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Psoriatic Patients at the Department of Dermatology at Kuopio University Hospital: A Retrospective Statistical Study of Treatments during 2001–2022

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Abstract

Psoriasis is a diverse and chronic skin disease. Decades ago, psoriasis was largely treated with topical treatments and UVB/PUVA-phototherapies alongside traditional drugs. These treatments are still being used, but nowadays there are also newer medication options available.

This is a retrospective study regarding the medication of psoriatic patients in the Dermatology Clinic at Kuopio University Hospital. The patients were 2–100 years of age. The material of the study included 560 psoriasis patients' treatment information between years 2001 and 2022. All patients used topical treatment alone or combined with various systemic medication.

For most patients, only topicals or first-line medications were used, but one patient had even 13 different medications. About half of the patients had used one or more first-generation medication (acitretin, methotrexate or cyclosporin). Five over 60-year-old patients had used efalizumab which is now discontinued due to severe side effects previously experienced abroad. 8.9 % of patients had used apremilast. TNF-alfa-inhibitors, including biosimilars, had used 16.1 % of patients and these were statistically used more in men. 19.6 % of patients had used newer interleukin inhibitors as biologics.

The use of medications in psoriasis has depended on what medications have been available and how they have been accessible regarding to financial reimbursement policy. With the development of medications, there has been a shift towards apremilast and especially to biologics, which are significantly more effective and have fewer and more manageable side effects.

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1. Introduction

Psoriasis is a diverse and chronic inflammatory skin disease with multifactorial aetiology of genetics and inflammatory processes existing world-wide. Also, external factors, like environment, trauma, stress, and infections are known to provoke the exacerbation of psoriasis [1,2].

Decades ago, psoriasis was largely treated with topical treatments and UVB/PUVA-phototherapies alongside traditional drugs, e.g., acitretin, methotrexate and cyclosporin. These treatments are still being used, but nowadays there are also newer medication options available as oral, like apremilast, and very effective biologics as TNF-alfa and numerous interleukin inhibitors.

2. Aim of the study

A retrospective statistical study was performed for psoriatic patients obtained from electronic patient files during 2001 to 2022, to evaluate treatments used with a special reference to age and sex.

3. Methods

A total of 580 patients were collected by search of ICD-10 code of L40.* (whether main or side diagnosis to find all patients) from the electronic patients' files during 2001 to 2022 in the Kuopio University Hospital. The misdiagnosis and typo error filings were excluded, as well as patients with only L40.3 palmoplantar pustulosis without other forms of psoriasis, thus, 560 patients were included in this retrospective study. Their all-time patient histories were recorded. The same patients had often used numerous medications during course of their disease, some even multiple parallel medications. The electronic diagnosis-based search for patients was conducted during Dec 1, 2017, to March 31, 2020.

For safety and anonymity in the data processing, the patients' data were loaded into an Excel table file only by sex, birth year and medications used. The possible concomitant medications for other diseases (like diabetes, blood pressure, etc.) were not recorded. The data material was analyzed by IBM SPSS-program version 26.0. The age groups were established by year 2019 as starting point to calculate the age from the birth year. There might be some small shift to different age groups into both directions, but likely does not play a marked role for the results in statistical analysis. Numeric variables were expressed as means or medians with ranges and categorical variables as frequencies and ranges. Numeric variables were compared by Mann Whitney U-test and categorical variables by Chi-Square test. P-values <0.05 were considered as statistically significant.

The study was approved by the Ethical Committee from the Kuopio University Hospital.

4. Results

The mean age of 560 patients in this study was 54.8 years (range 2–100 years), 256 females and 304 males. The biggest age group was 60–69-year-old patients, and the smallest ≤17-year-old and ≥80-year-old patients and (Table 1, 2). Table 2 shows the number of different medications in age groups. The highest number of different medications was 10 in females, and 13 in males (Table 3).

Table 1: Number of patients by age groups and sex.

Age group / years	≤17	18-29	30-39	40-49	50-59	60-69	70-79	≥80
Total (N=560)	25	31	56	76	116	144	86	26
Total males	12	17	31	47	68	75	40	14
Total females	13	14	25	29	48	69	46	12

Table 2: Number of medications used by age groups.

Age group / years	**≤17**	**18–29**	**30–39**	**40–49**	**50–59**	**60–69**	**70–79**	**≥80**
Number of medications								
0	23	17	24	35	42	49	42	8
1	0	0	14	7	24	27	13	7
2	1	6	3	6	14	23	11	6
3	1	3	5	7	9	16	6	2
4	0	2	5	10	6	7	8	0
5	0	0	3	4	7	12	1	1
6	0	1	1	3	9	7	3	2
7	0	0	1	1	3	1	1	0
8	0	2	0	1	0	1	0	0
9	0	0	0	1	1	1	0	0
10	0	0	0	1	0	0	1	0
11	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0
13	0	0	0	0	1	0	0	0
Total	25	31	56	76	116	144	86	26
Medication number zero means topical treatments, including phototherapies.								

Table 3: Number of medications by sex.

Number of medication used	**Females N=256**	**Males N=304**
0	115	125
1	53	39
2	27	43
3	17	32
4	10	28
5	17	11
6	10	16
7	2	5
8	1	3
9	2	1
10	2	0
11	0	0
12	0	0
13	0	1
Medication number zero means topical treatments, including phototherapies.		

In this retrospective study, diagnosis of psoriasis arthropathica with simultaneous skin psoriasis was set for 67 patients (12.0 %), having one or more medications commonly used in the rheumatology (leflunomide, hydroxychloroquine, azathioprine, mesalazine, sulfasalazine, golimumab). A few patients had used a Phase-III investigational drug briakinumab, that did not come to the market, thus it was omitted from further evaluations.

Some medications used in the past were excluded from analysis when not used anymore in Finland, such as gold-based auranofin (Ridaura) and sodium aurothiomalate (Myocrisin). In addition, for group analysis, mesalazine was combined with sulfasalazine and golimumab as used mainly by a rheumatologist. Medications used by the patients in the present retrospective study being possible useable medications in the future did not contain dimethylfumarate, and biologic medications certolizumab pegol, bimekizumab and tildrakizumab, since those were not available at the time for patients due to lack of reimbursement policy.

The first-generation medication (acitretin, methotrexate, cyclosporin) was used by majority of patients (307 patients, 54.8 %). Table 4 shows the number of patients by age group and sex with topical treatments, acitretin, methotrexate, and cyclosporine. The young age of ≤17-year old used only topical treatments instead of these conventional medications. Acitretin was seldom used in men up to 29-yeasrs of age, and females up to 29-years of age due to teratogenicity. Cyclosporin was not often used in any age group. Patients of ≥80 years, used oral conventional treatments rather seldom.

Table 4: Number of patients by age groups and sex with topical treatments, acitretin, MTX and CsA.

Age group / years	≤17	18-29	30-39	40-49	50-59	60-69	70-79	≥80
Total topical only	23 (92%)	17 (55%)	24 (43%)	35 (46%)	42 (36%)	49 (34%)	42 (49%)	8 (31%)
Topical only males	10	9	13	20	19	25	24	4
Topical only females	13	8	11	15	23	24	18	4
Total acitretin	0 (0%)	4 (13%)	14 (25%)	22 (29%)	39 (34%)	68 (47%)	30 (35%)	14 (54%)
acitretin males	0	3	13	16	29	37	12	7
acitretin females	0	1	1	6	10	31	18	7
Total MTX	0 (0%)	14 (45%)	23 (41%)	35 (46%)	63 (54%)	71 (49%)	32 (37%)	10 (38%)
MTX males	0	8	11	22	41	35	11	6
MTX females	0	6	12	13	22	26	21	4
Total CsA	0 (0%)	5 (16%)	7 (13%)	14 (18%)	17 (15%)	24 (17%)	9 (10%)	5 (19%)
CsA males	0	3	2	8	11	13	1	5
CsA females	0	2	5	6	6	11	8	0

MTX, metotrexate, CsA, cyclosporin

Topical treatments include emollients, Class I-IV steroids, calcineurin inhibitors and phototherapies. Data from phototherapies (SUP, UVB, PUVA, climate) was not available due to administrative re-strictions by the present Data Protection Law.

Percentages of patients in each age group are of total number of patients in the same age group.

The same patients may have used one or more of these conventional oral psoriasis drugs.
In this study, youngest females treated with acitretin, MTX, or CsA were at ages of 28, 20, and 22, respectively, whereas youngest males were at ages of 23, 22 and 18, resapectively.

Table 5 Shows the Number of Different Medications Used by Patients. Because the Same Patients Had Used Up To 13 Different Drugs for Treatment of Psoriasis, Thus the Total Number Exceeds the Patient Number.

Table 5: Number of patients using certain medications at any time point during the course of treatment of psoriasis.

	Medication	**Number of patients using a specific medication**
1st generation	Neotigason, acitretin	191
	Trexan, methotrexate	240
	Sandimmun Neoral, cyclosporin	82
Medications used in rheumatology	Arava, leflunomide	20
	Oxiklorin, hydroxychloroquine	13
	Asacol, mesalazine Salazopyrin, sulfasalazine Simponi, golimumab	53
	Azamun, azathioprine	13
PDE-4-blocker	Otezla, apremilast	50
T-cell blocker	Raptiva, efalizumab	5
TNF-alfa-blockers	Remicade, infliximab	28
	Enbrel, etanercept	27
	Humira, adalimumab	71
IL-12/23-blockers	Stelara, ustekinumab	23
IL-23-blockers	Tremfya, guselkumab	32
	Skyrizi, risankizumab	23
IL-17-blockers	Taltz, ixekizumab	51
	Kyntheum, brodalumab	4
	Cosentyx, secukinumab	42
When available, biosimilars are included in the calculations of appropriate medications.		

For group analysis, artificial treatment groups were established, as in Table 6. Apremilast was used by 50 patients (8.9 %). TNF-alfa blockers, including their biosimilars, were used by 90 patients (16.1 %). Newer biologic medications, i.e., IL-17-, IL-12/23 ja IL-23 blockers, were used by 110 patients (19.6 %), of which IL-12/23 blocker ustekinumab only 23 patients (4.1 %). IL-23 blocker guselkumab and/or risankizumab was used by 49 patients (8.8 %). Any of IL-17 blockers was used by 80 patients (14.3 %) (Table 6).

Table 6: The use of medication in group analysis. Only topical treatments in Group 1, Other groups contain medications based on mechanism of action.

Group	Number of patients	Portion (%) Nmax =560
1) topical treatments only	240	42.9
2) acitretin, metotrexate, cyclosporine	307	54.8
3) medications used mainly in rheumatology: leflunomide, hydroxychloroquine, mesalazine azathioprine	67	12.0
4) apremilast	50	8.9
5) efalizumab	5	0.9
6) infliximab, adalimumab, etanercept	90	16.1
7) secukinumab, ustekinumab, guselkumab, ixekizumab, brodalumab, risankizumab	110	19.6
8) risankizumab, guselkumab	49	8.8
9) ixekizumab, brodalumab, secukinumab	80	14.3
10) ustekinumab	23	4.1
Total number of treatments go over the number of 560 patients and also the percentage over 100% since the same patients are in different groups.		

A statistically significant relation was found between age groups and medications Groups 2, 5, 8 and 9 (Table 7). At age Group of ≤ 17-years, the patients made only 8% in Group 2 medications. In older age groups, Group 2 medications were used by 45.2% - 65,4% of patients. Young patients use these 1st generation medications considerably seldom as compared to older patients. This is likely expected since the disease has seldom proceeded to a severe disease needing a systemic treatment.

Table 7: Portion of used medication by patients (%) / age groups.

	Group 2 1st Generation medication	Group 5 T-cell blockers	Group 8 IL-23-blockers	Group 9 IL-17-blockers
Portion of used medication by patients (%) / age group				
Age group				
≤ 17	8.0	0	0	4.0
18–29	45.2	0	6.5	22.6
30–39	55.4	0	0	8.9
40–49	48.7	0	19.7	18.4
50–59	62.1	0	6.9	18.1
60–69	63.9	1.4	10.4	17.4
70–79	48.8	1.2	7.0	8.1
≥80	65.4	7.7	11.5	0
p-value	<0,001	0,019	0,004	0,027
p-value as compared for age group ≤ 17 years. 1st generation meditation includes methotrexate, acitretin and cyclosporin.				

Table 7 shows that T-cell blocker efalizumab (Raptiva) was used statistically significantly by patients of over 60 years old patients. Efalizumab was used in 2005–2008 only in 5 patients being 48–75 years of age at that time. Use of efalizumab was ceased in 2009 due to serious adverse events in the USA.

Group 8 medications, i.e., the use of IL-23 blockers became more frequent in older ager groups. At less than 39 years, the use was between 0 % to 6.5 %, whereas at age group over 40 years, their portion was between 6.9 % to 19.7 %, being significantly more frequent (p=0.004).

Group 9 medications, i.e., the use of IL-17 blockers was more frequent at age of less than 70 years between 4.0 % to 22.6 %, whereas at age of over 70 years, their portion was between 0 % - 8.1 % being markedly less frequent (Table 7).

In the Group 6 (i.e., TNF-alfa blockers), males had used statistically significantly more often medication as compared to females, 19.1 % vs 12.5%, p=0.035. No correlation was found between other Groups and sex. There was a statistically significant difference (Table 7) between age groups in Medication Groups 2, 5, 8 ja 9, but not in others (data not shown).

Table 8 shows the number of medications used by patient divided by sex. There was a statistically significant predominance for men by use of acitretin and azathioprine.

Table 8: The use of medication in group analysis. Only topical treatments in Group 1, Other groups contain medications based on mechanism of action.

Group	Number of patients	Females vs Males	p-value
1) topical treatments	240	115 vs. 125	0.365
2) acitretin, methotrexate, cyclosporine	(307)	74 vs. 117 115 vs. 135 38 vs. 44	0.017 0.419 0.902
3) in rheumatology: leflunomide, hydroxychloroquine, mesalazine azathioprine	(67)	12 vs. 8 8 vs. 5 19 vs. 34 1 vs. 12	0.192 0.247 0.130 0.005
4) apremilast	50	18 vs. 32	0.148
5) efalizumab	5	1 vs. 4	0.246
6) infliximab, adalimumab, etanercept	(90)	13 vs. 15 26 vs. 45 13 vs. 14	0.938 0.100 0.795
7) secukinumab, ustekinumab, guselkumab, ixekizumab, brodalumab, risankizumab	(110)	18 vs. 24 12 vs. 11 14 vs. 18 21 vs. 30 2 vs. 2 8 vs. 15	0.699 0.525 0.818 0.495 0.863 0.283
8) risankizumab, guselkumab	49		
9) ixekizumab, brodalumab, secukinumab	80		
10) ustekinumab	23		
Total number goes over 560 and percentage go over 100% since the same patients are in different groups.			

Table 9 presents the number of medications used by each patient in the whole patient group. The average of number of medications is 1.73 when also zero-medication patients are included, and the average is 3.03 if only "true" medication users are counted. The range was 1-13, and median 3.69. Most of the patients (N=240, 42.9%) used only topical treatments. A few patients had used simultaneously more than one medication at the same time (data not shown).

Table 9: Number of different medications used by patients.

Number of medication used	Number of patients (N=560)	Portion % (N = 560)
0	240	42.9
1	92	16.4
2	70	12.5
3	49	8.8
4	38	6.8
5	28	5.0
6	26	4.6
7	7	1.3
8	4	0.7
9	3	0.5
10	2	0.4
11	0	0
12	0	0
13	1	0.2
Zero medication contains topical treatments only (including photo therapies).		

5. Discussion

This retrospective study consists of patient entered to the Kuopio University Hospital by referral from specialists but also from general practice doctors, for evaluation of treatments needed for patients. Many patients N=240, 42.9%, F=115, M=125) still were evaluated to cope with topical treatments. The classical first-generation medication (acitretin, methotrexate, cyclosporin) was used by majority of patients (N=307, 54.8 %).

This retrospective study from a certain time point (here fixed to year 2019) reflects backwards the total number of used medications where the change in the medication availability and development is simultaneously proceeded, thus changing these figures during time.

Initially, decades ago, the treatment of psoriasis was based on topical treatment (various strength corticosteroids, 5-fluorouracil, D-vitamin and its analogues), phototherapies (SUP, UVB, PUVA), and so-called conventional medications (acitretin, methotrexate, cyclosporin). The treatments were initiated with the best available medications, but they did often lack of efficacy or brought adverse events. Thus, more effective medications have been developed having a better efficacy and less harmful side effects. The progress has led to oral apremilast and to various biologics, first to TNF-alfa blockers and thereafter to various IL-blockers. Also, the governmental financial reimbursement policy has had a delayed effect on the practical availability of medication for the patients.

However, it has been difficult to choose a certain medication to predict a desired effect and a complete or permanent outcome, as is our clinical experience; many medications have had a loss of efficacy during the time. The mean number of medications was 3,03, but the range was very wide from 1 to 13 (see Table 9).

Although many the patients in this study were referrals from colleague specialist and GPs, many patients were still evaluated to cope with topical treatments. As by clinical experience, some few patients have stopped oral or biologic medications and shifted back to topical treatments. It should be pointed out that patients with any medication could have been using also topical treatments, but as by practical experience, it is not very widely used, especially when the medication has produced PASI-value 90 or more leading to better physical and mental health, and less need for topical treatments.

Properties between different medications, such as injection intervals or costs, may have an effect of choosing a specific medication. The newest biologic medications can be administered more seldom which can reflect to a better compliance for treatments. In addition to this point of view, the overall effect and possible side adverse effects may explain that the patient has been individually treated until a “proper” treatment has been found. However, the exact reason(s) for changes from medication to another was not evaluated in this study. The medical field is continuously proceeding, thus the use of older topical treatments like 5-fuorouracil, bath PUVA and also UVB treatments have been markedly decreased as by personal clinical experience, but formal exact statistical data is very hard practically to obtain because of the present strict bureaucratic legislation. Also, the sales of drugs as numbers and financial aspects are classified information. Newer medication likely with a better efficacy and with less adverse effects will become available to market during time, thus changes in the treatments are expected, like bimekizumab is the newest used for treatment of psoriasis. However, the local government reimbursement policies will have a marked effect for availability and thus, choosing and prescribing a medication for the patient.

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