Terri DeNeui, DNP, ACNP, APRN-BC
Justin Graves, RPh

SUBCUTANEOUS TESTOSTERONE PELLET IMPLANTS

UNDERSTANDING THE ROLE OF TRIAMCINOLONE

Impacting lives globally through medical wellness initiatives is the focus of EVEXIAS Health Solutions (EHS). A primary mission of EHS is to introduce advances discovered over the years treating tens of thousands of patients successfully with subcutaneous hormone pellet therapy.

One such discovery is a revolutionary new testosterone hormone pellet containing trace amounts of a placatory substance, triamcinolone, which has been formulated and utilized successfully in thousands of implant procedures.

This white paper will address the issue of post pellet insertion complications related to the inflammatory response and present the safety and efficacy of testosterone pellets infused with low dose triamcinolone as an adjunct to counter these effects. A substantial literature review regarding side effects of triamcinolone use is also presented.

The Issue: ***Inflammatory response to subcutaneous pellet insertion***

A common complaint of many males and females receiving pellet therapy is the post insertion discomfort and scar tissue build up secondary to the inflammatory response[1]. This complication may deter patients from continuing the therapy over a long period of time. Further, the inflammatory response and resulting scar tissue build up may lead to erratic hormone absorption rates and pellet extrusions that cost practices thousands of dollars over time.

A common complaint from patients receiving pellet therapy is post insertion discomfort and scar tissue build up.

It is well established that post insertion pain and extrusion of the hormone pellet are common side effects[2] . Pellet extrusion rates have been reported in the literature as high as 12%[3]. The differences between men and women in post insertion pain and extrusion rates have been observed clinically, with men experiencing post insertion complications 30:1 over women. This increased rate of post insertion complications in men is theorized to be secondary to the volume of pellets inserted and the resulting inflammatory response, although provider technique, placement location and body composition are all known variables [4] .

Complications from the inflammatory response can cost thousands of dollars over time.

Triamcinolone Use, Safety & Efficacy: ***A Literature Review***

In an expansive literature review regarding the use of triamcinolone in various forms and formulations, the corticosteroid was shown to be safe and effica-

[1] McMahon, et.al., 2017

[2] Conners, et.al., 2011; Kelleheler, et.al., 1999

[3] Cavender & Fairall, 2009.

[4] Conners, et.al., 2011; Kelleheler, et.al., 1999; McMahon, 2017

cious in a variety of settings, modalities, doses, and uses. A concerning side effect reported in the literature as it pertains to subcutaneous leakage or use of triamcinolone is the possibility of fat necrosis, fat atrophy and skin hypo-pigmentation. The observation has been made from a number of studies dating back to the 1950's that higher doses of triamcinolone, 40mg/ml given intramuscularly, had rare presentations of fat atrophy and hypo-pigmentation secondary to leakage into the subcutaneous tissue; there have been 4 reports of fat necrosis out of over 6400 patients studied (0.06%) and these effects appear to be dose related[5]. The standard dose for dermatologic use of triamcinolone is 10mg/ml; all studies reported use at this dilution to be safe, effective and without the dermal complications of fat atrophy or necrosis noted at higher doses [6] .

An expansive literature review has shown triamcinolone use to be safe and efficacious in a variety of settings, including subcutaneous injections.

Compared to systemic corticosteroid injections, local corticosteroid injection complications are extremely rare, less than 1%, and all reported skin or subcutaneous complications, including subcutaneous atrophy, spontaneously resolve within 6-30 months post injection[7].

In a study of over 120 patients, abnormal scarring post rhinoplasty was treated with triamcinolone injections 10mg/ml with 85% success rate and zero reported complications from the injections[8]. In a systematic review of adverse effects of soft tissue injections of corticosteroids, 37 prospective studies, 10 of which utilized triamcinolone 10 mg/ml, reported minimal adverse events with skin pigment changes reported as the second most common adverse outcome after pain at injection site; skin changes noted reversed over time[9]. In the same systematic review, triamcinolone 1% was used in one study and reported zero adverse outcomes, including zero skin hypo pigmentation, infection or atrophy; the authors of this systematic review concluded soft tissue injections of corticosteroids to be a safe intervention.

A recent study utilizing 10mg/ml of triamcinolone injected subcutaneously for post herpetic neuralgia revealed no major adverse outcomes; minor complications such as bruising and discomfort were noted, patients were observed for 6 months post injections[10].

At reduced doses of corticosteroid, complications of skin hypo-pigmentation and atrophy can be eliminated.

---

[5] Beardwell, 1967; FDA-AERS, 2018; Fisherman, et.al., 1962; Pariser, et.al., 1963

[6] Hayward, et.al., 2018

[7] Brinks, et.al., 2010; Hanasono, et.al., 2002; Kanbe, et.al., 2016; Martins, et.al., 2017; Neal, et.al., 2017; Pace, et.al., 2018; Parveen, et.al., 2015; Park, et.al., 2013.

[8] Hanasono, et.al., 2002

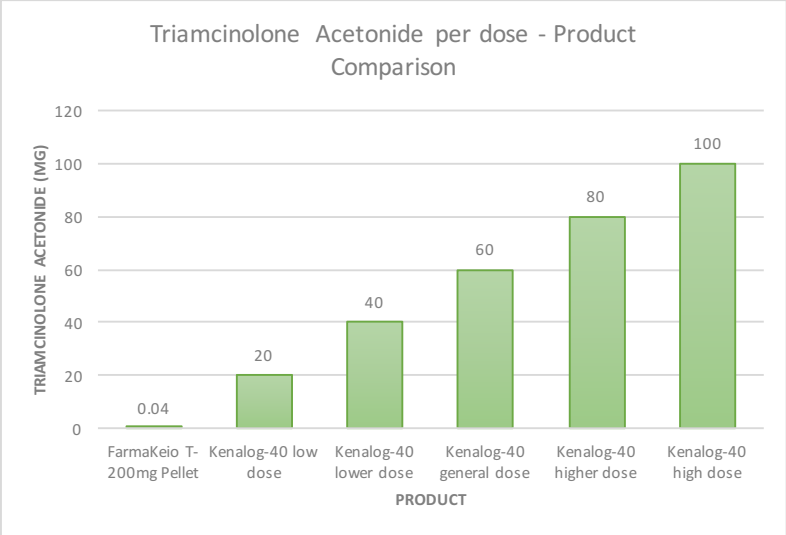
[9] Brinks, et.al., 2010

[10] Ni, et.al., 2017

The conclusion based on available literature on this topic is all complications of skin hypo pigmentation and fat atrophy may be greatly reduced if appropriate potency, dosage and solubility are used, and utilization of very low doses of corticosteroid, less than 1mg/ml, can negate these adverse outcomes.[11]

Subcutaneous Testosterone/Triamcinolone Pellets: *The Amount Matters*

As noted in the literature review, the adverse outcomes of subcutaneous leakage and/or use of triamcinolone include many variables. A primary variable noted in the studies was dosage used as it pertained to the specific adverse outcome of skin hypo-pigmentation and/or atrophy. All studies with the reported side effect of fat atrophy utilized the 40mg/ml dose.



The maximum amount of triamcinolone a patient may receive, at the maximum dosage of testosterone pellets for a male, 2400 mg, is 0.5 mg total, dissolved slowly over 5 months.

This equates to approximately 0.008 mg per pellet released subcutaneously per month, totaling 0.1 mg triamcinolone absorbed per month.

Subcutaneous Testosterone/Triamcinolone Pellets: *Yielding Better Outcomes*

In a retrospective chart review of males and females receiving hormone pellet therapy, over 1400 males and over 4500 females received testosterone implants infused with trace amounts of triamcinolone. The rates of post insertion pellet extrusions was reduced by greater than 50% over the prior year of reported extrusion rates.

50% reduction in post insertion extrusion rates was noted in a retrospective chart analysis of over 5000 pellet implant recipients.

Further, zero adverse events from the triamcinolone infused pellets were observed and patients reported less discomfort at insertion site post procedure compared to prior insertions without triamcinolone.

[11] Neal, et.al., 2017; Park, et.al., 2013; Wu & Goldman, 2018.

Frequently Asked Questions: ***Testosterone/Triamcinolone Pellets***

Are the pellets bio-identical? **T**he active hormone is bio-identical testosterone derived from wild yams. The addition of triamcinolone has no effect on the active hormone, nor do the binders and lubricating agents used in all pellet formulations, such as stearic acid or cholesterol.

Can triamcinolone infused pellets cause fat atrophy or necrosis? The trace amount of triamcinolone used in the pellets has **not been shown** to cause any adverse effects in over 5000 insertions. Triamcinolone used subcutaneously in doses of 10mg/ml or less have shown **zero side effects of fat atrophy or necrosis** and have been deemed safe and efficacious.

Will triamcinolone infused pellets cause an elevation in blood glucose? It is a well known fact that long term, chronic steroid use may alter blood glucose levels. In the retrospective chart analysis of over 5000 patients, there were no changes noted from baseline levels of HGA1C and no reported increases in blood glucose levels.

Final Thoughts

When dosed and monitored appropriately, androgen therapy with subcutaneous hormone pellets is highly effective in alleviating symptoms of age related hormone decline such as fatigue, depression, anxiety, mood swings, brain fog, memory loss and insomnia, thereby improving over-all sense of well-being and quality of life.

The side effects of subcutaneous hormone pellet insertions are primarily related to the inflammatory process and can prove to be a barrier for continuing the therapy long term. With the use of an evidence based, revolutionary new pellet technology many of the untoward side effects of traditional implantations may be avoided, yielding better outcomes and increased patient satisfaction- both of which directly impact the medical practice bottom line.

The revolutionary pellet technology has been shown to decrease many untoward side effects, directly impacting patient satisfaction and yielding better outcomes.

Based on years of experience using evidence based treatment modalities, collaborating with top medical providers and researchers in the field of menopausal and andropausal hormone therapies, and spearheading the training of hundreds of practitioners across the country, EVEXIAS Health Solutions is passionate about sharing what we have learned with other like-minded healthcare providers whose focus is to increase the quality of life and sense of well being, and offer hope to every patient they serve.

Bibliography

Beardwell, Ann. "Subcutaneous atrophy after local corticosteroid injection." *British medical journal* 3.5565 (1967): 600.

Brinks, Aaltien, et al. "Adverse effects of extra-articular corticosteroid injections: a systematic review." *BMC musculoskeletal disorders* 11.1 (2010): 206.

Cavender, Richard K., and Melissa Fairall. "ENDOCRINOLOGY: Subcutaneous Testosterone Pellet Implant (Testopel®) Therapy for Men with Testosterone Deficiency Syndrome: A Single–Site Retrospective Safety Analysis." *The journal of sexual medicine* 6.11 (2009): 3177-3192.

Conners, William, Kevin Flinn, and Abraham Morgentaler. "Outcomes with the "V" implantation technique vs. standard technique for testosterone pellet therapy." *The journal of sexual medicine* 8.12 (2011): 3465-3470.

FDA Adverse Event Reporting System, 2018. Retrieved from: https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm

Fisherman, Elmer W., Alan R. Feinberg, and Samuel M. Feinberg. "Local subcutaneous atrophy." *JAMA* 179.12 (1962): 971-972.

Hanasono, Matthew M., et al. "Correction of the soft tissue pollybeak using triamcinolone injection." *Archives of facial plastic surgery* 4.1 (2002): 26-30.

Hayward, W. A., Sibbitt, W. L., Sibbitt, R. R., Muruganandam, M., Rolle, N. A., Fangtham, M., ... & Kettwich, S. K. (2018). Intralesional Injection of Triamcinolone Acetonide for Subcutaneous Lipoma causing Musculoskeletal and Neurologic Symptoms. *The Journal of clinical and aesthetic dermatology*, *11*(5), 38.

Kanbe, Katsuaki, et al. "Simultaneous treatment with subcutaneous injection of golimumab and intra-articular injection of triamcinolone acetonide (K-method) in patients with rheumatoid arthritis undergoing switching of biologics: retrospective case–control study." *Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders* 9 (2016): CMAMD-S38442

Kelleher, S., et al. "Extrusion of testosterone pellets: a randomized controlled clinical study." *CLINICAL ENDOCRINOLOGY-OXFORD*- 51 (1999): 469-472.

Martins, Nádia, et al. "Treatment of Persistent Cutaneous Atrophy After Corticosteroid Injection With Fat Graft." *Reumatologia clinica* (2017).

McMahon, Chris G., Neil Shusterman, and Brian Cohen. "Pharmacokinetics, clinical efficacy, safety profile, and patient-reported outcomes in patients receiving subcutaneous testosterone pellets 900 mg for treatment of symptoms associated with androgen deficiency." *The journal of sexual medicine* 14.7 (2017): 883-890.

Neal, Danielle, Jason Arnold, and Tyler Moss. "Serpiginous hypopigmentation secondary to intra-articular corticosteroid injection." *Dermatology online journal* 23.4 (2017)

Ni, Jiaxiang, et al. "Subcutaneous Injection of Triamcinolone and Lidocaine to Prevent Postherpetic Neuralgia." *Pain physician* 20.5 (2017): 397-403.

Pace, Collier S., Nadia P. Blanchet, and Jonathan E. Isaacs. "Soft Tissue Atrophy Related to Corticosteroid Injection: Review of the Literature and Implications for Hand Surgeons." *The Journal of hand surgery* (2018).

PARISER, HARRY, and PHILIP F. MURRAY. "Intralesional injections of triamcinolone: Effects of different concentrations on psoriatic lesions." *Archives of dermatology* 87.2 (1963): 183-187.

Park, Sun-Kyung, Yun Suk Choi, and Hyun-Jung Kim. "Hypopigmentation and subcutaneous fat, muscle atrophy after local corticosteroid injection." *Korean journal of anesthesiology* 65.6 Suppl (2013): S59-S61.

Parveen, Shagufta, et al. "Comparison of subcutaneous extralesional and intralesional triamcinolone injection for the treatment of chalazion." *Pakistan Armed Forces Medical Journal* 4 (2015): 502.

Wu, Douglas C., and Mitchel P. Goldman. "Randomized, Double-Blinded, Sham-Controlled, Split-Hand Trial Evaluating the Safety and Efficacy of Triamcinolone Acetate Injection After Calcium Hydroxylapatite Volume Restoration of the Dorsal Hand." *Dermatologic Surgery* 44.4 (2018): 534-541.