



RESEARCH PAPER



## Stage I and II Stress Incontinence (SIC): High dosed vitamin D may improve effects of local estriol

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### ABSTRACT

After the age of 55 almost every third woman suffers from conditions of the incapability to retain urine when the intra-abdominal pressure is raised by different causes. So called stress incontinence. It's caused by a predisposition in the family, weakness of the tissue, physical strain, deficiency in the metabolism, especially an increasing local estrogen deficiency and a local and systemic vitamin D deficiency. **Patients:** We evaluated the data of 60 meno- and postmenopausal female patients with a stress incontinence (SIC). All had a SIC in spite of a former local estriol treatment with a treatment of OeKolp® forte (= 0.5 mg estriol/ov), 3 times a week, for 6 weeks and in spite of a regular pelvic floor exercise for 6 weeks in the morning and in the evening, according to the protocol. Thirty were in stage I SIC and 30 were in stage II SIC. **Method:** We evaluated vitamin-D-levels in serum of our 60 postmenopausal women. Only 20% of this group had good vitamin D-levels. The medical intervention combined estriol (0.5 mg) together with high dosed vitamin D (12.500 I.U.) locally 3 times a week for a period of 6 weeks. The patients also had the instruction to continue their daily exercises in pelvic floor (morning and evening, due to their protocol). After six weeks of treatment the vitamin D level in serum was defined and correlated to the patients condition (symptomatic of stress incontinence, protocol of micturitions, Pad-test). **Results:** About one-third of women from our test assigned to be now capable of retaining urine. More than one-third of our patients cleared a profit of treatment. They reported minimum regression about 25% of volume of incontinence. Therefore more than 2-third of our women being incapable of retaining urine improved their body conditions by using a combination of locally administered estriol and high dosed vitamin D. **Conclusion:** Stress incontinence (being incapable of retaining urine when the intra-abdominal pressure arises) in lower and middle grade, improves their body conditions under a combination of local administered estriol and vitamin D. This small study is not representative. We need much bigger studies with much more dates and with a follow up.

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### Stress incontinence - A common illness

In gynecological practice we are daily confronted with load incontinence (SIC), very often in connection with pelvic floor weakness (BBS). About each third woman is affected by it. That means alone in Germany several million are concerned, so that of a common illness can be spoken of.

### Causes

The causes of the SIC are various. It is very often accompanied with pelvic floor weakness and general weakness of

connective tissue. This arises familiarly frequently. The symptoms of the SIC often are strengthened by hypotrophy of connective tissue and/or their "atrophy. This arises in the context of increasing metabolic disturbances, particularly in menopause. Cofactors are then above all hard manual labor, heavy lifting, rapidly sequential births, pregnancies with heavy children etc.

### Diagnostics

The first diagnosis of the SIC was primarily placed anamnestic (see symptoms), secondarily by the general

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CAUTION: At the moment we do not know, if the high dose vitamin D treatment with 12500 IE is possible in pregnancy. We have no experience. Therefore we recommend an effective contraception during the application.

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and gynecological investigation, including evaluation of the pelvic floor, pelvimetric by means of ultrasonic CT (pelvic floor status, electronic Cystoscopy), protocol of micturition (at least 2 days), urine laboratory (rapid test, culture, sediment), PAD-test, urographic excretion, urethroscopy and urodynamic investigation. As a function of the anamnesis we also make individual laboratory analyzes, like minerals, vitamins and hormones. From our view the following hormones can be of special importance for the metabolism of connective tissue: estradiol, estrone, estriol, progesterone, testosterone, cortisol, DHEA, serotonin, homocysteine, T3, T4, TSH, TBG. With suspicion on SIC in connection with BS we analyze structures of connective tissue with Kollagenoson® method. With our ultrasonic CT we can determine sonographically various urodynamic parameters for the evaluation of the different functions capability of the different functions with and without stress (measurement of the pelvic floor in relaxation and under maximum contraction) quantitatively.

## The SIC study

### Our patients

We evaluated the data of 60 meno- and postmenopausal female patients who suffer from mild and moderate SIC. All suffered despite preceding local estriol therapy with OeKolg® (= 0.5 mg estriol per ovula, 3 times a week, for 6 weeks) and despite regular pelvic floor exercises (6 weeks long, in the morning and in the evening, according to their protocol) from mild and/or moderate stress incontinence.

### Protocols of micturition

All SIC female patients had been asked, to keep protocols of micturition and to make a PAD test (= standardized diaper test, 24 hours): The used templates/diapers were weighed, the unloaded weight was deducted and the urine quantities were computed and differentiated in light, moderate and heavy:

- Stage I: light, urine loss quantity maximally until 10 g/24 hr.
- Stage II: moderate, urine loss quantity of 11 to 50 g/24 hr.
- Stage III: heavy, urine loss quantity over 50 g/24 hr.

Our patients were separated in a group of SIC 1 and SIC 2

Thirty female patients had a mild SIC Stage I (incontinence when coughing, sneezing, laughter, small urine loss quantity, PAD test before the therapy: up until maximally 10 g/24 hr.).

Thirty female patients had a moderately severe SIC Stage II (incontinence when coughing, sneezing, laughter as well as with abrupt body movements, when rising and/or moving, before the therapy small up to middle urine loss quantity, PAD test: until maximally 50 g/24 hr.).

Suffering from heavily urine loss (degree of 3 SIC) was a criterion of exclusion.

## Methodology

We put into practice a combined vaginal high-dose estriol (0.5 mg) and vitamin D (12500 I.U.) treatment for at least 6 weeks.

The following prescription was formulated in a compounding pharmacy:

Vaginal suppository with vitamin D and estriol, e.g. "OVID E"

Rp. 0.5 mg estriol (according to the dosage in OeKolg® forte)

12500 I.E. vitamin D in an oily base

Middle chain triglycerides, adeps solidus q.s.

XII/XXIV ovula, ad 2 g

The patients were administered to use the suppositories vaginally at night, 3 times a week. In the morning the material of the suppositories was completely absorbed. After six weeks serum levels of vitamin D were determined according to therapy. Conditions of the female patients were evaluated (SIC symptomatology, protocol of micturition, PAD test, etc.). Compliance was very good. All female patients indicated to get on well with the method.

## Results

### Serum levels of vitamin D before therapy

The serum levels of vitamin D before therapy were measured in all female patients (n = 30) degree of 1. The standard values for 25-Hydroxy-Vitamin D in serum<sup>2,7</sup>

<30 ng/ml	unsatisfying
30–50 ng/ml	Satisfying
50–70 ng/ml	sufficient
>70 ng/ml	good

We stated that most female patients had a lack in vitamin D. Only **about 20%** of the female patients had good values of vitamin D. From the tested 60 patients (SIC 1 together with SIC 2) about **one third** had unsatisfying, **one third** satisfying, **about 10.0%** sufficient and **about 20.0%** comparable levels of vitamin D in serum. It seems evident, that beginning with the menopause and advanced age, levels of vitamin D are continuously decreasing: The UV-dependant production of vitamin D-through different organs (skin, liver, kidney) and the utilization of food resources in the gastrointestinal, metabolic, endocrine and weakness of transportation increases during advanced life drastically.

### Symptoms after therapy

**SIC I group:** After treatment of 6 weeks the SIC I group showed the following results (Stage I, incontinence when coughing and/or sneezing, small urine loss quantity, PAD test: until maximally 10 g/24 hr). **Almost half of women:** no more incontinence while coughing and sneezing. **About one-third:** less incontinence and problems, urine loss quantity was reduced around 30%–50% (PAD test) while coughing and sneezing. **About 20.0%:** no difference, urine loss quantity comparable.

That means, according to their own statements, almost 80% of SIC Stage I female patients, our therapy was of measurable benefit to them.

**SIC 2 group:** SIC 2 group showed the following result after the treatment of 6 weeks. **About 20.0%:** no more incontinence. **About 20.0%:** remarkable decreasing problems (= no more incontinence with abrupt body movements). **About 25%:** mild decreasing problems (= less incontinence problems with abrupt body movements). Smaller average urine loss quantity (about 25%–30% less, PAD test). **About one-third:** No difference, urine loss quantity didn't change, PAD test).

That means that according to their own statements one-third of the SIC I patients and about 20% of the SIC II patients indicated after the therapy to be again continent. Furthermore **more than one-third** of the female patients indicated at least 25% smaller average of urine loss quantity. Thus **more than 2-third** from SIC patients had a benefit using the combination therapy of local estriol and high-dosed vitamin D.

### Serum levels of vitamin D after treatment of 6 weeks

The majority of the female patients were better in vitamin D after 6 weeks of therapy than before beginning of the therapy. Thus the high-dose application of vaginal vitamin D in combination with estriol can be recommended for the prophylaxis and therapy of vitamin D lack with many female patients. Ten female patients remained within unsatisfactory values after the therapy. We must confirm that the vaginal absorption of lipophilic nutrients varies individually. It is interesting that 8 of these 10 female patients, who were therapy failures, did not improve the symptoms of SIC.

### Discussion

The outcome of therapy of the SIC depend on the stage and form of being incapable of retaining urine. All forms of therapy are complex and include different ways of approach. Measures in general include changing of life style and dietetic principles. In detail food watch, body mass index, weight reduction, pelvic floor training and - exercise, sports, methods of biofeedback, application of incontinence assistance, vaginal or anal electrical stimulation therapy, dutch caps, vaginal muscle training with special weights. There are also various medicamentous and surgical approaches, e.g., TVT, implantation therapy or implantation of an sphincter in addition. We demonstrated that combined high-dose estriol together with vitamin D seems to be a good recommendation in SIC degree 1 and SIC degree 2. We examined 60 female patients suffering from mild and/or moderate stress incontinence. They all had been pre-treated with a local estriol therapy (OeKolg® = 0.5 mg estriol, 3 times the week, 6 weeks long) and although they had made additionally pelvic floor exercise (according to protocol, 6 weeks long, in the morning and in the evening), they were stable in their stage of being incapable of retaining urine.

As we could find...

- most patients of that group had a lack of vitamin D,
- vitamin D was absorbed vaginally administered by suppositories
- combination of high-dosed vitamin D brought a partial improvement to therapy with single estriol.

The explanation?

At that moment each second woman suffers from concomitant symptoms of a vitamin D lack.<sup>7,17,18,20</sup> At the same time the incidences of SIC rises.<sup>1,2,3,6,7,13</sup> While getting older the skin-production of vitamin D, which constitutes in younger persons up to 80–90% of demand, decreases. Even our life style causes lack of vitamin D, because we work and live no longer under the natural sun and outdoors. Supplying vitamin D by food (egg, fish, mushrooms, etc.) is not very effective, and it seems, that elder people do metabolize more weakly in general.<sup>16</sup> Since a long time it is well-known that vitamin D is very important for the entire bone and metabolism of the connective tissue. Calcium absorption depends on a sufficient serum level of Cholecalciferol. Also the balance between osteoblasts and osteoclasts, between calcitonin and parathyroid hormone is dependently adjusted through vitamin D. Recently published research articles of high interest underline the anti-inflammatory, immune-modulating and anti-oxidative effects of the vitamin D.<sup>17,18,20</sup> Studies also proved that vitamin D obviously has a key function for cancer prevention and - therapy as well.<sup>4,5,15</sup> A sufficient daily supply of vitamin D (1.000 I.U.) reduces the risk for colon carcinoma to a half. A daily intake of 2.000 I.U. Vitamin D lowers the risk even to a third.<sup>4,5,15</sup> Chronic deficiency in vitamin D can - with the appropriate predisposition - promote emergence of hormone-dependant tumors: Vitamin D lack increases the risk for Mamma carcinoma,<sup>4</sup> in addition, for ovarian and prostate gland carcinomas. Recent studies show this for carcinoma of bronchus, bladder, esophagus, stomach, rectum, larynx and pancreas.<sup>46-48</sup> In vitro studies with cultured cells of the prostate gland showed that vitamin D can stop their growth. After effective supply of vitamin D prostate gland cancer cells increase uncontrolled growth, but grow normally and regularly furthermore.<sup>12</sup> Colon- and mamma-ca cells react exactly in the same manner. Mice, with artificially inoculated large intestine cancer had a clearly smaller tumor growth after administration of vitamin D.<sup>4</sup> In a study 44 of 60 female patients (=73.3%) had a respectively benefit regarding the SIC by locally therapy of estriol and high-dosed vitamin D. The protocol and the prescription, which has been developed, is suitable thus for the prophylaxis and therapy of the SIC. As we recently also showed, the vaginale application of vitamin D also might be

suitable for the treatment and prophylaxis of chronically recurrent therapy-resistant colpitis, cervicitis and several dysplasias.<sup>19</sup> Based on the research as it stands, it seems that vaginal application of high dosed vitamin D in combination with progesterone may balance hormone conditions on a good level. Our protocol includes improvement of healing after surgery of gynecological and gynaecourological interventions.

### Individually formulation for compounding pharmacies

The suppositories can be fomulated by all pharmacies, especially by compounding pharmacies.

Vaginal Ovula vitamin D and estriol, e.g. "OVID E" p.

Estriol	0,0005g
Vitamin-D in an oily base	12.500 I.U. (ref. Vitamin D3)
Middle chain triglycerides and adeps solidus	q. s.
XXII / XXIV Ovula (2g)	

### Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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