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DIFFERENTIAL DIAGNOSIS OF PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS USING INFRARED MICROSPECTROSCOPY

Hypothesis / aims of study

The diagnosis of painful bladder syndrome/interstitial cystitis (IC) currently is hampered by the lack of reliable biological markers. We have previously reported the feasibility of using infrared microspectroscopic analysis (IRMS) of dry serum films (DSF) to differentiate patients with IC from healthy subjects [1]. We now report the results of comparisons between healthy women, those with IC, and those with other urological disorders.

Study design, materials and methods

Serum samples were collected from female human subjects using the capillary finger-stick puncture technique. Subjects consisted of 7 IC patients, 8 healthy controls and 12 patients with other urological disorders (Comparison group), including stress incontinence (8), neurogenic bladder (2), chronic bacterial cystitis (1), and history of transitional cell carcinoma (1). NIDDK criteria were used by a single clinician to diagnose those with IC, all of whom were on active treatment with oral, intravesical, or combination oral and intravesical therapy, and stable symptoms. Women without IC were screened with a Urogenital Distress Inventory (UDI-6) questionnaire, and were excluded if they reported any bladder, suprapubic, or vaginal pain, any baseline pelvic pain, or another chronic pain condition. Sera were used to prepare DSF using a 1:5 serum/water solution. The serum solution was loaded onto a cellulose membrane filter device with a 10,000 nominal molecular weight limit and fractionated at 16,000 x g for 10 min. The filtrates (0.5 µL) were applied to microscope slides (SpectRIM™) with a highly reflective surface and no detectable IR background signal, and films were obtained by vacuum drying. Ultrafiltration and IRMS was performed 3 separate times for each subject sample. IR spectra collected from the DSF were used to create classification models using Soft Independent Modeling by Class Analogy (SIMCA) [2].

Results

A total of 27 subject serum samples were analyzed. Mean age of all subjects was 48.3 years (range 28-71). Mean age for IC patients was 45.6 years (33-61), for comparison subjects 50.0 (28-71), and for healthy volunteers 33.6 (25-45). Mean duration from IC diagnosis was 14.2 years (5-30). Films prepared by ultrafiltration showed a marked decrease in the IR absorption bands in the 1400-1800 cm^{-1} region when compared to serum spectra, probably due to the removal of large proteins (Figure 1). The SIMCA models correctly classified spectra based on subject condition (healthy/IC/Comparison group) in 100% of the subjects with high discrimination power (Figure 1). The predominant and consistent discrimination of IC from non-IC patients was associated with frequencies at 1550-1600 and 1360 cm^{-1}, bands normally associated with tryptophan and pyridine-carboxilic acids (Figure 2).

Interpretation of results

Using a SIMCA model, IRMS was consistently able to differentiate between patients with IC, other urologic conditions, and healthy controls. The pattern of IR discriminatory frequency suggests that derivatives from tryptophan may be linked to IC.

Concluding message

This research substantiates the potential of the IRMS as a cost-effective, simple and minimally-invasive approach to diagnose IC, and to differentiate patients with IC from those with other urological disorders.

Figure 1: SIMCA model showing 100% discrimination between IC, healthy, and non-IC urologic disorders (Comparison group).

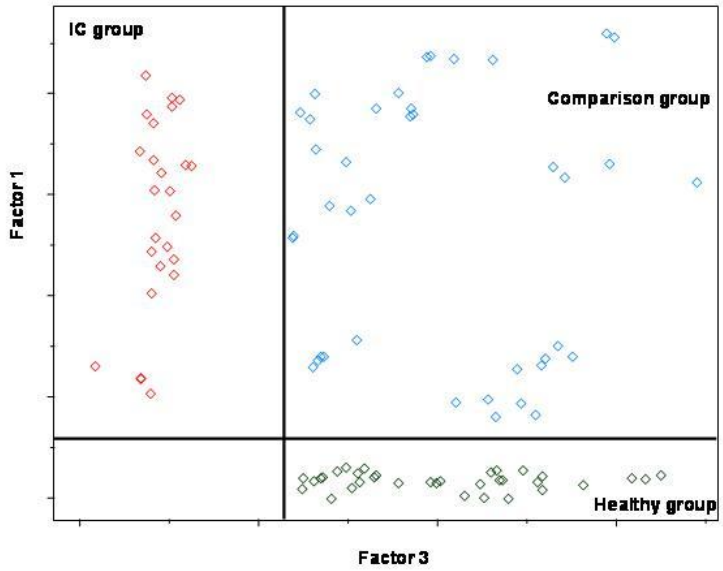
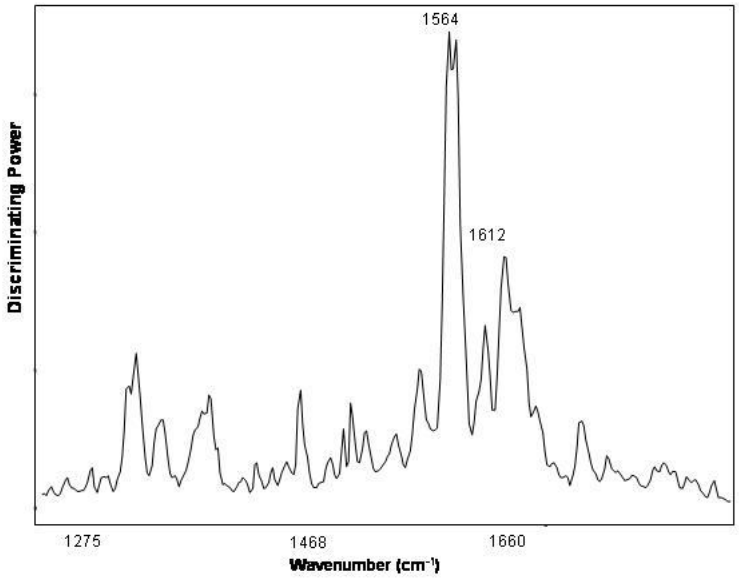


Figure 2: Area of consistent discrimination between IC and non-IC subjects on infrared microspectroscopy spectrum (IRMS) of human serum films in the 1550-1600 and 1360 cm^{-1} region.



References

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2. Sakudo A, Kuratsune H, Kobayashi T, et al. Spectroscopic diagnosis of chronic fatigue syndrome by visible and near-infrared spectroscopy in serum samples. Biochem Biophys Res Commun, 345: 1513, 2006

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**The Ohio State University Institutional Review Board**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**