

Commentary

Lessons Learned in Best Practice Infertility Treatment

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In this special issue of Clinical and Experimental Obstetrics and Gynaecology focusing on infertility, it seems an appropriate place to consider our past and current attitudes to how we as scientists and clinicians gather, interpret and use the evidence available to inform clinical practice in assisted reproduction. In an industry that has been criticised for being highly commercial, poor value for money when cost is weighed against chances of success, and not holding the patient at the center of care, how do those providing care counteract these observations in their daily practice? Insight was provided recently in a CEOG article entitled *Use of Endometrial Scratching in IVF/IUI – A Worldwide* Opinion and Clinical Practice Survey where the authors report on clinicians' attitudes to using endometrial scratching (ES), a debated infertility treatment, following the publication of several recent randomised controlled trials that showed no or limited improvement in patient outcomes [1–

The study demonstrated that confusion created through a lack of definitive practice guidelines had a significant impact on the current use of ES, with many clinicians abandoning or reducing the frequency that they perform the procedure. Even so, 57.2% of respondents still believed that ES could increase implantation rate in selected patient groups. Inconsistencies between studies in experimental design, methodology, patient cohorts and measured outcomes led the authors to conclude that further investigation is required to truly elucidated the scientific mechanisms at work. Yet it is not just that more data is required, but rather that more consistent and high-quality data is generated in response to the high risk of bias identified in many ES studies through quality assessment and meta-analysis [5].

While true that the scientific framework guiding our use of ES has not been closely adhered to, is there a reason that this should be more prevalent in the field of clinical infertility treatment than other areas of medical science? Endometrial biopsy/scratching/injury became part of clinical practice following the publication of a single, nonrandomised trial in 2003 [6]. Shoham *et al.* [1] demonstrate in their study that ES was used by 85% of survey respondents who represented an estimated 124,200 cycles conducted annually across the globe, a sample of about 5% of the industry. This data is supported by a 2015 study where survey respondents from Australia, New Zealand and the

UK reported an 83% usage of ES showing a similar uptake in the technology is a narrower sample population [7]. A follow-up study published in 2019 reported ES usage to decline to just 34%, and like the survey respondents in the Shoham *et al.* [1] study, it was predominantly being used only with an indication of recurrent miscarriage [8]. While it's encouraging to see a shift in the use of ES to reflect the data available, what made this procedure so successful in its initial uptake requires some scrutiny.

Like with many wicked problems in society there are other factors influencing the use of this treatment in daily practice. These have been discussed in the literature more broadly when referring to "add-ons"—infertility treatments that are not a core component of the IVF/ICSI cycle, and usually come at an additional cost to the end-user. To better understand the use of add-ons, stakeholder attitudes and opinions have been the subject of recent analysis, with some conflicting observation—medical directors claiming that patients are often the ones driving the use of add-ons [9], yet patients cite they first heard about the add-ons at the clinic [10]. Care must be taken in linking these observations as data were captured in different market settings, yet both scenarios are likely to hold true to some effect, the questions being: why are consumers designing their own treatment without medical guidance, and why are clinics offering treatments that don't have clear practice guidelines?

A lot of this might come down to the unknown unknowns of assisted reproduction. With an estimated 40% of infertilities idiopathic, and 70-80% of treatments unsuccessful in producing a live birth, there lies a large and unexplained grey area of 'hope' whereby both clinician and patient want to create opportunity for success. With much of the industry privately funded, within a free market, consumer autonomy is supported by commercialised business, both by medical device companies selling treatments and by clinics trying to offer competitive advantage. Regulatory bodies such as the HFEA in the UK have tried to support consumer decision making by setting up a traffic light system to expose the evidence-based nature of add-ons (none receiving a green light), and time will tell how much of a success this is. Historically, the biggest shift in infertility treatment practice has been from multiple to single embryo transfer (SET) and was driven financially through the subsidised treatment of SET, and later by data-driven example, reducing the complications resulting from pregnancies with

multiple foetuses [11].

Steps can be made to reduce the uptake of technologies that don't have strict practice guidelines in place. This can first be done by assuring that the scientific data collected is done so with integrity, and in collaboration instead of competition—we would be better informed with more registered, multi-centred trials with large sample sizes and consistent protocols than statistically groomed metaanalyses and quality assessments that confirm high risk of bias and heterogeneity of included studies. Next, we may need to change our funding approaches to encourage such rigorous testing of new technologies and procedures, and in markets where public funding does apply restrict it to technologies with clear indications for success. This also allows for benchmarking to take place in real populations, offering an opportunity to lead both public and private practice by example. Studies like those conducted by Shoham et al. [1] and others cited in this article offer an insight into the limitations of our current systems and a lag in the legacy left behind by obstreperous practice.

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KHB conceptualized, drafted and approved the final manuscript.

Ethics Approval and Consent to Participate

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Conflict of Interest

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