SES02.4

260 therapeutic drug monitorings (TDM) in relation to compliance and co-medication in psychiatric treatment

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The issues of patient-compliance with prescribed medication and utility of a multitude of different drugs at the same time are always pertinent pharmacological problems in everyday clinical psychiatry. Estimates of non-compliance amounting to even a majority the patients prescribed psychoactive drugs are found in the literature. With a total pharmacopoea of perhaps several thousands of drugs being available for general clinical prescription and an average use of as much as 5.8 such drugs per patient in hospitalised psychiatric patients (data from Sweden 1997), the number of permutations possibilities for such co-medication therapies are outside the reach for any reasonable controlled trial design to investigate as a foundation for evidence-based medicine. Still, the everyday clinical problems of unknown non-compliance and drug-drug interactions lingers and can be envisaged to cause both a substantial number of situations with lack of treatment effect as well as unnecessary and even dangerous side-effects. How to cope with these problems?

Fortunately, the established tradition of frequently applying TDM-procedures in clinical psychopharmacology, not only in research but also in clinical practice has previously been shown useful to older psychoactive drugs. Here, the TDM-procedures were mainly based on potential toxicity of older drugs in higher concentrations and of concentration-effect relationships being established. Moreover, though, using TDM for older psychoactive drugs have simultaneously been found useful to detect non-compliance and uncover unknown drug-drug interactions in clinical practice. Accordingly, since newer clinical drugs in psychiatry are likely to also render non-compliance and drug-drug interaction problems, the use of development for TDM-procedures for the newer drugs and their rapidly expanding use during the past decade(s) in psychiatry seems highly rational. However, this has not been the case and for this reason the everlasting matter of non-compliance and drug-drug interactions in modern clinical psychopharmacology is a grossly neglected aspect of therapy. Hence, better focus on the non-compliance and drug-drug interaction scenario by developing and using TDM-procedures have a potential major impact to both treatment success-rates for patients, relative

SES02.5

The importance of drug metabolic pheno- and genotype in psychiatric co-medication issues

P. Baumann. *Switzerland*

No abstract was available at the time of printing.

IS01. Novel approaches to the patient with treatment-resistant depression

Chairs: M. Trimble (GB), T.E. Schlaepfer (CH)

IS01.1

Treatment-resistant depression

M. Trimble*. *Institute of Neurology, London, UK*

The presentation will begin with a discussion of the concept of resistant depression and its designation in standardised statistical diagnostic manuals. It will be noted that although our present classifications, that is ICD 10 and DSM IV contain reference to a group of patients with chronic and remitting disorder, the concept of resistant depression is rather poorly developed.

A definition of resistant depression from a clinical point of view will be attempted. The criteria will embrace both symptoms of depression, and the longitudinal course, embracing relapses and remissions.

Taking a model from epilepsy, it will be argued that patients with the chronic form of the disorder differ from those with acute non-recurrent episodes of depression, suggesting that the pathogenesis of the disorder is different.

There are several factors that might underlie the development of resistant depression, which will then be considered. These include:
genetic factors
the underlying personality
associated psychopathologies
associated neurobiologies

Factors likely to be associated with resistant depression will be delineated, and the impact of these on treatment outcome discussed. Personality variables and neurobiological problems seem the most important. The former leads to group of patients with a chronically melancholic lifestyle intertwined with recognisable personality disorders, the latter not only serving the ongoing depression but interfering with treatment for example though non-compliance and drug polytherapy with misuse.

The neurobiological variables include subtle cerebral damage, possibly longstanding, or in an elderly age group secondary to, for example, cerebrovascular disease. Evidence that patients with resistant depression reveal cerebral change on brain imaging, especially MRI will be reviewed.

Finally it will be concluded that patients with resistant depression, who probably have a differing psychosocioneurobiological underpinning to their disorder than other patients with depression, need differing treatment strategies, and fail to be adequately managed with conventional psychotropic drugs and psychotherapy.

IS01.2

Pharmacological approaches to resistant depression

P.J. Cowen*. *University Department of Psychiatry, Warneford Hospital, Oxford, UK*

Pharmacological approaches to the treatment of resistant depression consist of three main approaches: (1) increase the antidepressant dose (2) switch antidepressant (3) augment with another compound. It is worth noting that meta-analyses suggest that some pharmacologically less selective drugs such as amitriptyline and venlafaxine are slightly more effective than selective agents such as SSRIs. The most validated augmentation strategy is lithium addition. Tri-iodothyronine (T3) augmentation can also be used, but

https://doi.org/10.1016/S0924-9338(02)80014-1 Published online by Cambridge University Press

randomised trial data are not compelling and there are no controlled studies with newer anti-depressant agents such as SSRIs. There has been recent interest in the augmenting action of pindolol, because animal experimental studies suggest that certain β-adrenoceptor antagonists can enhance the effects of SSRIs on serotonin neurotransmission through 5-HT1A autoreceptor blockade. However, clinical data from controlled trials are not encouraging and PET imaging indicates that the dose of pindolol generally employed in SSRI augmentation studies (7.5mg daily) is probably insufficient to occupy human 5-HT1A receptors. Recently atypical antipsychotic drugs have been used as SSRI augmenting agents with olanzapine producing clinically useful effects in one small controlled trial.

IS01.3

An overview of the antidepressant properties of transcranial magnetic stimulation

T.E. Schlaepfer*, M. Kosel, C. Frick-Schröter, H.-U. Fisch. *University Hospital Bern, Department of Psychiatry, Psychiatric Neuroimaging Group, Switzerland*

The possibility of focal and noninvasive stimulation of the brain has been an appealing vision that for a couple of years seems to be realized: Repetitive Transcranial magnetic stimulation (rTMS) holds promise as a tool to study localization of function, connectivity of brain regions, and pathophysiology of neuro-psychiatric disorders. Transcranial magnetic stimulation involves placing an electromagnetic coil on the scalp. High-intensity cur-rent is rapidly turned on and off in the coil through the discharge of capacitors. This produces a time-varying magnetic field that lasts for about 100 to 200 microseconds. The magnetic field typically has a strength of about 2 Tesla (40 000 times the earth's magnetic field, or about the same intensity as the static magnetic field used in clinical magnetic resonance imaging).

This technique has been used in Neurology as an investigative tool for more than a decade, but as potential effects on mood have become apparent, interest has grown in its use in treatment and assessment of major depression. Since the technique is non-invasive and can be applied to a non-anesthetized patient it would be extremely promising as an antidepressant modality, since other methods of therapeutic brain stimulation such as electroconvulsive therapy (ECT) are much more invasive.

IS01.4

Vagus nerve stimulation: a potential new treatment for treatment resistant depression?

A. Zobel*, J. Wellmer, N. Freymann, W. Maier. *University of Bonn, Department of Psychiatry, Germany*

Because of the fact that up to 20 % of depressed patients do not respond to the currently available therapies, new treatment options are desirable.

Subjective observations from treatment of patients with epilepsy leaded to the idea that vagus nerv stimulation (VNS) has antidepressive effects. Although the basic mechanism of action of VNS is unknown, both clinical and animal studies indicate a mechanism that is likely to affect the same neurotransmitter systems that are thought to be involved in depression. Furthermore PET scan data showed modulations of cerebral blood flow in humans in key brain structures for depression. An american randomized open-label trial study with 30 patients confirmed these first suggestions and demonstrated a 40% response rate.

We now investigate the first treatment refractory depressed patients in Europe in an open label, non-randomized multi-center study. In addition to weekly psychopathometric ratings we investigate the reactivity of the HPA system using the combined dex/CRH test and the cerebral perfusion performing HMPAO-SPECTs after one and after four weeks of stimulation for monitoring neurobiological parameters of depression under VNS treatment. Preliminary data will be presented.

S01. Major European research networks on schizophrenia

Chairs: W. Gaebel (D), H.-J. Möller (D)

S01.1

The German Network Research on Schizophrenia

W. Gaebel*, W. Wölwer. *Department of Psychiatry, University of Düsseldorf, Germany*

The German Research Network On Schizophrenia is one of three psychiatric "Competence Networks" funded by the German Ministry of Education and Research in order to improve the horizontal and vertical collaboration between research institutions and the psychiatric care system. The schizophrenia network is organized, with respect to illness development, into two main "Project Networks" (PN), focussing primarily on the treatment and need for care in the prodromal phase preceeding the first episode (PN I), and after first hospitalization (PN II). In total, about 30 research projects aim at the improvement of early detection and intervention (PN I), or at the optimization of acute and long-term treatment, especially in first episode patients, including rehabilitation strategies, especially in patients with residual symptoms (PN II). Furthermore, there is a "Special Network" on molecular genetics, together with several more general projects on health economy, fighting stigma and discrimination, postgraduate training, quality assurance, and methodology. More than 20 psychiatric university departments, 14 state hospitals, six psychiatric and primary care networks, and further organizations like self-help associations of relatives collaborate in the network.

S01.2

The Swedish HUBIN Project on Schizophrenia

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The HUBIN (Human Brain Informatics) project is a national interdisciplinary collaborative effort to explore genetic and environmental mechanisms involved in the etiology and pathophysiology in Swedish patients with schizophrenia. Two different subject materials are used in this approach. The first is a case-control material of subjects from the Stockholm area. The second is a unique Swedish material of sib-pairs with schizophrenia. Standard electronic protocols are used to determine, (1) perinatal risk factors from birth records, (2) phenotypic characteristics of the disorder,

https://doi.org/10.1016/S0924-9338(02)80014-1 Published online by Cambridge University Press