Warming Echovist contrast medium for hysterocontrastsonography and the effect on the incidence of pelvic pain. A randomized controlled study

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BACKGROUND: Hysterocontrastsonography (HyCoSy) is a simple effective investigation of tubal patency. One common side effect is pelvic pain at the time of the procedure. The temperature of the contrast media used may be a causative agent for pelvic pain. This study was designed to assess the effect of warming the contrast to body temperature compared to room temperature on the incidence of pelvic pain. METHODS: A randomized controlled trial was carried out at the Cardiff Assisted Reproduction Unit. Following ethical approval, all women having HyCoSy for tubal assessment were asked if they would be willing to participate in the study. Computer-generated numbers were placed in opaque sealed envelopes, which were opened by the fertility nurse at the time of procedure. The women were randomized into two arms to receive the contrast medium at either room temperature or at body temperature. Randomization was done according to CONSORT guidelines. The pain experienced was then recorded by the patient on a 10-cm visual analogue scale. RESULTS: The mean pain scores in the room temperature and the body temperature arms were 5.1 and 3.86, respectively. This was statistically significant \( P = 0.006 \). CONCLUSION: Warming of Echovist contrast media to body temperature is a simple and effective intervention in reducing discomfort at the time of HyCoSy.

Key words: Echovist/hysterocontrastsonography/pain/temperature/tubal

Introduction

Tubal aetiology is a significant factor contributing to subfertility in 25% of couples attending for investigation and treatment of subfertility (Serafini and Batzolin, 1989). It is pivotal to assess tubal patency before undergoing assisted reproduction therapies for several reasons. The presence or absence of tubal patency determines not only the modality of treatment but also allows some prediction of prognosis (Mol et al., 1999). Even if IVF is contemplated, it is important to note the presence of hydrosalpinges as this significantly adversely affects the pregnancy rate (Zeyneloglu et al., 1998). A recent meta-analysis strongly supports the surgical removal of hydrosalpinges before embryo transfer as this significantly improves the chance of conception (Johnson et al., 2005).

The gold standard for tubal assessment is formal laparoscopy and dye chromotubation (Swart et al., 1995). Although this allows excellent images of the pelvic anatomy, it is associated with significant logistic disadvantages; these include general anaesthesia, use of operative time and equipment and high financial cost to the health care providers. Although laparoscopy is often thought of as a simple procedure, it is not without significant risks. These include visceral trauma, damage to retroperitoneal structures, life-threatening haemorrhage, infection, surgical emphysema and peritonitis secondary to bowel damage (Tarik and Fehmi, 2004).

In view of the importance for accurate tubal assessment and the above risks, a more suitable investigative tool was required. This, coupled with the great advancements in imaging technology, has paved the way for alternative techniques.

Hystersalpingogram is a valid alternative but has some disadvantages including use of clinical radiography time, contrast media reactions, pelvic discomfort and vasovagal reactions (Ayida et al., 1996a).

A more recent modality for tubal assessment is hysterocontrastsonography (HyCoSy). This is a simple procedure that can be performed in an office outpatient setting (Exacoustos et al., 2003). It involves the introduction of a fine (5-French gauge) catheter via the cervical canal into the uterine cavity. A small balloon at the tip of the catheter keeps it in place. A special contrast medium called Echovist is used in this procedure. Echovist is a suspension of galactose microparticles in aqueous galactose solution and is an echogenic contrast media. Echovist is introduced into the uterine cavity via the catheter, and a transvaginal ultrasound scan is concurrently performed. The contrast under positive pressure in the uterine cavity flows...
through the fallopian tube to the peritoneal cavity. This can be clearly demonstrated on real-time ultrasound. This can be dynamically recorded electronically. One common yet significant problem associated with HyCoSy is pelvic pain occurring at the time of contrast infusion, even if patent tubes are present (Ayida et al., 1996b). It has been hypothesized that the pain is generated by excessive intrauterine pressure caused by infusion of large volumes or rapid infusion (Hamilton et al., 1998). It is recommended using only 1–2 ml intermittently to decrease the incidence and severity of pelvic pain. Even after applying this strategy, pelvic pain still seems to occur. One possible explanation is that the introduction of contrast media below body temperature causes uterine contractions, stimulation of pain receptors and vasovagal reactions.

Our hypothesis is that warming the contrast media to body temperature decreases the subjective pain experienced by women undergoing HyCoSy compared to contrast at room temperature.

Materials and methods

In this randomized controlled study, 149 women were recruited from the general fertility clinic at the Cardiff Assisted Reproduction Unit, University Hospital of Wales, Cardiff, UK. Following full approval from the local research and ethics committee, all women requiring tubal assessment for primary or secondary infertility who satisfied the inclusion/exclusion criteria were invited to participate in the study. Women were excluded from the study if laparoscopy was deemed to be more appropriate, such as previous pelvic inflammatory disease, history suggestive of endometriosis and the presence of gross hydro-salpinges or adnexal pathology. All women were given patient information leaflets explaining the study and a consent form to be completed at a later date after informed counselling. All women who were invited kindly agreed to participate in the study. The South Wales ethical committee approval was obtained for this study and the local research and development department informed. Randomization was carried out as per CONSORT guidelines. Computer-generated random numbers were generated and placed in sealed opaque envelopes. At the time of HyCoSy, one envelope was opened and, depending on the parity of the number, Echovist contrast at room temperature or body temperature was used for the procedure. Echovist used in the body temperature arm of the trial was warmed in a standard embryo media incubator at 37°C. The temperature was electronically monitored and thermostatically controlled. The room temperature was recorded with the aid of a mercuric thermometer. The randomization, selection and mixing of the Echovist were performed by one of the fertility nurses independent of the clinician performing the procedure and the patient. The study was double blinded with respect to the patient and the clinician. Patients were asked to grade the discomfort experienced with the aid of a 10-cm visual analogue scale, with 0 corresponding to ‘no pain experienced’ and 10 corresponding to ‘the maximum pain experienced’. The data were recorded on proformae by the patient and placed in a sealed box until the conclusion of the trial. The data were then collated by two researchers and analysed with the aid of the Statistical Package for the Social Sciences, version 11 for Microsoft Windows (SPSS Inc., Chicago, IL, USA). P-values were obtained with a Mann–Whitney U-test. A P-value of <0.05 was considered to be statistically significant. Power calculation performed at the design stage of the trial suggested that 71 subjects were required in each arm of the study if the prevalence of pelvic discomfort at HyCoSy is accepted as 30% with a 95% confidence and 80% power.

| Table I. Mean subjective pain score (scale 0–10) versus Echovist temperature |
|------------------|------------------|------------------|--------------|
| Visual analogue score | Echovist [mean score (95% CI)] | P-value |
| Pain score        | At room temperature | At body temperature |          |
| 5.1 (4.5–5.71)    | 3.86 (3.18–4.55)   | 0.006            |

CI, confidence interval.

Results

A total of 149 women were randomized to one or other arm of the trial. After randomization, 77 women underwent HyCoSy with the Echovist at room temperature, and 72 women underwent HyCoSy with the Echovist at 37°C. All procedures were satisfactorily carried out in both groups. There was no difference noted in the incidence of structural malformations of the cervix or uterus in the two groups. There were three women who experienced acute vasovagal episodes. All the three women were in the room temperature arm of the study. All were treated conservatively without pharmacological intervention. There were no episodes of vasovagal attack in the body temperature group, although, there is no statistical difference between the two groups (P = 0.246) with the aid of Fisher’s exact constant test. All women completed the visual analogue scale assessment correctly. The mean pain score recorded on the visual analogue scale in the room temperature arm of the study was 5.1, and the mean pain score recorded in the body temperature arm was 3.86 (Table I). This was statistically significant (P = 0.006) with the aid of a Mann–Whitney U-test.

Discussion

HyCoSy is a simple and cost effective investigation to assess tubal patency. It is likely to have a significant role in office gynaecology in the future as well as in assisted conception units. The main disadvantages include pelvic pain and vasovagal attack. The study clearly supports the hypothesis that the temperature of the Echovist media is a causative agent of pelvic pain at the time of the procedure. More specifically, increasing the Echovist temperature to 37°C results in a statistically significant reduction in the incidence of pelvic pain compared to when Echovist is used at room temperature. Warming of the Echovist for a sufficient time before the procedure is a simple, cheap, non-pharmacological, effective method to reduce pelvic pains without any side effects. One possible logistical problem is that although warming incubators are readily available with no additional financial costs in assisted conception units, this may not be the case in the outpatient gynaecology setting. This potential cost may be offset by increased patient compliance, patient satisfaction and less pharmacological requirements. To date, there has been no studies reported in literature assessing Echovist temperature as a modifiable cause of pain at HyCoSy. Vasovagal attacks are another possible significant side effect of HyCoSy. It may be that temperature is also another causative factor in this. This has not yet been assessed in literature. In this study, there was no statistical difference noted in the incidence of vasovagal
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episodes between the two arms of the study. This result is likely to be due to the fact that the study was not designed to assess this phenomenon and is therefore underpowered to assess the incidence of vasovagal episodes. A larger future study is recommended. Another hypothesis is that a reduced temperature of Echovist media compared to body temperature may be associated with an increased incidence of tubal spasm. This would result in increased incidence of false tubal occlusions and its subsequent inappropriate management. Again, this hypothesis has not been assessed in the current literature. This study has not been designed to assess this and therefore is underpowered. Future studies are urgently required.

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References


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