

Is St. John's wort (SJW) an Evidenced Based Treatment-Alternative for Depressed Minors - Facts and Prescribing Trends in Germany

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The FDA Public Health Advisory of spring 2004 about side effects of antidepressant medication in adolescence emphasizes the need of pharmacotherapeutic alternatives to SSRI. In traditional medicine in Asia and, based on ecological movement, in Germany, herbal medicine is considered as a therapeutic alternative without side effects (Woolfe 2003). The best examined herbal medicine against mood disorder is St. John's wort (*Hypericum perforatum*, SJW). Its use is more common in Europe than in the USA (Beckmann et al. 2000). SJW seems to be often used without involving physicians in self-medication (Cala et al. 2003).

Data show that the use of SSRI is less common in Germany than e.g. in the USA or in the Netherlands (Kito et al. In prep.). A high rate of use of SJW could explain this difference. If there is a relevant prescription-rate of SJW by physicians this would mean that in Germany an alternative psychopharmacological treatment of mood disorders in childhood and adolescence is common.

This leads to questions about safety-data, labeling-aspects, rationales for indication and evidence based treatment of SJW.

We examined whether there is a relevant use, and especially a relevant off-label-use in minors of this drug prescribed by physicians.

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As a first step to investigate safety and effectiveness of SJW, we examined the prescribing patterns for outpatient children. We performed a retrospective analysis of 1.74 million prescriptions, written in January through March 1999 for 27% of all children aged 0 to 16 years in Baden-Wuerttemberg by 6886 practitioners of general, internal and pediatric medicine at the expense of the Allgemeine Ortskrankenkasse Baden-Wuerttemberg (a health-insurance). Prescriptions for St. John's wort were categorized in terms of their licence-status for age groups and Anatomical Therapeutic Chemical Classification groups.

DATE FOR REF (1999)	All age-groups 0-16y	% of prescriptions of antidepressants	Age-groups				
			0-11m	1y-2y	3-6y	7-11y	12-16y (total)
All prescriptions antidepressants	281	100,00%					
St. John's wort	268	59,35%	0	2	99	161	198
Compound preparation of St. John's wort	96	19,10%	0	0	10	30	55
Floxedine	11	3,88%	0	0	0	4	17

DATE FOR REF (1999)	All age-groups	% of all prescriptions in relation to prescription-day specific off-label-use	Age-groups				
			0-11m	1y-2y	3-6y	7-11y	12-16y (total)
off-label prescription antidepressants	276	36,31%	0	0	10	11	165
St. John's wort	267	35,87%	0	0	10	11	165
Compound preparation of St. John's wort	81	10,87%	0	0	10	11	55

RESULTS:

In the sample, 268 prescriptions of SJW and 96 prescriptions of compound preparations were found. Together these are over 50% (53,45%) of all prescriptions of antidepressant drugs in the age-group of 0-16 years.

Overall 54,9 % of the prescriptions of SJW and 26,0 % of compound preparations were off-label.

DISCUSSION

1) These prescribing-data show the relevance of SJW in physician initiated drug therapy of mood disorders in childhood. More over half of the prescribed drugs were preparations with SJW.

2) The data suggest a small but relevant off-label use of SJW in minors. Compound products may have more side effects than pure extracts of SJW. They are prescribed even for very young children.

RESULTS

SJW is a compound of various substances. The antidepressant activity of SJW seems to be performed by hyperforin and/or hypericin (Butterweck et al. 2001). There are effects on various brain receptors (e.g. GABA_A, 5HT₁ & 5HT₂). SJW interacts with Cytochrome-P450 and other enzymes; interactions with many other drugs (esp. changes of plasma-levels) has been described (Merkowitz et al. 2003). Gastroenterological problems and dermatological reactions (increases sensitivity to sunlight) are the most common side-effects (Kasper 2001).

Data about efficacy and benefits of treatment with St. John's wort are very inhomogeneous. Data from trials conducted in USA and Europe, especially in Germany, differ. While trials in USA report about no or less effects of SJW (e.g. Hypericum Depression Trial Study Group 2002), findings in Germany recognize effects for the treatment with SJW in mild or moderate depression. Reports sign ineffectiveness by preparations with low doses of SJW (Kasper 2001).

As we can recognize only one study reported about effectiveness of SJW in mild depression in childhood (Huebner et al. 2001). Further studies conducted with minors about effectiveness and safety of SJW can not be found (see also Kasper 2001).

Preparations of SJW are labelled in Germany for children 12 years and older. By the fact, that SJW is a pharmacological active substance interacting with other drugs and causing side-effects there should be clear therapeutic rationales for a drug therapy. Data about effects, side-effects and long-term safety for SJW in treatment of minors should be generated.

