CONCORDANCE OF MANAGEMENT OF GOUT IN FRANCE WITH THE 2006 EULAR RECOMMENDATIONS. THE GOSPEL 1000 STUDY.

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- **As reported in the UK and Germany, treatment of acute and chronic gout in France is suboptimal and only partly concordant with EULAR recommendations.**
- **Primary and postgraduate medical education of physicians should be enforced for appropriate gout management.**
- **Implementation of current EULAR recommendations has to be improved.**
- **Due to additional acquired data related to gout disease since 2006 (vitamin C, sugared sodas, etc.) updating EULAR recommendations would result in further improvement in gout management.**

INTRODUCTION

Gout is the most frequent intermittent inflammatory arthritis in adults. Currently its prevalence is increasing both in Western and emerging countries. Several mechanisms are involved: ageing, use of drugs such as diuretics, lifestyle including diet, in association with uric acid handling renal dysfunction of genetic origin.

In 2006, a dedicated EULAR task force validated and published recommendations for the gout diagnosis [1] and management [2]. Significant management deviations were recently observed in 3 EU countries (UK, Germany, Ireland) and EULAR recommendations (EULARr) appeared to be not sufficiently implemented.

In France, these recommendations have been issued through few CME actions (articles in general practice and rheumatology journals / local and national meetings).

AIM OF THE STUDY

To describe and compare current procedures and knowledge of gout management in France with the 2006 EULAR recommendations.

METHODS

National prospective and transversal epidemiological study of current management on a population of gouty patients (pts) referred to GPs and PRs.

Physicians

Random selection from a national data base used for observational studies (representative geographic survey). 398 GPs and 109 PRs included 2 pts each between October 2008 and September 2009.

Patients

Inclusion criteria: outpatients > 18 y/o, after informed consent, with known gout or with inflammatory arthritis diagnosed as gout by their GP or PR.

Non inclusion criteria: impossibility to fill self-administered questionnaires (SAQ).

Methods

Case report forms (CRF) and SAQ filled in respectively by GP/PR and pts were used to identify adverse lifestyle, associated co-morbidities (CM) and risk factors (RF) and to assess pts education, CM/RF management and implementation of lifestyle modification. Physical examination [BMI, BP, waist circumference], metabolic syndrome/[FID criteria], recent (<1yr) available blood results [serum uric acid (SUA), lipids, fast blood glucose, HbA1c, creatinine and calculated clearance], and current medications were recorded.

As a marker for management, drug changes, any biological or imaging tests prescribed by the end of the visit were recorded.

Pts filled in a SAQ, including a lifestyle questionnaire, personal physician advices, and a quality of life assessment.

Non pharmacological and pharmacological management were compared to the EULARr proposals 2, 3, 4, 5, 7, 8, 9, 10, 11 & 12.

Statistical methods

Descriptive statistics provided quantitative and qualitative variables.

Results

1009 patients were included but 1003 (810 from GPs and 193 from PRs) **were analysed** (6 major deviations)

DEMOGRAPHICS AND PATIENTS' CHARACTERISTICS

879 males (88%) and 124 females (12%)

Males: mean age 61.6±11.0 years, with 13.3% over 75 years

Females: mean age 70.2±11.9 years, with 42.0% over 75 years

BMI (kg/m²)

Total population:	28.4±4.1	Normal weight (BMI<25):	19.8%
Male population:	28.4±3.8	Overweight (BMI :[25-30[):	51.5%
Female population:	28.2±5.7	Obesity (BMI>30):	28.7%

Mean age at diagnosis of hyperuricemia: 54.4 ±12.9 yrs

Mean age at diagnosis of gout: 54.5 ±12.9

Duration of hyperuricemia: 8.2±8.4 yrs

Duration of gout: Total population: 8.0±8.3 yrs
Population followed by GP: 7.9±8.1 yrs
Population followed by PR: 8.6±9.2 yrs

Patient condition at study entry

With gout attack: 48.6% (487/1003 pts : 427 with GPs, 60 with PRs)

Mean number of previous gout attacks/yr:
1.9±1.5 total population; 1.8±1.4 GP population; 2.4±2.0 PR population

Diagnostic criteria

Diagnosis of gout was based on physician criteria at study entry
Confirmed diagnosis: 857 Pts (87.3%)
Suspected diagnosis: 125 Pts (12.7%)
ACR criteria were present in 85.2% of patients

ACR criteria

> 6/11 or MSU crystals)	GP N	GP %	PR N	PR %	Total N	Total %
Yes	707	87.3	148	76.7	855	85.2
No	103	12.7	45	23.3	148	14.8

Co-morbidities

	GP N	GP %	PR N	PR %	Total N	Total %
Hypertension	443	55.0	100	52.1	543	54.5
Coronary Heart Disease	71	8.9	16	8.4	87	8.8
CerebroVascular Accident	28	3.5	3	1.6	31	3.1
Diabetes mellitus	129	16.1	19	10.0	148	14.9
Dyslipidemia	402	50.1	66	34.7	468	47.2
Metabolic syndrome	392	51.9	48	27.0	440	47.2
Renal impairment (RI) (reported by physician)	32	4.0	19	10.0	51	5.2
RI (n=697) according to creatinine clearance					300	43

Relationship consistency between RI reported by physicians and creatinine clearance

Creatinine clearance	RI identified by physicians N	RI identified by physicians %	RI not identified N	RI not identified %	Total N	Total %
< 15 ml/mn: terminal	1	2.0	-	-	1	0.1
[15 - 30[severe	8	16.0	1	0.2	9	1.3
[30 - 60[moderate	35	70.0	90	14.0	125	18.1
[60 - 80[mild	4	8.0	158	24.6	162	23.4
≥ 80 ml/mn	2	4.0	392	61.2	394	57.0

EULAR AND CURRENT GOUT MANAGEMENT IN FRENCH PATIENTS

***Proposal 2:** « Patient education and appropriate lifestyle advice regarding weight loss if obese, diet, and reduced alcohol (especially beer) are core aspects of management.»*

Obesity (BMI> 30) was present in 286 pts (28.7%). Overweight (BMI: [25-30[) and obesity were only mentioned by physicians in 5.9%.

Increased calories intake was identified in 27.2%.

Advices for diet modifications were proposed to 149/286 (56%) of obese pts and to 22.6% of the whole population.

High beer intake (n=56 pts) and **high alcohol intake** [>21 U/wk for men (52.4%), and 14 U/wk for women (22.8%)] were reported by GP/PRs in **7%** and **49%** of patients, respectively.

Advices for alcohol consumption reduction were only offered to 12.6% of pts.

Physical activity was recommended in 54 pts **(6.0%)** (39 : GPs/15 : PRs)

***Proposal 3:** « Associated comorbidity (CM) and risk factors such as hyperlipidaemia, hypertension, hyperglycaemia, obesity and smoking should be addressed as an important part of the management of gout. »*

Cardiovascular CM were present in 693 pts (71.3%). Treatment was already appropriate or given in 87.2% of these pts, with differences between GP **(89%)** and PR **(78.7%)** practices.

Metabolic syndrome was present in 46.0% males and 55.8% females.

Management of co-morbidities (2006 EULAR proposal 3)

	GP N	GP %	PR N	PR %	Total N	Total %
DYSLIPIDEMIA						
No	400	50.6	124	65.6	524	53.5
Yes without drug treatment	39	4.9	19	10.1	58	5.9
Yes with drug treatment	352	44.5	46	24.3	398	40.6
DIABETES						
No	672	83.9	171	90.0	843	85.1
Yes without drug treatment	19	2.4	5	2.6	24	2.4
Yes with drug treatment	110	13.7	14	7.4	124	12.5
HYPERTENSION						
No	362	45.2	92	48.4	454	45.8
Yes without drug treatment	5	0.6	4	2.1	9	0.9
Yes with drug treatment	434	54.2	94	49.5	528	53.3
OVERALL MANAGEMENT						
No co-morbidity	217	27.7	62	32.8	279	28.7
All co-morbidities treated	504	64.4	100	52.9	604	62.1
At least one co-morbidity treated	62	7.9	27	14.3	89	9.2

***Proposals 4 & 5:** « Oral colchicine and/or NSAIDs are first line agents for systemic treatment of acute gout. In the absence of contraindications an NSAID is a convenient and well accepted option ». « High doses of colchicine lead to side effects, and low doses (for example 0.5 mg three times daily) may be sufficient for some patients with acute gout » .*

In France, for the treatment of gout attack, Colchicine C is widely used and recommended at a maximal dose of 3mg on the first day.

National regulatory agency (AFSSAPS) has issued recommendations for dosage adjustment according to creatinine clearance.

Usual reported treatment for attacks are : C = 72.3%, NSAIDs = 4.3%, or combination = 22.4%.

At day 1, total colchicine dose was 3mg for 86.1% pts (89.2% GP; 71.7 PR) and > 3mg for 3.9% of pts only.

In pts with creatinine clearance < 60ml/mn, the colchicine 3mg dose regimen at day 1 was applied in 93.6% (103/110) (GP: 88/91 pts; PR: 15/19 pts) and **NSAIDs** were proposed to 17.3% of pts (21/118) (GP: 17/98; PR: 4/20)

Treatment for acute gout attacks

Colchicine: initial dosage at day 1	GP N	GP %	PR N	PR %	Total N	Total %
1mg	21	3.0	18	11.8	39	4.5
2mg	28	3.9	19	12.5	47	5.4
3mg	**634**	**89.2**	**109**	**71.7**	**743**	**86.1**
4mg	22	3.1	6	3.9	28	3.2
6mg	6	0.8	-	-	6	0.7

Colchicine: initial dosage at day 1 adjusted to creatinine clearance	<60 ml/mn N	<60 ml/mn %	≥ 60 ml/mn N	≥ 60 ml/mn %
General practitioners				
1mg	2	2.2	12	2.9
2mg	2	2.2	13	3.1
3mg	83	92.2	374	89.3
4mg	1	1.1	18	4.3
6mg	2	2.2	2	0.5
Rheumatologists				
1mg	2	10.5	9	12.9
2mg	2	10.5	8	11.4
3mg	13	68.4	51	72.9
4mg	2	10.5	2	2.9

***Proposal 7:** « Urate lowering therapy is indicated in patients with recurrent acute attacks, arthropathy, tophi, or radiographic changes of gout. »*

According to EULARr, **severe gout** was present in **81.1%** (n=805) of pts. **Allopurinol**, as a first choice urate lowering therapy (ULT), **was prescribed in 77.5%** (616/791) of these pts. Only 2/3 of pts were given ULT. ULT combination was prescribed in 21 pts (EULAR #10). 19.3% (GP) and 13.1% (PR) of pts with severe gout were never prescribed ULT.

Indication for ULT and current or prescribed treatment at study entry

A. Patients with at least one reason for ULT (N> 3 attacks or tophus or chronic arthropathy or X-rays changes)	GP N	GP %	PR N	PR %	Total N	Total %
YES	**647**	**80.9**	**158**	**81.9**	**805**	**81.1**
NO	153	19.1	35	18.1	188	18.9
B. Correlation of ULT prescription to proper indication according to EULAR recommendations						
Indicated-prescribed	484	62.0	132	72.1	616	63.9
Indicated – not prescribed	151	19.3	24	13.1	175	18.2
Not indicated – administered	95	12.2	15	8.2	110	11.4
Non indicated – not prescribed	51	6.5	12	6.6	63	6.5

***Proposal 8:** "The therapeutic goal of urate lowering therapy is to promote crystal dissolution and prevent crystal formation. This is achieved by maintaining the serum uric acid below the saturation point for monosodium urate (≤360 µmol/l or ≤6 mg/dl)."*

Recent (<1 year) SUA level was only available in 77.5% CRF (GP=76.0%; PR=83.8%). **Current and sustained target level (SUA<360 µmol/l, 6.0 mg/dl) was only achieved in 32.7% and 41.5% of patients followed by GPs and PRs, respectively.**

***Proposal 9:** « Allopurinol is an appropriate long term urate lowering therapy. It should be started at a low dose (100 mg daily) and increased by 100 mg every two to four weeks if required. The dose must be adjusted in patients with renal impairment. If allopurinol toxicity occurs, options include other xanthine oxidase inhibitors, a uricosuric agent, or allopurinol desensitisation (the latter only in cases of mild rash). »*

These are **key quality indicators. Allopurinol** was the main ULT used at time of the study as **first line ULT.** New prescriptions were available in 44 pts.

- **Initial ULT dosage was not appropriate** with initial dosing >100mg/d in **58.1% GP pts and 53.9% PR pts.**
- **Creatinine clearance**, needed for allopurinol optimal dosage determination, **was available in 2/3 of pts** followed by GPs and **in all pts** followed by PRs.

***Proposal 10:** « Uricosuric agents such as probenecid and sulphinpyrazone (not available in France) can be used as an alternative to allopurinol in patients with normal renal function but are relatively contraindicated in patients with urolithiasis. Benzbromarone can be used in patients with mild to moderate renal insufficiency on a named patient basis but carries a small risk of hepatotoxicity. »*

Probenecid was given to 31 pts (23 in GP and 8 in PR):

- Combination was prescribed with allopurinol in 25 pts (GPs, n=17 pts; PRs, n=8 pts).
- Switch from allopurinol to probenecid in 8 pts
- First ULT drug was probenecid in 6 pts by GPs, none by PRs.

Benzbromarone was not given in this series.

***Proposal 11:** « Prophylaxis against acute attacks during the first months of urate lowering therapy can be achieved by colchicine (0.5 to 1 mg daily) and/or an NSAID (with gastro-protection if indicated). »*

Prevention with colchicine was recorded only in 38% of GP pts and in 100% of PR pts starting allopurinol (n=40, 4 missing data).

Duration of prophylaxis was not appropriate according to EULARr:

- GP pts = 7.7±4.7 weeks (range 4.3-12.9 weeks)
- PR pts = 11.2±7.8 weeks (1.4-25.7 weeks).

***Proposal 12:** « When gout associates with diuretic therapy, stop the diuretic if possible. For hypertension and hyperlipidaemia consider the use of losartan and fenofibrate, respectively (both have modest uricosuric effects). »*

Diuretic agents were prescribed in 220 pts, whom 195 pts had hypertension and 25 had chronic heart failure.

Diuretic use was identified as risk factor only in 62/220 pts (6.7% GP pts, and 6.1% PR pts).

Diuretics for hypertension were only discontinued by GPs in 7/194 pts (3.6%, 1 missing data), but not by PRs.

DISCUSSION

1. The GOSPEL study is the first community study on gouty patients in France, with specific emphasis on general practice, describing management by GPs and PRs. This series also shows the potential severity of the disease, including more than 80 % of patients with ULT and 20% with tophi.
2. It shows also the high prevalence of comorbidities since more than 50% of pts had metabolic syndrome. Hypertension was more frequent in French gouty pts than in the UK or Germany.
3. There is clearly a place for management improvement through lifestyle modification advices, adaptation of drugs to renal function, discontinuation of diuretics, and regular monitoring of SUA and creatinine levels.

References

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