

Aldactazide®

(spironolactone 25 mg/
hydrochlorothiazide 25 mg.)

WARNING

Spironolactone, an ingredient of Aldactazide, has been shown to be a tumorigen in chronic toxicity studies in rats (see *Warnings*). Aldactazide should be used only in those conditions described under *Indications*. Unnecessary use of this drug should be avoided.

Fixed-dose combination drugs are not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Indications: Cirrhosis of the liver accompanied by edema and/or ascites. Essential hypertension, edema of congestive heart failure and the nephrotic syndrome, when other measures are considered inappropriate.

Contraindications: Anuria, acute renal insufficiency, significant impairment of renal function, hyperkalemia or acute or severe hepatic failure. Allergy to thiazide diuretics or to other sulfonamide-derived drugs.

Warnings: Excessive potassium intake may cause hyperkalemia. Potassium supplements should not be given with Aldactazide. Do not administer concurrently with other potassium-sparing diuretics. Sulfonamide derivatives including thiazides have been reported to exacerbate or activate systemic lupus erythematosus.

Spironolactone has been shown to be a tumorigen in chronic toxicity studies in rats. In one study using 25, 75 and 250 times the usual daily human dose (2 mg./kg.) there was a statistically significant dose-related increase in benign adenomas of the thyroid and testes. In female rats there was a statistically significant increase in malignant mammary tumors at the mid-dose only. In male rats there was a dose-related increase in proliferative changes in the liver. At the highest dosage level (500 mg./kg.) the range of effects included hepatocytomegaly, hyperplastic nodules and hepatocellular carcinoma; the last was not statistically significant.

Precautions: Patients should be carefully evaluated for possible disturbances of fluid and electrolyte balance. Hyperkalemia may occur in patients with impaired renal function or excessive potassium intake and can cause cardiac irregularities which may be fatal. Hypokalemia may develop as a result of profound diuresis, particularly when Aldactazide is used concomitantly with loop diuretics, glucocorticoids or ACTH. Transient elevation of BUN may occur. Dilutional hyponatremia or rarely low-salt syndrome may develop. Gynecomastia may develop and in rare instances some breast enlargement may persist.

Thiazides may alter the metabolism of uric acid and carbohydrates with possible hyperuricemia, gout and decreased glucose tolerance. Vascular responsiveness to norepinephrine is reduced. Thiazides may also increase the responsiveness to tubocurarine. Thiazides may decrease serum PBI levels and prolonged therapy may induce hypercalcemia and hypophosphatemia.

Spironolactone may and hydrochlorothiazide does cross the placental barrier. Use in pregnant women requires that the anticipated benefit be weighed against possible hazards to the fetus. Breast feeding should be discontinued when Aldactazide is being used.

Adverse Reactions:

Associated with spironolactone: Gynecomastia is observed but infrequently. Gastrointestinal symptoms including cramping and diarrhea, drowsiness, lethargy, headache, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, ataxia, inability to achieve or maintain erection, irregular menses or amenorrhea, postmenopausal bleeding, hirsutism and deepening of the voice. Carcinoma of the breast has been reported but a cause-and-effect relationship has not been established.

Associated with thiazides: Gastrointestinal symptoms (anorexia, nausea, vomiting, diarrhea, abdominal cramps), purpura, thrombocytopenia, leukopenia, agranulocytosis, dermatologic symptoms (cutaneous eruptions, pruritus, erythema multiforme), paresthesia, acute pancreatitis, jaundice, dizziness, vertigo, headache, xanthopsia, photosensitivity, necrotizing angitis, aplastic anemia, orthostatic hypotension, muscle spasm, weakness and restlessness.

Adverse reactions are usually reversible upon discontinuation of Aldactazide.

Dosage and Administration

Edema in adults: The usual maintenance dose is one tablet four times daily but may range from one to eight tablets daily depending on the response to the initial titration.

Edema in children: The usual daily maintenance dose should be that which provides 0.75 to 1.5 mg. of spironolactone per pound of body weight (1.65 to 3.3 mg./kg.).

Essential hypertension: Usually two to four tablets daily depending on results of the titration of the individual ingredients.

SEARLE

Searle & Co.

San Juan, Puerto Rico 00936

Address medical inquiries to:

G. D. Searle & Co.

Medical Communications Department
Box 5110, Chicago, Illinois 60680

Letters to the Editor

The Journal welcomes Letters to the Editor; if found suitable, they will be published as space allows. Letters should be typed double-spaced, should not exceed 400 words, and are subject to abridgment and other editorial changes in accordance with journal style.



Foot Deformities in Children

To the Editor:

The area of foot deformities has long suffered not only from a cornucopia of confusing terminology, but also from a lack of rigorous, systematic examination which necessarily encompasses all of the lower extremities and not just the foot. If we borrow from behavioral science and invoke the technique of catastrophic expectations, ie, what is the worst that could happen should these conditions continue on untreated, we might find that the endpoints of neglect are poorly defined.

The portion of Dr. Paul's paper (*Paul GR: Common foot deformities in infancy and childhood. J Fam Pract 3:537, 1976*) dealing with metatarsus adductus highlights the use of stretching exercises as the initial step in the management of metatarsus adductus. This area is not referenced, and in searching the literature I was unable to find documentation of the efficacy of these maneuvers. Controversy regarding the use of corrective shoes and/or parental exercises exists, and a portion of the literature suggests that these methods are not only ineffective but possibly harmful.^{1,2} Further research revealed that there was no more documentation to this statement than to the efficacy of the modalities it eschews.

There is little controversy regarding the need for treatment of clubfoot. However, the lack of controlled longitudinal studies on the management of lesser conditions responsible for intoeing leaves an obvious vacuum. Indeed, intoeing may bestow on its owner an advantage as personified by Bob Hayes, professional football player and winner of an Olympic Gold Medal in sprinting.

My concern is for our role as family practitioners in dispelling the mythology which constantly complicates our relations with our patients. For this reason I question the use of stretching exercises in the treatment of metatarsus adductus. Reassurance and placebo may be indicated as balm to the worried parent, but the use of stretching exercise in the treatment of metatarsus adductus should be documented before it is further dignified in our literature.

William MacMillan Rodney, MD
University of California
Los Angeles

References

1. Connolly J, Regen E, Hillman JW: Pigeon-toes and flatfeet. *Pediatr Clin N Am* 17:291, 1970
2. Tachdjian MO: *Pediatric Orthopedics*, vol 2. Philadelphia, WB Saunders, 1972, pp 1331-1332

The preceding letter was referred to Dr. Paul who responds as follows:

Dr. Rodney raises two issues requiring specific comment. The first involves the treatment of metatarsus adductus. Standard orthopedic textbooks^{1,2} state that passive stretching exercises may be the definitive treatment for mild metatarsus adductus. If there is little fixed adduction deformity, which can be easily abducted with minimal resistance, then repeated abduction stretching exercises several times daily has proven to be effective definitive treatment. This assumes that the parents are trained well enough in the process to perform it; also, it requires adequate follow-up to see that the condition continues to improve. There is no controversy regarding such use of exercises. More emphatically, to state that stretching exercises are "not continued on page 18

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only ineffective but possibly harmful" is a misstatement. Shoes should be considered as holding devices, and not vises with which to gain reduction.

Stretching exercises should not, however, be considered as the initial treatment for severe metatarsus adductus. Indeed, serial plaster castings after manipulation of the forefoot into further and further abduction remains the initial, and usually the definitive, treatment for metatarsus adductus for any significant degree of fixed deformity.

A second area requiring comment is intoeing. Intoeing is caused by a myriad of conditions involving both foot or forefoot deformities but, more importantly, rotational abnormalities of the lower extremities, such as femoral anteversion or, less frequently, internal tibial torsion. Intoeing has been observed in sprinters and other athletes in whom speed is vital, and the intoeing has been ascribed as an important factor in the strong push-off responsible for their speed. This has not, however, been documented in any way. Regardless, intoeing of any significant degree produces a biomechanically uneconomical and cosmetically undesirable gait.

One cannot undertake the treatment of intoeing as an entity itself without understanding the many conditions producing it. Some conditions, such as the structural deformities in the foot, require active immediate treatment; whereas, most rotational deformities of the lower extremity producing intoeing spontaneously remodel with normal childhood development.

Lastly, to cite a person in the public eye (Bob Hayes) for an alleged deformity, without benefit of examination to determine the cause of the deformity, or even to determine if such deformity exists, and then to ascribe a benefit to it, gives support to the very issue Dr. Rodney purports to challenge in the opening sentence of his letter.

*G. Richard Paul, MD
University Hospital
Boston, Massachusetts*

References

1. Sage FP: Congenital anomalies. In Crenshaw AH (ed): Campbell's Operative Orthopedics ed 5. St. Louis, CV Mosby, 1971, p 1903
2. Tachdjian MO: Pediatric Orthopedics, vol 2. Philadelphia, WB Saunders, 1972, pp 1331-1332