovulation before end of amenorrhoea was retrospectively identified as likely infertile because of luteal insufficiency, evidenced by only 9 days of post-ovulatory raised temperature (Döring 1969). After that, the patient was followed for the complete period of pregnancy contraindication lasting 12 consecutive cycles. Statistics of those cycles are shown in Table 1. All these cycles were assessed as ovulatory and met luteal sufficiency criteria in all but one.

Fourteen months post-transplantation, the couple wished a new baby. During her clinical suitability evaluation pregnancy was temporarily contraindicated for subclinical CMV infection. Five months later, antiviral treatment had negativized viremia while clinical condition remained stable. Due to its teratogenic potential (European-Medicines-Agency 1996), mycophenolate mofetil was discontinued and after a 6-week washout time, the patient was released from pregnancy contraindication. During her first cycle of attempts, directed sexual intercourses during the fertile phase led to the intended pregnancy without a need of progestin supplementation.

From that time point onwards the patient was carefully monitored at her transplantation hospital by a multidisciplinary team composed of liver-transplant physicians and high-risk pregnancy unit obstetricians. The patient experienced an episode of acute rejection right after conception, which was successfully treated with methyl-prednisone boluses. Her evolution showed normal and stable graft function, without gestational diabetes or other medical events, and she remained normotensive. After premature rupture of membranes, the

Table 1. Statistical analysis of the main fertility associated indicators of the patient during the first 12 cycles after the end of amenorrhoea.

Total number of cycles (<i>n</i>)	12	
Number of biphasic cycles (<i>n</i>)	12	
Number of cycles with luteal phase ≥ 10 days (<i>n</i>)	11	
Number of cycles with marital intercourse (<i>n</i>)	12	
Number of cycles with marital intercourse during clinical fertility window (<i>n</i>)	0	
Cycle length (days post-menstruation; median and 95% C.I.)	32.5	(29.8–35.3)
First day with mucus (days post-menstruation; median and 95% C.I.)	8	(7.4–9.1)
First-day temperature rise (days post-menstruation; median and 95% C.I.)	22.5	(20.8–25.8)
Clinical fertility window (number of days in a cycle; median and 95% C.I.)	18	(15.5–21.7)
Number of infertile days double check (luteal phase) (days pre-menstruation; median and 95% C.I.)	6.0	(4.4–6.8)
Total number of infertile days double check (number of days in a cycle; median and 95% C.I.)	14.0	(13.1–14.9)

patient gave birth by vacuum-assisted vaginal delivery to a 35 + 6-week-old, 2.5 kg heavy healthy girl.

Postpartum, the patient continued monitoring her BFI. After the end of amenorrhoea her cycles were ovulatory, normal in length and without luteal insufficiency. Patient's hepatic allograft function stood stable and without any hospital admission or meaningful medical event. As documented in her charts, the couple was sexually active and compliant with STM rules, avoiding further pregnancies, for now, more than 6 consecutive years. Considering that sexually active couples at our patient's age without the use of contraception have a Pearl Index of 85% (Trussell 2011), sexual continence during all their CFW periods is likely the major cause of pregnancy-free outcome. Awareness of the CFW allowed self-confidence and consequent satisfactory marital life, without any anxiety or fear of becoming pregnant.

Larger prospective series are needed to confirm a favourable risk to benefit ratio as a basis for evidence-based recommendation. Using this patient as a proof of concept we think that applicability of this method should not differ from the general population. Discrepancy between perfect and typical use should be lower because their serious condition may contribute to the couple's motivation to avoid pregnancy. However, fertility-awareness methods should be recommended carefully, after considering the following eligibility criteria: (a) motivated couples willing to adhere to the method and associated continence during CFW; (b) transplant centres in association with experienced teaching personnel; (c) appropriate and validated combined use of BFI, excluding single indicator-based methods; (d) close ambulatory follow-up of the patient, at least during the whole learning process; and (e) special precaution during immediate post-transplantation or puerperal periods.

Concomitant use of CFW identification with barrier methods proposed by some authors in general population should be recommended with caution in transplanted patients. Undoubtedly, such approaches will increase efficacy rates in uncompliant STM users, but are known to reduce efficacy in general population as compared with strictly compliant couples (Frank-Herrmann et al. 2007).

Newest developments in fertility-awareness-based methods go beyond the evaluation of BFI in favour of direct hormonal pattern monitoring (Bouchard et al. 2013). Provided

evidence-based and validated methods can be used, such technologies might further simplify identifying the upcoming ovulation and spread the use of these methods, especially during the puerperal phase.

In summary, this publication shows that the complex clinical situation during postnatal transplantation did not preclude from using STM as a safe and efficacious pregnancy avoiding approach. BFI also were used to achieve an intended pregnancy after careful clinical evaluation. Further details on background, methodology used, clinical management and evolution can be found online as [Supplemental Material](#).

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