

HPV DNA Screening Could Help Limit Surgery

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WHITE SULPHUR SPRINGS, W. VA. — A treatment algorithm based on DNA identification of high-risk human papilloma virus subtypes could eliminate much unnecessary surgical intervention for women eventually found to have no cervical abnormality, William Irvin, M.D., reported. “If the initial HPV DNA screening is negative, the likelihood that the patient

harbors a high-grade squamous cervical lesion is very low, and rather than continue with diagnostic loop electrosurgical excision or conization, we would recommend conservative follow-up,” Dr. Irvin of the University of Virginia, Charlottesville, said at the annual meeting of the South Atlantic Association of Obstetricians and Gynecologists.

“It’s hoped that by following this algorithm, we can reduce or avoid unnecessary conization and electrosurgical excision

procedures in women who are truly at low risk for cervical or endocervical lesions.” (See box.)

Dr. Irvin based his suggestions on the results of two studies. A 1999 Kaiser Permanente study of 137 women with cytologic atypical glandular cells (AGC) found that HPV DNA testing identified 94% of those with high-grade squamous intraepithelial lesions (HSIL) and 100% of those with endocervical adenocarcinoma in situ (Hum. Pathol. 1999;30:816-25).

And his own small study of 28 women with cytologic AGC found that the DNA testing had both a 100% sensitivity for detecting cervical intraepithelial neoplasia and a 100% negative predictive value for ruling out dysplasia.

“The take-home message of our study is that when a patient presents with cytologic AGC, and the HPV testing is negative [for high-risk strains], the likelihood of a high-grade endocervical lesion is exceedingly small, and you could consider that smear to be either reactive in nature or, if pathologic, most likely to be arising from lesions of

the endometrium or adnexa,” he said.

Dr. Irvin prospectively analyzed 28 women who presented to a colposcopy clinic from 2002 to 2004. All of the women had a repeat ThinPrep System Pap smear for cytology and HPV testing, a colposcopy, and Fischer electrosurgical conization, followed by Pipelle endometrial biopsy.

A total of 58% of the group had significant pathologic abnormalities. Squamous intraepithelial lesions occurred in 50% of the group; 11 of those were HSIL, and 3 were low-grade squamous intraepithelial lesions. One woman had endocervical adenocarcinoma in situ, and one had endometrial hyperplasia.

Normal cells were found in 42% of the group. No cancers were found in study participants. Four of the HPV DNA samples were contaminated with blood, so results were available for 24 patients. Of those, 17 were positive for high-risk HPV, including all 13 dysplastic patients. Seven of the tests were negative for high-risk HPV, and none of the patients with negative test outcomes had dysplasia. ■

and a one-year study of once weekly FOSAMAX® (alendronate sodium) 70 mg the rates of discontinuation of therapy due to any clinical adverse experience were 2.7% for FOSAMAX 10 mg/day vs. 10.5% for placebo, and 6.4% for once weekly FOSAMAX 70 mg vs. 8.6% for placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in ≥2% of patients treated with either FOSAMAX or placebo are presented in the following table.

| | Osteoporosis Studies in Men Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥2% of Patients | | | |
|------------------------------------|---|------------------------|--|------------------------|
| | Two-year Study | | One-year Study | |
| | FOSAMAX 10 mg/day % (n=146) | Placebo % (n=95) | Once Weekly FOSAMAX 70 mg % (n=109) | Placebo % (n=58) |
| <i>Gastrointestinal</i> | | | | |
| acid regurgitation | 4.1 | 3.2 | 0.0 | 0.0 |
| flatulence | 4.1 | 1.1 | 0.0 | 0.0 |
| gastroesophageal reflux disease | 0.7 | 3.2 | 2.8 | 0.0 |
| dyspepsia | 3.4 | 0.0 | 2.8 | 1.7 |
| diarrhea | 1.4 | 1.1 | 2.8 | 0.0 |
| abdominal pain | 2.1 | 1.1 | 0.9 | 3.4 |
| nausea | 2.1 | 0.0 | 0.0 | 0.0 |

Prevention of osteoporosis in postmenopausal women

The safety of FOSAMAX tablets 5 mg/day in postmenopausal women 40-60 years of age has been evaluated in three double-blind, placebo-controlled studies involving over 1,400 patients randomized to receive FOSAMAX for either two or three years. In these studies the overall safety profiles of FOSAMAX 5 mg/day and placebo were similar. Discontinuation of therapy due to any clinical adverse experience occurred in 7.5% of 642 patients treated with FOSAMAX 5 mg/day and 5.7% of 648 patients treated with placebo.

In a one-year, double-blind, multicenter study, the overall safety and tolerability profiles of once weekly FOSAMAX 35 mg and FOSAMAX 5 mg daily were similar.

The adverse experiences from these studies considered by the investigators as possibly, probably, or definitely drug related in ≥1% of patients treated with either once weekly FOSAMAX 35 mg, FOSAMAX 5 mg/day or placebo are presented in the following table.

| | Osteoporosis Prevention Studies in Postmenopausal Women Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥1% of Patients | | | |
|---|--|----------------------|-------------------------------|---|
| | Two/Three-Year Studies | | One-Year Study | |
| | FOSAMAX 5 mg/day % (n=642) | Placebo % (n=648) | FOSAMAX 5 mg/day % (n=361) | Once Weekly FOSAMAX 35 mg % (n=362) |
| <i>Gastrointestinal</i> | | | | |
| dyspepsia | 1.9 | 1.4 | 2.2 | 1.7 |
| abdominal pain | 1.7 | 3.4 | 4.2 | 2.2 |
| acid regurgitation | 1.4 | 2.5 | 4.2 | 4.7 |
| nausea | 1.4 | 1.4 | 2.5 | 1.4 |
| diarrhea | 1.1 | 1.7 | 1.1 | 0.6 |
| constipation | 0.9 | 0.5 | 1.7 | 0.3 |
| abdominal distention | 0.2 | 0.3 | 1.4 | 1.1 |
| <i>Musculoskeletal</i> | | | | |
| musculoskeletal (bone, muscle or joint) pain | 0.8 | 0.9 | 1.9 | 2.2 |

Concomitant use with estrogen/hormone replacement therapy

In two studies (of one and two years' duration) of postmenopausal osteoporotic women (total: n=853), the safety and tolerability profile of combined treatment with FOSAMAX 10 mg once daily and estrogen ± progestin (n=354) was consistent with those of the individual treatments.

Treatment of glucocorticoid-induced osteoporosis

In two, one-year, placebo-controlled, double-blind, multicenter studies in patients receiving glucocorticoid treatment, the overall safety and tolerability profiles of FOSAMAX 5 and 10 mg/day were generally similar to that of placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in ≥1% of patients treated with either FOSAMAX 10 mg/day (n=157), FOSAMAX 5 mg/day (n=161), or placebo (n=159), respectively, were: *Gastrointestinal*: abdominal pain (3.2%; 1.9%; 0.0%), acid regurgitation (2.5%; 1.9%; 1.3%), constipation (1.3%; 0.6%; 0.0%), melena (1.3%; 0.0%; 0.0%), nausea (0.6%; 1.2%; 0.6%), diarrhea (0.0%; 0.0%; 1.3%); *Nervous System/Psychiatric*: headache (0.6%; 0.0%; 1.3%).

The overall safety and tolerability profile in the glucocorticoid-induced osteoporosis population that continued therapy for the second year of the studies (FOSAMAX: n=147) was consistent with that observed in the first year.

Paget's disease of bone

In clinical studies (osteoporosis and Paget's disease), adverse experiences reported in 175 patients taking FOSAMAX 40 mg/day for 3-12 months were similar to those in postmenopausal women treated with FOSAMAX 10 mg/day. However, there was an apparent increased incidence of upper gastrointestinal adverse experiences in patients taking FOSAMAX 40 mg/day (17.7% FOSAMAX vs. 10.2% placebo). One case of esophagitis and two cases of gastritis resulted in discontinuation of treatment.

Additionally, musculoskeletal (bone, muscle or joint) pain, which has been described in patients with Paget's disease treated with other bisphosphonates, was considered by the investigators as possibly, probably, or definitely drug related in approximately 6% of patients treated with FOSAMAX 40 mg/day versus approximately 1% of patients treated with placebo, but rarely resulted in discontinuation of therapy. Discontinuation of therapy due to any clinical adverse experience occurred in 6.4% of patients with Paget's disease treated with FOSAMAX 40 mg/day and 2.4% of patients treated with placebo.

Laboratory Test Findings

In double-blind, multicenter, controlled studies, asymptomatic, mild, and transient decreases in serum calcium and phosphate were observed in approximately 18% and 10%, respectively, of patients taking FOSAMAX versus approximately 12% and 3% of those taking placebo. However, the incidences of decreases in serum calcium to <8.0 mg/dL (2.0 mM) and serum phosphate to <2.0 mg/dL (0.65 mM) were similar in both treatment groups.

Post-Marketing Experience

The following adverse reactions have been reported in post-marketing use:

Body as a Whole: hypersensitivity reactions including urticaria and rarely angioedema. Transient symptoms of myalgia, malaise and rarely, fever have been reported with FOSAMAX, typically in association with initiation of treatment. Rarely, symptomatic hypocalcemia has occurred, generally in association with predisposing conditions.

Gastrointestinal: esophagitis, esophageal erosions, esophageal ulcers, rarely esophageal stricture or perforation, and oropharyngeal ulceration. Gastric or duodenal ulcers, some severe and with complications have also been reported (see WARNINGS, PRECAUTIONS, Information for Patients, and DOSAGE AND ADMINISTRATION).

Skin: rash (occasionally with photosensitivity), pruritus, rarely severe skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Special Senses: rarely uveitis, rarely scleritis.

For more detailed information, please read the complete Prescribing Information.
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Management Tips for Women With Cytologic Atypical Glandular Cells

- ▶ For women older than 35 years, women younger than 35 years who have abnormal bleeding, and women with AGC that “favors endometrial cells”: Perform endometrial sampling.
- ▶ If AGC “favors endocervical adenocarcinoma in situ”: Perform cold-knife conization and subsequent cervical curettage.
- ▶ For AGC not otherwise specified: Perform HPV DNA testing.

If the patient is negative for high-risk HPV, repeat cytology at 6-month

intervals until two consecutive normal results are obtained. If abnormal cytology persists, refer the patient to colposcopy.

If the patient is positive for high-risk HPV, the likelihood of a dysplastic cervical lesion—typically high-grade—is high. Perform colposcopy, biopsy as indicated, and obtain endocervical samplings. Base further management on the results of the evaluation.

Source: Dr. Irvin

Study Suggests Hormonal Contraceptives Do Not Cause Women to Gain Weight

WASHINGTON — Women's perceptions that they gain weight when taking hormonal contraceptives are not realities, according to a randomized study.

Data from a poster presented at the annual meeting of the Association of Reproductive Health Professionals refuted the long-held association between use of hormonal contraception and weight gain, showing that women's perceived weight changes didn't match their actual weight changes while using contraceptives.

Concerns about weight gain may lead women to discontinue hormonal contraception, according to Lauren Osborne, a graduate student, and colleagues at Columbia University, New York. No significant weight changes occurred from baseline among women who used hormonal contraception in the form of either a pill or the vaginal ring in their randomized study of 201 subjects.

Overall, 167 of the 201 women completed three menstrual cycles using either

oral contraception in the form of Ortho TriCyclen Lo (ethinyl estradiol and norgestimate) or a vaginal contraceptive ring (ethinyl estradiol and etonogestrel). The study was supported by a grant from Organon Pharmaceuticals Inc., maker of the NuvaRing vaginal contraceptive ring.

On average, the women who participated in the study gained 2.8 pounds, regardless of baseline weight or BMI and type of contraceptive used. The 34 women who reported a “bad change” in weight at the study's end had gained an average of 4.4 pounds, while the 112 women who reported “no change” had gained 2.2 pounds, and the 14 women who reported a “good change” had gained 3.3 pounds.

The mean weight of all the women studied was 146 pounds, and included women with BMIs in the healthy (less than 25), overweight (from 25 to 30), and obese (greater than 30) range.

—Heidi Splette