

IVF Sperm Origin No Factor in Cognitive Risks

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WASHINGTON — Children who were conceived from surgically retrieved sperm had no greater risk of cognitive and behavioral problems than did those conceived from ejaculated sperm, according to a study of 3-year follow-up data from 874 children.

Surgically retrieved sperm have been associated with an increased risk of ge-

netic defects in previous studies. Because intracytoplasmic sperm injection (ICSI) is the technique of choice in cases of male infertility, concerns have been raised about an increased risk of developmental delays in children conceived from surgically retrieved sperm.

But the clinical implications of this study are that the origin of the sperm was not a factor in the percentage of IVF children who were at risk for cognitive and behavioral problems, Queenie V. Neri, a

biologist at the Center for Reproductive Medicine and Infertility at the Cornell University Medical School, New York, reported in a presentation at the annual meeting of the American Society for Reproductive Medicine.

To investigate the cognitive and behavioral profiles of children conceived using assisted reproductive technology according to sperm origin, Ms. Neri compared data from 74 children conceived via ICSI with surgically retrieved sperm, 516 chil-

dren conceived via ICSI with ejaculated sperm, and 284 children conceived via IVF but not ICSI.

Ms. Neri worked under the guidance of Dr. Zev Rosenwaks and Dr. Gianpiero D. Palermo, both of Cornell University.

The Ages & Stages Questionnaire (ASQ) and Social Skills Rating System (SSRS) were used to assess the children's communication skills, fine motor skills, gross motor skills, social skills, and problem-solving skills at 3 years of age.

Overall, 87.1% of the children had ASQ scores in the normal range, compared with 12.9% who scored in the at-risk range (meaning at risk for further developmental delays or abnormalities). The at-risk

Children who were conceived from surgically retrieved sperm actually scored significantly higher on ASQ measures of gross and fine-motor skills.

group included 10.4% of the IVF children, 11.4% of the children conceived via ICSI with ejaculated sperm, and significantly fewer (2.8%) of the children conceived via ICSI with surgically retrieved sperm.

Within the subset of at-risk children conceived via ICSI, those conceived from surgically retrieved sperm scored significantly higher on measures of gross and fine-motor skills on the ASQ than did those conceived from ejaculated sperm.

These children also scored higher on measures of communication, problem solving, and personal/social development, but the differences were not statistically significant.

Similarly, 81.8% of the children overall had SSRS scores in the normal range, compared with 18.2% of children in the at-risk range.

The at-risk group included 17.2% of the IVF children, 20.1% of the children conceived via ICSI from ejaculated sperm, and 15.8% of those conceived via ICSI from surgically retrieved sperm.

In the subset of children conceived via ICSI, the percentage of children at risk for problems with social skills was significantly lower among those conceived with surgically retrieved sperm, compared with those who were conceived with ejaculated sperm.

In addition, children who were part of multiple gestations were significantly more likely to be in the at-risk score range for the SSRS in both the IVF (non-ICSI) group and the ICSI group conceived from ejaculated sperm.

However, the difference in at-risk SSRS scores between multiples and singletons was not significant for children who were conceived via ICSI with surgically retrieved sperm.

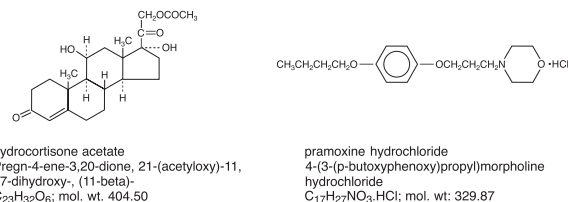
Although the results from this study suggest that there is no negative association between sperm characteristics and child development, ongoing follow-up is important in detecting malformations that appear after birth, Ms. Neri said. ■

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CLINICAL PHARMACOLOGY: Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Pramoxine hydrochloride is a topical anesthetic agent which provides temporary relief from itching and pain. It acts by stabilizing the neuronal membrane of nerve endings with which it comes into contact.

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses. (See DOSAGE AND ADMINISTRATION.)

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE: Topical corticosteroids are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS: Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

PRECAUTIONS: General: Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients. Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area and under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids. Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. (See Precautions-Pediatric Use.)

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly the corticosteroid should be discontinued until the infection has been adequately controlled.

Information for the Patient: Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions especially under occlusive dressings.
5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

Laboratory Tests: The following tests may be helpful in evaluating the HPA axis suppression: Urinary free cortisol test
ACTH stimulation test

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids. Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

Pregnancy: Teratogenic Effects: Pregnancy Category C: Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers: It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable amounts in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities NOT likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

Pediatric Use: Pediatric patients may demonstrate greater susceptibility to topical corticosteroid induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS: The following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence:

Burning	Hypertrichosis	Maceration of the skin
Itching	Acneiform eruptions	Secondary infection
Irritation	Hypopigmentation	Skin atrophy
Dryness	Perioral dermatitis	Striae
Folliculitis	Allergic contact dermatitis	Miliaria

OVERDOSAGE: Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects. (See PRECAUTIONS.)

DOSAGE AND ADMINISTRATION: Topical corticosteroids are generally applied to the affected area as a thin film three to four times daily depending on the severity of the condition. Occlusive dressings may be used for the management of psoriasis or recalcitrant conditions. If an infection develops, the use of occlusive dressings should be discontinued and appropriate antimicrobial therapy instituted.

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