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DIE BEHANDELING VAN *TRICHOMONAS VAGINALIS*

Elke geneesheer wat gedurende die afgelope aantal jare met die probleem van trichomonas-infeksie te doen gekry het, weet maar te goed hoe hardnekkig dit kan aanhou en hoe dit steeds weer by herhaling bly voorkom. Tot nog maar onlangs kon verligting slegs verkry word deur die herhaalde gebruik van vaginale spoelmiddels en steekpille. 'n Vroeëre middel wat per mond geneem kon word, het teleurstellende resultate opgelewer.

Die jongste middel (metronidasol — ‚flagyl') wat vir die behandeling van hierdie toestand beskikbaar is, skyn baie suksesvol te wees, en dit wil voorkom of die versigtige, vroeë aansprake oor die doelmatigheid van dié middel vir die behandeling van trichomonas-infeksie in albei geslagte, bevestig is. Vier gekombineerde Britse reekse het aangetoon dat 85% van 258 pasiënte, wat onder goed-gekontroleerde omstandighede behandel is, genees is, met 'n herhalingsyfer van 15%. Hierdie herhalingsyfer sluit in 4·6% van gevalle waar daar primêr geen respons op behandeling was nie, en 10·5% wat na skynbare genesing in die begin tog weer herhaal het. Al die pasiënte het die standaardkursus van 600 mg. daagliks vir 1 week ontvang, en is as genees beskou as hulle 3 maande lank vry van infeksie gebly het. Al die manlike pasiënte, soos blyk uit kleinere reekse, is genees na een kursus van behandeling.

Watt en Jennison[1] rapporteer dat net 1 van hulle 200 pasiënte nie in staat was om die standaarddosis te verdra nie. Dit was soms moeilik om genoegsame samewerking te verkry van die mans van vrouens by wie herhaalde aanvalle van infeksie voorgekom het. Hierdie ondersoekers het in 6·8% van hul gevalle 'n primêre mislukking van die behandeling gevind. As moontlike redes vir dié mislukking kan die volgende genoem word: die gebrek aan stamsensitiwiteit van die betrokke organisme, en ook gebrekkige absorbering van die middel in die gevalle van pasiënte wat wel die middel in die regte dosis geneem het. Die vlak van die middel in die serum het egter aangetoon dat gebrekkige absorbering nie 'n belangrike faktor by primêre mislukking van die behandeling was nie.

Laat herhalings van infeksie (19·8%) is waarskynlik die gevolg van reïnfeksie of van die voortbestaan van 'n ‚nes' van infeksie wat moontlik by die man voorkom. (Dit was die geval by 53% van die mans wat ondersoek is.) Dit is egter ook bewys dat die trichomonas organismes kan bly voortleef selfs op lewelose voorwerpe, en dit moet ook gemeld word dat 2% van die pasiënte ongetroude vroue was wat geen geslagsomgang gehad het nie.

Die gelyktydige behandeling van die mans het 87% van die gevalle van laat herhalings by die vroue genees, terwyl herhaalde behandeling van die vrou suksesvol was in 65% van gevalle. Wat plaaslike, kompliserende faktore betref, meen die skrywers[1] dat swangerskap en 'n onlangse verlossing (miskraam of voltydig) die respons mag beïnvloed. Ginekologiese abnormaliteite wat simptome veroorsaak en toevallig met die trichomonas-infeksie saamgeval het, het skynbaar geen uitwerking op die respons tot behandeling gehad nie.

Op grond van die bevindings lyk dit of dit nie nodig is om mans ook as 'n roetinemaatreël saam met die vrouens te behandel nie. Die behandeling van mans is egter nodig in gevalle waar daar 'n laat herhaling van die infeksie by vrouens is. Mans is oor die algemeen onwillig om hulle aan behandeling te onderwerp, en dié onwilligheid by mans, wat dikwels geen simptome toon nie, om 'n voorgeskrewe kursus van behandeling te volg, kan inderdaad 'n herhaling wees van die geskiedenis van die gebruik van die sulfonamides vir gonorree.

Ligte gastroïntestinale newe-uitwerkings het in 10% van gevalle voorgekom (slegte smaak in die mond, aangepakte tong, ens.), hoofpyn in 3·1% van gevalle, en daar was enkele, geïsoleerde gevalle van duiseligheid, bedruktheid, slaperigheid, opwinding, gejeuk van die vel, en 1 geval van huiduitslag wat egter spontaan opgeklaar het. By een pasiënt het 'n akute hervatting van haar psoriase voorgekom, en swangerskap het die mate waarin die middel verdra kon word nie beïnvloed nie.

Watt en Jennison besluit dat ‚metronidazole has so far proved non-toxic and has rendered obsolete the methods of treatment in most cases of trichomoniasis in the female'. Hulle sê dat daar nie bewyse is dat primêre weerstand voorkom nie, maar waarsku dat sulke weerstand teoreties moontlik is en dat dit tog dalk in die hand gewerk kan word deur ongenoegsame dosisse.

1. Watt, L. en Jennison, R. F. (1962): Brit. Med. J., **1**, 276.

COLCHICINE

The colchicum plant (the autumn crocus) has been known botanically and pharmacologically since early times. Its active constituent is the alkaloid colchicine. Extracts have been used in the treatment of acute gouty arthritis for about 1,500 years; today the alkaloid is used for this purpose. The alkaloid and related compounds also have important effects on cell division that are mainly of academic interest and importance.

The structure of colchicine, which consists of three rings, and its analogues and their effects on acute gouty arthritis, have been the subject of extensive studies. Certain analogues are effective, and others less potent, or ineffective, as regards antigout activity. Comparatively little is known about the metabolism of colchicine because of difficulties in measuring the content of the alkaloid in body fluids and tissues during the treatment of gout. Labelled colchicine extracted from the colchicum plant grown in an atmosphere containing radioactive carbon dioxide, has

been used in some studies. Less sensitive methods for determining colchicine have also been used, such as colorimetric determinations.

It may be stated that colchicine by mouth is absorbed in the gastro-intestinal tract, passes through the liver, and re-enters the intestine in the bile. Some is reabsorbed from the intestine. It disappears rapidly from the blood. Further studies on its metabolic fate in man and its mode of action in acute gout are needed. The mechanism of action in gout is poorly understood. Until the pathogenesis of the acute attack of gout is itself established, it is doubtful that any exact knowledge about the action of the drug will be obtained. When given in therapeutic doses it does not appear to have any significant effect on uric-acid metabolism nor on adrenal-cortex function. It exerts no significant influence on uric-acid excretion, it is not a uricosuric drug, and has no significant effect on the serum concentration or the miscible pool of uric acid. It seems unlikely that it influences gout through the 'pituitary-adrenal axis'. Colchicine has been shown to act in a variety of enzyme systems. It is possible that its potent action in gout may be related to this type of action. The drug also has a distinct action on the central nervous system. It is evident that there is a great deal to be learned about the clinical pharmacology of colchicine in gout.[1]

The antimitotic activity of colchicine has not been shown to be related to its antigout effects. Separation of these effects has been accomplished in an analogue of colchicine, trimethyl colchicinic acid, which is potent in gout and not antimitotic, except in very large doses. The typical effect of colchicine on cell division, namely arrest of cell division in the metaphase, is known as the Dustin effect.[2] The action is essentially on the achromatic substance of the cell, i.e. on the spindle fibres necessary for normal chromosome division; these fail to develop. There is disorganization of the orientation of the spindle micelles, most likely through breaking down of some chemical bond in or between the micelles. The chromosomes may show some changes, although they may remain intact; with high concentrations pyknosis of chromatin material occurs and the cell degenerates. The discovery of this action on cell division led to its investigation as a possible anti-neoplastic agent. Certain tumours are affected, but the therapeutic results in animals and man do not suggest that colchicine is of any significant value.

In acute gouty arthritis colchicine has both diagnostic and therapeutic value. No other acute arthritis responds to this agent. It should be given as soon as symptoms appear, since delay of even a few hours may increase the severity or prolong the duration of the acute episode. A significant number of patients may fail to respond to the drug. To some extent this may be due to delay in starting treatment. In recurrent acute gouty arthritis small doses given several times a week or daily exert a prophylactic effect.

Colchicine has toxicity in addition to the well-known gastro-intestinal effects. In sensitive subjects it may rarely produce leucopenia and depression of the bone marrow, loss of hair, damage to the nervous system, and death.

A tremendous amount of work has been done in attempts to elucidate the action of colchicine in acute gout, yet its use in this disease is still on an empirical basis.

1. Wallace, S. L. (1961): Amer. J. Med., **30**, 439.
2. Robson, J. M. and Keele, C. A. (1956): *Recent Advances in Pharmacology*. London: J. & A. Churchill Ltd.