Barbiturate Dependence: The Cycle of Tolerance and Withdrawal

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With regular use of barbiturates, barbiturate dependence develops. This in turn may lead to a need for increasing doses of the drug to get the original desired pharmacological or therapeutic effect. Barbiturate use can lead to both addiction and physical dependence, and as such they have a high potential for abuse. Psychological addiction to barbiturates can develop quickly. The GABAA receptor, one of barbiturates' main sites of action, is thought to play a pivotal role in the development of tolerance to and dependence on barbiturates, as well as the euphoric "high" that results from their abuse. The mechanism by which barbiturate tolerance develops is believed to be different than that of ethanol or benzodiazepines, even though these drugs have been shown to exhibit cross-tolerance with each other. The management of a physical dependence on barbiturates is stabilisation on the long-acting barbiturate phenobarbital followed by a gradual titration down of dose. The slowly eliminated phenobarbital lessens the severity of the withdrawal syndrome and reduces the chances of serious barbiturate withdrawal effects such as seizures. Antipsychotics are not recommended for barbiturate withdrawal (or other CNS depressant withdrawal states) especially clozapine, olanzapine or low potency phenothiazines e.g. chlorpromazine as they lower the seizure threshold and can worsen withdrawal effects; if used extreme caution is required.