

Oxytocin: bringing magic into nipple aspiration

A large need remains for new noninvasive breast cancer screening modalities. Nipple fluid, that contains breast epithelial cells, is produced in the breast ducts of nonlactating women and can be collected by vacuum aspiration. Previous studies failed to obtain nipple fluid in a considerable proportion of women.

We assessed the feasibility of carrying out oxytocin-supported nipple aspiration on 67 healthy female volunteers. Nipple fluid was aspirated through use of a vacuum system after administration of oxytocin nasal spray.

Nipple aspiration was successful in 94% of women. Volumes ranged from 5 to >100 µl, containing ~2000 ng DNA, which showed to be largely enough for carrying out a quantitative methylation-specific polymerase chain reaction for multiple genes. The procedure was very well endured.

Oxytocin-supported nipple aspiration provides a valuable tool for accessing mammary epithelium, providing sufficient DNA for a broad spectrum of analysis in the large majority of women.

New noninvasive breast cancer screening modalities are urgently needed. In high-risk women, current screening modalities miss one out of four breast tumors [1]. Nipple fluid, that contains breast epithelial cells and proteins secreted by them, is produced in small amounts in the breast ducts of nonlactating women and can be collected by noninvasive vacuum aspiration. Analyzing genomic changes in nipple fluid could cause a breakthrough in breast cancer screening and prevention.

Historically, successful nipple fluid aspiration was reported in only 39%–66% of women [2, 3], clearly limiting its potential. Other approaches to obtain ductal cells such as ductal lavage and random fine needle aspiration are more invasive, cause more discomfort and cost more time and money [2]. Zhang et al. [4] previously suggested from a pilot of nine volunteers, that the use of nasal oxytocin spray potentially increased the yield of nipple aspirate fluid. Oxytocin stimulates and facilitates emptying of the breast glands.

After approval of the study protocol by the Hospital's Ethics Committee, we assessed the feasibility of carrying out oxytocin-supported nipple aspiration on 67 healthy female volunteers. After warming of the breast and scrubbing of the nipple, nipple fluid was aspirated with a vacuum system within half an hour after administration of four IE oxytocin nasal spray. Participants rated the experienced discomfort during different stages of the procedure from 0 to 10.

Participants were 18–60 years old (mean 29 years). 12% of the women were postmenopausal, 75% were nulliparous, 19% had previously breast-fed and 7 of 67 participants (10%) reported a history of spontaneous nipple discharge. Nipple aspiration was successful in 63 of 67 women (94%). For 13 women (19%), fluid was only obtained unilaterally; from the remaining 50 women (75%) fluid was obtained bilaterally (Table 1).

The only predictor for fluid yielding during aspiration was a history of spontaneous nipple discharge ($P < 0.005$ and $P = 0.05$ for the right and left breast, respectively). Other features such as age, previous breast-feeding, hormonal/reproductive factors and history of breast surgery showed no predictive value for the volume of nipple fluid that was produced. No combination of factors identified women ineligible to participate in this procedure.

After proteinase K digestion of the first 20 randomly selected samples, an average of 2000 ng of DNA (range 500–6800 ng) was obtained, which was largely sufficient for carrying out a quantitative methylation-specific polymerase chain reaction [5] for multiple genes. When splitting the samples, enough material is left to screen for other epigenetic, genetic and proteomic changes.

The procedure was very well tolerated. No oxytocin side-effects were reported. 66 of 67 participants (99%) would undergo the procedure again and would recommend the procedure to others. Mean discomfort rating for the total procedure was 1.3. For women that had previously undergone mammography or had breast-fed, the mean discomfort rating was only 0.9, which is significantly lower than the discomfort experienced during breast-feeding (1.9) or mammography (4.3).

In conclusion, oxytocin-supported nipple aspiration provides sufficient DNA and fluids for a broad spectrum of

Table 1. Volume of nipple fluid that was obtained for right and left breasts separately

| Volume nipple fluid | Right breast | | Left breast | |
|---------------------|--------------|-----|-------------|-----|
| | N | % | N | % |
| Nothing | 12 | 18 | 9 | 13 |
| <5 µl | 13 | 19 | 9 | 13 |
| 5–10 µl | 26 | 39 | 26 | 39 |
| 10–50 µl | 11 | 16 | 18 | 27 |
| 50–100 µl | 4 | 6 | 3 | 5 |
| >100 µl | 1 | 2 | 2 | 3 |
| Total | 67 | 100 | 67 | 100 |

genomic analyses in almost all women and therefore could mean a breakthrough in noninvasive breast cancer screening.

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